PATIENT INFORMATION		SPECIMEN DETAILS		PROVIDER INFORMATION
NAME:	**Carl Cardio**	**SPECIMEN TYPE:**	Buccal Swab	Genesys
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

Pharmacogenetic Cardiology Report

Current Patient Medications

Warfarin, Simvastatin, Metoprolol, Plavix, Clopidogrel

Clopidogrel
Plavix®

Significantly Reduced Response to Clopidogrel (CYP2C19: Poor Metabolizer) — ACTIONABLE

Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

Plavix
Clopidogrel

Significantly Reduced Response to Clopidogrel (CYP2C19: Poor Metabolizer) — ACTIONABLE

Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

Simvastatin
Zocor®

High Myopathy Risk (SLCO1B1: Poor Function) — ACTIONABLE

Simvastatin plasma concentrations are expected to be elevated. **Consider avoiding simvastatin** and prescribe an alternative statin or another hypolipidemic drug, or consider prescribing simvastatin at a lower starting dose (20 mg/day). Routine creatine kinase (CK) monitoring is also advised. **The FDA recommends against the 80 mg daily dose.** Although the association between the SLCO1B1 521T>C variant and myopathy risk is not clearly established for other statins such as atorvastatin, pitavastatin, rosuvastatin, and pravastatin, caution is advised if high doses of these statins are used in this patient. Fluvastatin plasma levels are not affected by the SLCO1B1 521T>C variant.

Metoprolol
Lopressor®

Significantly Increased Exposure to Metoprolol (CYP2D6: Poor Metabolizer) — ACTIONABLE

The patient's genotype is associated with an increased metoprolol exposure following standard dosing. When compared to a normal metabolizer, a poor metabolizer may require a 75% dose reduction. If metoprolol is prescribed, be alert to adverse events (e.g., bradycardia or cold extremities).

Warfarin
Coumadin®

Dosing Adjustments are Expected (CYP2C9 *1/*5; VKORC1 -1639G>A G/A) — ACTIONABLE

When initiating warfarin treatment for indications with a target INR of 2-3, consider using pharmacogenetic algorithms/calculators (available at www.warfarindosing.org) to estimate dosing requirements:

Caucasians and Asians: Use the patient's demographics and other clinical factors along with CYP2C9 and VKORC1 genotypes to calculate the expected therapeutic dose. Consider an additional 15-30% decrease to the calculated dose.

Africans and African Americans: Use the patient's demographics and other clinical factors along with CYP2C9 and VKORC1 genotypes to calculate the expected therapeutic dose. Consider an additional 15-30% decrease to the calculated dose.

The provided recommendations in Africans and African Americans apply only when all the following CYP2C9 alleles are tested: *5, *6, *8, *11.

PATIENT INFORMATION

NAME: **Carl Cardio**
ACC #: 1039
DOB: 1/1/1900
SEX: Male

A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.	**ACTIONABLE**	Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA, EMA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as knowledge arises.
Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.		
The medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.	**INFORMATIVE**	There are insufficient or contradictory findings documenting the impact of a given genetic polymorphism or drug interaction. Recommendations are informative and implementation in a clinical setting is optional.

PATIENT INFORMATION

NAME: Carl Cardio
ACC #: 1039
DOB: 1/1/1900
SEX: Male

Risk Management

Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

The patient does not carry the MTHFR c.665C>T variant or MTHFR c.1286A>C variant. MTHFR enzyme activity is normal.

Based on results for the MTHFR c.665C>T and c.1286A>C variants, the patient has normal MTHFR activity and is unlikely to have elevated plasma levels of homocysteine. Hyperhomocysteinemia is associated with a risk for venous thromboembolism (VTE). Unless other risk factors are present, the patient is not expected to have an increased risk for VTE.

MTHFR enzyme activity is normal.

Thrombophilia

Increased Risk of Thrombosis

The patient carries two copies (homozygous) of the F5 c.1601G>A variant (also known as Factor V Leiden) and does not carry the F2 c.*97G>A variant (also known as Factor II 20210G>A).

The patient's risk of thrombosis is 18 to 80 times higher than average (average risk of clotting is about 1 in 1000 for anyone in a year). Homozygous patients tend to develop thrombosis at a younger age. Other risk factors may have additive effects on thrombotic risk, increasing it further.

Anticoagulation:

Post-VTE patients with a low or moderate bleeding risk: long-term anticoagulation may be considered with periodic reevaluation to assess risks versus benefits.

Asymptomatic individual without a history of thrombosis: a short course of prophylactic anticoagulation may be considered in high-risk settings such as surgery, pregnancy, or prolonged immobilization. Decisions regarding prophylactic anticoagulation should be based on a risk/benefit assessment.

Estrogen-containing contraceptive and hormone replacement therapy: women with or without prior history of thrombotic events should avoid estrogen containing contraception and hormone replacement therapy.

Type III Hyperlipoproteinemia

Associated with Type III Hyperlipoproteinemia

The patient is negative for the APOE c.388 T>C (Cys130Arg) mutation and positive for the APOE c.526 C>T (Arg176Cys) mutation. The patient's genotype is ε2/ε2 (frequency: 0.2-2%).

Homozygosity for APOE ε2 allele is strongly associated with type III hyperlipoproteinemia. Over 90% of individuals presenting the type III hyperlipoproteinemia have the rare ε2/ε2 genotype. However, only 1-5% of individuals ε2/ε2 develop type III hyperlipoproteinemia. Although individuals with the APOE ε2/ε2 genotype are at a higher risk of premature vascular disease, they may never develop the disease because this genotype is only one of the risk factors.

In normolipidemic individuals, the APOE ε2 allele is associated with lower serum cholesterol concentrations, and may confer a protection against hypercholesterolemia.

Dietary adjustment and statin drugs are the preferred agents for lipid-lowering therapy. Useful drugs for treatment of type III hyperlipoproteinemia include nicotinic acid, fibric acid derivatives, and statins.

PATIENT INFORMATION

NAME: Carl Cardio
ACC #: 1039
DOB: 1/1/1900
SEX: Male

Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Cardiovascular	Angiotensin II Receptor Antagonists	Azilsartan (Edarbi®, Edarbyclor®) Candesartan (Atacand®) Eprosartan (Teveten®) Irbesartan (Avapro®) Losartan (Cozaar®, Hyzaar®) Olmesartan (Benicar®) Telmisartan (Micardis®) Valsartan (Diovan®, Entresto®)		
	Antianginal Agents		Ranolazine (Ranexa®)	
	Antiarrhythmics	Amiodarone (Nexterone®, Pacerone®) Disopyramide (Norpace®) Quinidine (Quinidine®) Sotalol (Betapace®, Sorine®, Sotylize®)	Flecainide (Tambocor®) Mexiletine (Mexitil®) Propafenone (Rythmol®)	
	Anticoagulants	Apixaban (Eliquis®) Betrixaban (Bevyxxa®) Dabigatran Etexilate (Pradaxa®) Edoxaban (Savaysa®) Fondaparinux (Arixtra®) Rivaroxaban (Xarelto®)	Warfarin (Coumadin®)	
	Antiplatelets	Prasugrel (Effient®) Ticagrelor (Brilinta®) Vorapaxar (Zontivity®)		Clopidogrel (Plavix®)
	Beta Blockers	Atenolol (Tenormin®) Bisoprolol (Zebeta®) Carvedilol (Coreg®) Labetalol (Normodyne®, Trandate®) Nebivolol (Bystolic®) Propranolol (Inderal®)	Metoprolol (Lopressor®) Timolol (Blocadren®)	
	Diuretics	Torsemide (Demadex®)		
	Statins		Atorvastatin (Lipitor®) Fluvastatin (Lescol®) Lovastatin (Mevacor®, Altoprev®, Advicor®) Pitavastatin (Livalo®) Pravastatin (Pravachol®) Rosuvastatin (Crestor®)	Simvastatin (Zocor®)

PATIENT INFORMATION

NAME: Carl Cardio
ACC #: 1039
DOB: 1/1/1900
SEX: Male

Dosing Guidance

Atorvastatin
Lipitor®

Increased Myopathy Risk (SLCO1B1: Poor Function) — ACTIONABLE

The patient's genotype is associated with reduced SLCO1B1 function which results in elevated atorvastatin plasma concentrations. If atorvastatin is used in this patient, consider closer monitoring of myopathy, serum creatine kinase and liver function.

If the patient has additional myopathy risk factors, consider an alternative statin that is not influenced by SLCO1B1. Other myopathy risk factors include advanced age (65 and older), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female sex.

Clopidogrel
Plavix®

Significantly Reduced Response to Clopidogrel (CYP2C19: Poor Metabolizer) — ACTIONABLE

Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

Flecainide
Tambocor®

Significantly Increased Exposure to Flecainide (CYP2D6: Poor Metabolizer) — ACTIONABLE

The patient's genotype is associated with an increased flecainide exposure following standard dosing. Consider prescribing a lower flecainide dose for therapeutic indications. When compared to a CYP2D6 normal metabolizer, a poor metabolizer may require a 50% dose reduction. Careful titration with ECG recording and monitoring of flecainide plasma concentrations are recommended until a favorable clinical response is achieved.

Dose adjustments are not required when flecainide is utilized for diagnostic uses.

Fluvastatin
Lescol®

Possible Increased Fluvastatin Exposure (CYP2C9: Intermediate Metabolizer) — INFORMATIVE

Increased fluvastatin plasma concentrations due to reduced CYP2C9 activity may occur, resulting in myopathy/hepatotoxicity. Consider monitoring the patient for treatment-related adverse effects, and adjust dose based on tolerability and response. Other adverse events and predisposing factors include advanced age (65 and older), diabetes, hypothyroidism, renal or hepatic impairments, high statin dose, CYP2C9 inhibitors, ABCG2 inhibitors, and female sex.

Lovastatin
Mevacor®, Altoprev®, Advicor®

Increased Myopathy Risk (SLCO1B1: Poor Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated lovastatin acid plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high lovastatin doses in this patient should be avoided. If lovastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (65 and older), uncontrolled hypothyroidism, renal impairment, comedications, and female sex.

Metoprolol
Lopressor®

Significantly Increased Exposure to Metoprolol (CYP2D6: Poor Metabolizer) — ACTIONABLE

The patient's genotype is associated with an increased metoprolol exposure following standard dosing. When compared to a normal metabolizer, a poor metabolizer may require a 75% dose reduction. If metoprolol is prescribed, be alert to adverse events (e.g., bradycardia or cold extremities).

Mexiletine
Mexitil®

Significantly Increased Sensitivity to Mexiletine (CYP2D6: Poor Metabolizer) — ACTIONABLE

Consider prescribing a lower mexiletine dose. A slow titration with ECG recording and monitoring of mexiletine plasma concentrations are recommended until a favorable clinical response is achieved.

Pitavastatin
Livalo®

Increased Myopathy Risk (SLCO1B1: Poor Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated pitavastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pitavastatin doses in this patient should be avoided. If pitavastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (65 and older), uncontrolled hypothyroidism, renal impairment, comedications, and female sex.

Pravastatin
Pravachol®

Increased Myopathy Risk (SLCO1B1: Poor Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated pravastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pravastatin doses in this patient should be avoided. If pravastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (65 and older), uncontrolled hypothyroidism, renal impairment, comedications, and female sex.

Propafenone
Rythmol®

Increased Exposure to Propafenone (CYP2D6: Poor Metabolizer) — ACTIONABLE

The patient's genotype is associated with an increased propafenone exposure following standard dosing. Consider a 70% dose reduction in the propafenone initial dose and monitor ECG and plasma concentrations.

Dose adjustments with co-medications: increased exposure to propafenone may lead to cardiac arrhythmias and exaggerated beta-adrenergic blocking activity. Concurrent use of propafenone in CYP2D6 poor metabolizers along with CYP3A4 inhibitors may significantly increase the plasma concentration of propafenone increasing the risk of proarrhythmia and other adverse events. Therefore, avoid simultaneous use of propafenone with a CYP3A4 inhibitor for CYP2D6 poor metabolizers.

Ranolazine
Ranexa®

Increased Sensitivity to Ranolazine (CYP2D6: Poor Metabolizer) — ACTIONABLE

Ranolazine is metabolized mainly by CYP3A4, and to a lesser extent by CYP2D6. At 500 mg twice daily, subjects lacking CYP2D6 activity (poor metabolizers) had 62% higher ranolazine exposure than subjects with normal CYP2D6 activity. The corresponding difference at 1000 mg twice daily dose was 25%.

The risk for increased exposure leading to adverse events is higher in patients lacking CYP2D6 activity (i.e., poor metabolizers). The recommended initial oral dose is 375 mg twice daily. **A slower up titration and additional monitoring is recommended in these patients.** Exposure related side effects might include nausea, vomiting, syncope, and dizziness. If a patient experiences treatment-related adverse events, down titration of the dose to 500 mg or 375 mg twice daily may be required. If symptoms do not resolve after dose reduction, treatment should be discontinued.

Ranolazine is a QTc prolonging drug. Caution should be observed when treating: 1- patients with a history of congenital or a family history of long QT syndrome, 2- patients with known acquired QT interval prolongation, and 3- patients treated with drugs affecting the QTc interval. Administration of CYP3A4 inhibitors increases the exposure of ranolazine significantly. As a consequence, the QTc prolongation by ranolazine in the presence of potent CYP3A inhibitors is significantly elevated relative to when the drug is administered alone.

Rosuvastatin
Crestor®

Increased Myopathy Risk (SLCO1B1 521T>C C/C) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated rosuvastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high rosuvastatin doses in this patient should be avoided. If rosuvastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (65 and older), uncontrolled hypothyroidism, renal impairment, comedications, and female sex.

Simvastatin
Zocor®

High Myopathy Risk (SLCO1B1: Poor Function) — ACTIONABLE

Simvastatin plasma concentrations are expected to be elevated. **Consider avoiding simvastatin** and prescribe an alternative statin or another hypolipidemic drug, or consider prescribing simvastatin at a lower starting dose (20 mg/day). Routine creatine kinase (CK) monitoring is also advised. **The FDA recommends against the 80 mg daily dose.** Although the association between the SLCO1B1 521T>C variant and myopathy risk is not clearly established for other statins such as atorvastatin, pitavastatin, rosuvastatin, and pravastatin, caution is advised if high doses of these statins are used in this patient. Fluvastatin plasma levels are not affected by the SLCO1B1 521T>C variant.

PATIENT INFORMATION

NAME: Carl Cardio
ACC #: 1039
DOB: 1/1/1900
SEX: Male

Timolol
Blocadren®

Increased Sensitivity to Timolol (CYP2D6: Poor Metabolizer) — **INFORMATIVE**

Potentiated systemic beta-blockade (e.g., bradycardia) has been reported during timolol treatment by patients with decreased CYP2D6 activity. Monitor patient for treatment-related adverse effects.

Warfarin
Coumadin®

Dosing Adjustments are Expected (CYP2C9 *1/*5; VKORC1 -1639G>A G/A) — **ACTIONABLE**

When initiating warfarin treatment for indications with a target INR of 2-3, consider using pharmacogenetic algorithms/calculators (available at www.warfarindosing.org) to estimate dosing requirements:

Caucasians and Asians: Use the patient's demographics and other clinical factors along with CYP2C9 and VKORC1 genotypes to calculate the expected therapeutic dose. Consider an additional 15-30% decrease to the calculated dose.

Africans and African Americans: Use the patient's demographics and other clinical factors along with CYP2C9 and VKORC1 genotypes to calculate the expected therapeutic dose. Consider an additional 15-30% decrease to the calculated dose.

The provided recommendations in Africans and African Americans apply only when all the following CYP2C9 alleles are tested: *5, *6, *8, *11.

PATIENT INFORMATION

NAME: Carl Cardio
ACC #: 1039
DOB: 1/1/1900
SEX: Male

Test Details

Gene	Genotype	Phenotype	Clinical Consequences
Apolipoprotein E	ε2/ε2	Altered APOE function	5% of patients with this genotype develop type III hyperlipoproteinemia and subsequent premature cardiovascular disease
CYP2C19	*2/*2	Poor Metabolizer	Consistent with a significant deficiency in CYP2C19 enzyme activity. Exercise caution if CYP2C19 drug substrates are prescribed.
CYP2C9	*1/*5	Intermediate Metabolizer	Consistent with a moderate deficiency in CYP2C9 enzyme activity.
CYP2D6	*4M/*4M XN	Poor Metabolizer	Consistent with a significant deficiency in CYP2D6 enzyme activity. Exercise caution if CYP2D6 drug substrates are prescribed.
CYP3A4	*1/*1	Normal Metabolizer	Consistent with a typical CYP3A4 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
CYP3A5	*3/*3	Poor Metabolizer	Consistent with an absence of CYP3A5 enzyme expression (Non-Expresser). This phenotype is the most common in the general population.
F2 F5	rs1799963 GG rs6025 TT	Increased Risk of Thrombosis	The patient's genotypes for F5 c.1601G>A variant (also known as Factor V Leiden) and F2 c.*97G>A variant (also known as Factor II 20210G>A) predict an increased risk for thrombosis. Consider avoiding estrogen-containing preparations. A short course of prophylactic anticoagulation may be considered in high-risk settings such as surgery.
MTHFR	c.1286A>C TT c.665C>T GG	No Increased Risk of Hyperhomocysteinemia	The patient does not carry the MTHFR c.665C>T or c.1286A>C variant. Therefore, the patient has normal MTHFR function, and no elevation of plasma homocysteine levels is expected.
SLCO1B1	521T>C C/C	Poor Function	Consistent with a severely decreased SLCO1B1 transporter function. Exercise caution when certain SLCO1B1 drug substrates are prescribed.
VKORC1	-1639G>A G/A	Intermediate Warfarin Sensitivity	Consistent with a moderately decreased VKORC1 expression. Exercise caution with coumarin anticoagulants.

Alleles Tested: Apolipoprotein E ε2, ε4, (ε3 is reference); **CYP2C19** *2, *3, *4A, *4B, *6, *7, *8, *9, *10, *17; **CYP2C9** *2, *3, *4, *5, *6, *8, *11, *27; **CYP2D6** *2, *3, *4, *4M, *6, *7, *9, *10, *12, *14, *17, *29, *41, *114, *5 (gene deletion), XN (gene duplication); **CYP3A4** *2, *3, *12, *17, *22; **CYP3A5** *2, *3, *6, *7, *8, *9; **Factor II** rs1799963; **Factor V Leiden** rs6025; **MTHFR** c.1286A>C, c.665C>T; **SLCO1B1** 521T>C; **VKORC1** -1639G>A

PATIENT INFORMATION

NAME: **Carl Cardio**
ACC #: 1039
DOB: 1/1/1900
SEX: Male

Limitation: This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Absence of a detectable gene mutation does not rule out the possibility that a patient has different phenotypes due to the presence of an undetected polymorphism or due to other factors such as drug-drug interactions, comorbidities and lifestyle habits. Technical limitations include the possibility of laboratory error and inaccuracy of the test due to unknown rare variants.

Methodology: Bead array and e-sensor based assays detect listed alleles and most rare variants with known clinical significance and analytical sensitivity and specificity >99%.

Lab Disclaimer: Genesys Diagnostics Inc. has validated the Genotype Test. The performance characteristics of this test were determined by Genesys Diagnostics Inc. This test is an FDA modified and Lab Developed Test.

Translational Software Disclaimer: The information presented on this report is provided as general educational health information. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of the medications prescribed.

The pharmacogenetic assay involves use of reporting software and genotype-phenotype associations performed by Translational Software (www.translationalsoftware.com). The software has not been evaluated by the Food and Drug Administration. The software, and the report generated by the software, is not intended to diagnose, treat, cure, or prevent any disease. A qualified designee within the lab uses Translational Software to generate and subsequently review the report. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

Report was signed out electronically by Life Technologies Demo on 7/29/2014.

PATIENT INFORMATION

NAME: **Carl Cardio**
ACC #: 1039
DOB: 1/1/1900
SEX: Male

Patient Information Card

This is a summary genetic report for your patient to share with other healthcare providers. The card can be cut out along the dashed line and carried with the patient.

REPORT DETAILS

Name: Carl Cardio
DOB: 1/1/1900
ACC #: 1039

Pharmacogenetic Test Summary

Apolipoprotein E	ε2/ε2	Altered APOE function
CYP2C19	*2/*2	Poor Metabolizer
CYP2C9	*1/*5	Intermediate Metabolizer
CYP2D6	*4M/*4M XN	Poor Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*3/*3	Poor Metabolizer
Factor II	rs1799963 GG	Normal Thrombosis Risk
Factor V Leiden	rs6025 TT	High Thrombosis Risk
MTHFR	c.665C>T GG	Normal MTHFR Activity
MTHFR	c.1286A>C TT	Normal MTHFR Activity
SLCO1B1	521T>C C/C	Poor Function
VKORC1	-1639G>A G/G	Low Warfarin Sensitivity

For a complete report contact Genesys Diagnostics
www.gdilabs.com

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

Comprehensive Pharmacogenetic Report with DDI

Current Patient Medications

Warfarin, Simvastatin, Metoprolol, Plavix, Clopidogrel

Clopidogrel
Plavix®

Significantly Reduced Response to Clopidogrel (CYP2C19: Poor Metabolizer) — ACTIONABLE

Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

Plavix
Clopidogrel

Significantly Reduced Response to Clopidogrel (CYP2C19: Poor Metabolizer) — ACTIONABLE

Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

Simvastatin
Zocor®

High Myopathy Risk (SLCO1B1: Poor Function) — ACTIONABLE

Simvastatin plasma concentrations are expected to be elevated. **Consider avoiding simvastatin** and prescribe an alternative statin or another hypolipidemic drug, or consider prescribing simvastatin at a lower starting dose (20 mg/day). Routine creatine kinase (CK) monitoring is also advised. **The FDA recommends against the 80 mg daily dose.** Although the association between the SLCO1B1 521T>C variant and myopathy risk is not clearly established for other statins such as atorvastatin, pitavastatin, rosuvastatin, and pravastatin, caution is advised if high doses of these statins are used in this patient. Fluvastatin plasma levels are not affected by the SLCO1B1 521T>C variant.

Metoprolol
Lopressor®

Significantly Increased Exposure to Metoprolol (CYP2D6: Poor Metabolizer) — ACTIONABLE

The patient's genotype is associated with an increased metoprolol exposure following standard dosing. When compared to a normal metabolizer, a poor metabolizer may require a 75% dose reduction. If metoprolol is prescribed, be alert to adverse events (e.g., bradycardia or cold extremities).

Warfarin
Coumadin®

Dosing Adjustments are Expected (CYP2C9 *1/*5; VKORC1 -1639G>A G/A) — ACTIONABLE

When initiating warfarin treatment for indications with a target INR of 2-3, consider using pharmacogenetic algorithms/calculators (available at www.warfarindosing.org) to estimate dosing requirements:

Caucasians and Asians: Use the patient's demographics and other clinical factors along with CYP2C9 and VKORC1 genotypes to calculate the expected therapeutic dose. Consider an additional 15-30% decrease to the calculated dose.

Africans and African Americans: Use the patient's demographics and other clinical factors along with CYP2C9 and VKORC1 genotypes to calculate the expected therapeutic dose. Consider an additional 15-30% decrease to the calculated dose.

The provided recommendations in Africans and African Americans apply only when all the following CYP2C9 alleles are tested: *5, *6, *8, *11.

Clopidogrel & Warfarin

MODERATE

Use caution when administering platelet aggregation inhibitors concurrently with anticoagulants. Careful monitoring of appropriate laboratory values for the patient's anticoagulant (e.g. PTT for heparin, anti Xa levels for low-molecular weight heparins, INR for warfarin) as well as signs and symptoms of bleeding is warranted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

Plavix & Warfarin

MODERATE

Use caution when administering platelet aggregation inhibitors concurrently with anticoagulants. Careful monitoring of appropriate laboratory values for the patient's anticoagulant (e.g. PTT for heparin, anti Xa levels for low-molecular weight heparins, INR for warfarin) as well as signs and symptoms of bleeding is warranted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Simvastatin

MODERATE

Patients should be monitored for changes in prothrombin time when a HMG Co-A reductase inhibitor is added to or discontinued from warfarin therapy, or if the dosage of the HMG Co-A reductase inhibitor is adjusted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Unrecognized Medications: *None*

Highly elevated risk for indicated condition or adverse drug reaction. Medication can be prescribed with monitoring; alternative therapy may be needed.

Moderately elevated risk for indicated condition or adverse drug reaction. Medication can be prescribed with monitoring; therapy adjustment may be needed.

Typical risk for indicated condition or adverse drug reaction. Medication can be prescribed according to standard dosing guidelines.

PHARMACOGENETIC RESULTS

DRUG-DRUG INTERACTIONS

ACTIONABLE Recommendations are suitable for implementation in a clinical setting. Recommendations extracted from evidence based guidelines issued by international pharmacogenetic consortia, professional societies or regulatory bodies (CPIC, DPWG, FDA, EMA, CPNDA, ACMG).

INFORMATIVE Recommendations are informative and implementation in a clinical setting is optional. The evidence documenting these drug-gene associations may be limited or insufficient and may require further investigation. There are no established evidence based guidelines issued by international pharmacogenetic consortia, professional societies or regulatory bodies.

MODERATE Drug interactions of moderate severity. The clinician should assess the patient's characteristics and take action as needed.

SERIOUS Severe drug interaction or contraindicated drug combination which may produces serious consequences in most patients. This drug combination generally should not be dispensed or administered to the same patient. Action is required to reduce risk of severe adverse interaction.

Risk Management

Type III Hyperlipoproteinemia

Associated with Type III Hyperlipoproteinemia

The patient is negative for the APOE c.388 T>C (Cys130Arg) mutation and positive for the APOE c.526 C>T (Arg176Cys) mutation. The patient's genotype is ε2/ε2 (frequency: 0.2-2%).
Homozygosity for APOE ε2 allele is strongly associated with type III hyperlipoproteinemia. Over 90% of individuals presenting the type III hyperlipoproteinemia have the rare ε2/ε2 genotype. However, only 1-5% of individuals ε2/ε2 develop type III hyperlipoproteinemia. Although individuals with the APOE ε2/ε2 genotype are at a higher risk of premature vascular disease, they may never develop the disease because this genotype is only one of the risk factors.

In normolipidemic individuals, the APOE ε2 allele is associated with lower serum cholesterol concentrations, and may confer a protection against hypercholesterolemia.
Dietary adjustment and statin drugs are the preferred agents for lipid-lowering therapy. Useful drugs for treatment of type III hyperlipoproteinemia include nicotinic acid, fibric acid derivatives, and statins.

Hyperhomocysteinemia - Depression

No Increased Risk of Hyperhomocysteinemia

The patient does not carry the MTHFR c.665C>T variant. MTHFR enzyme activity is normal.
Patients diagnosed with depression often have low folate levels and homocysteine is a highly sensitive marker of folate status. Functional folate deficiency is indicated by elevated homocysteine. With a normal MTHFR activity, this patient can process folate normally and is unlikely to have elevated plasma levels of homocysteine.
Patients diagnosed with depression: as lower folate levels are associated with poorer antidepressant response, and baseline levels of folate within the normal range predict antidepressant response, testing for homocysteine levels and serum folate levels may be informative for this patient before prescribing methylfolate as an antidepressant-augmenting agent.

Thrombophilia

Increased Risk of Thrombosis

The patient carries two copies (homozygous) of the F5 c.1601G>A variant (also known as Factor V Leiden) and does not carry the F2 c.*97G>A variant (also known as Factor II 20210G>A).
The patient's risk of thrombosis is 18 to 80 times higher than average (average risk of clotting is about 1 in 1000 for anyone in a year). Homozygous patients tend to develop thrombosis at a younger age. Other risk factors may have additive effects on thrombotic risk, increasing it further.
Anticoagulation:
Post-VTE patients with a low or moderate bleeding risk: long-term anticoagulation may be considered with periodic reevaluation to assess risks versus benefits.
Asymptomatic individual without a history of thrombosis: a short course of prophylactic anticoagulation may be considered in high-risk settings such as surgery, pregnancy, or prolonged immobilization. Decisions regarding prophylactic anticoagulation should be based on a risk/benefit assessment.

Estrogen-containing contraceptive and hormone replacement therapy: women with or without prior history of thrombotic events should avoid estrogen containing contraception and hormone replacement therapy.

Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

The patient does not carry the MTHFR c.665C>T variant or MTHFR c.1286A>C variant. MTHFR enzyme activity is normal.
Based on results for the MTHFR c.665C>T and c.1286A>C variants, the patient has normal MTHFR activity and is unlikely to have elevated plasma levels of homocysteine. Hyperhomocysteinemia is associated with a risk for venous thromboembolism (VTE). Unless other risk factors are present, the patient is not expected to have an increased risk for VTE.
MTHFR enzyme activity is normal.

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

Potentially Impacted Medications

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	*Dutasteride (Avodart®)*	●			
	Finasteride (Proscar®)	●			
Alpha-Blockers for Benign Prostatic Hyperplasia	*Alfuzosin (UroXatral®)*	●			⚠
	Doxazosin (Cardura®)	●			⚠
	Silodosin (Rapaflo®)	●			
	Tamsulosin (Flomax®)		●		
	Terazosin (Hytrin®)	●			⚠
Angiotensin II Receptor Antagonists	Azilsartan (Edarbi®, Edarbyclor®)	●			
	Candesartan (Atacand®)	●			
	Eprosartan (Teveten®)	●			
	Irbesartan (Avapro®)	●			
	Losartan (Cozaar®, Hyzaar®)	●			
	Olmesartan (Benicar®)	●			
	Telmisartan (Micardis®)	●			
	Valsartan (Diovan®, Entresto®)	●			
Antiaddictives	Bupropion (Wellbutrin®, Zyban®, Aplenzin®, Contrave®)	●			⚠
	Lofexidine (Lucemyra®)		●		
	Naltrexone (Vivitrol®, Contrave®)		●		
Anti-ADHD Agents	Amphetamine (Adderall®, Evekeo®)		●		
	Atomoxetine (Strattera®)		●		
	Clonidine (Kapvay®)	●			⊗
	Dexmethylphenidate (Focalin®)	●			
	Dextroamphetamine (Dexedrine®)		●		
	Guanfacine (Intuniv®)	●			
	Lisdexamfetamine (Vyvanse®)		●		
	Methylphenidate (Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®)	●			
Antianginal Agents	Ranolazine (Ranexa®)		●		⚠ ⚠

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
Antiarrhythmics	*Amiodarone (Nexterone®, Pacerone®)*	●			⚠ ⚠ ⊗
	Disopyramide (Norpace®)	●			
	Flecainide (Tambocor®)		●		
	Mexiletine (Mexitil®)		●		
	Propafenone (Rythmol®)		●		⚠ ⚠
	Quinidine (Quinidine®)	●			⚠ ⚠
	Sotalol (Betapace®, Sorine®, Sotylize®)	●			

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
Anticoagulants	*Apixaban (Eliquis®)*	●			⊗ Plavix ⊗ Clopidogrel ⊗
	Betrixaban (Bevyxxa®)	●			⊗ Plavix ⊗ Clopidogrel ⚠ ⊗
	Dabigatran Etexilate (Pradaxa®)	●			⊗ Plavix ⊗ Clopidogrel ⚠ ⊗
	Edoxaban (Savaysa®)	●			⊗ Plavix ⊗ Clopidogrel ⚠ ⊗
	Fondaparinux (Arixtra®)	●			⚠ Plavix ⚠ Clopidogrel ⚠
	Rivaroxaban (Xarelto®)	●			⊗ Plavix ⊗ Clopidogrel ⊗
	Warfarin (Coumadin®)		●		⚠ Plavix ⚠ Clopidogrel ⚠

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
Anticonvulsants	Brivaracetam (Briviact®)		●		
	Cannabidiol (Epidiolex®)	●			
	Carbamazepine (Tegretol®, Carbatrol®, Epitol®)	●			⚠
	Eslicarbazepine (Aptiom®)	●			
	Ethosuximide (Zarontin®)	●			
	Ezogabine (Potiga®)	●			
	Felbamate (Felbatol®)	●			⊗ Plavix ⊗ Clopidogrel
	Fosphenytoin (Cerebyx®)	●			⊗
	Gabapentin (Neurontin®)	●			
	Lacosamide (Vimpat®)	●			⚠
	Lamotrigine (Lamictal®)	●			
	Levetiracetam (Keppra®)	●			
	Oxcarbazepine (Trileptal®, Oxtellar XR®)	●			
	Perampanel (Fycompa®)	●			
	Phenobarbital (Luminal®)		●		⚠ ⊗
	Phenytoin (Dilantin®)	●			⊗
	Pregabalin (Lyrica®)	●			
	Primidone (Mysoline®)		●		⚠ ⊗
	Rufinamide (Banzel®)	●			
	Tiagabine (Gabitril®)	●			
	Topiramate (Topamax®)	●			
	Valproic Acid (Depakene®)	●			⚠
	Vigabatrin (Sabril®)	●			
	Zonisamide (Zonegran®)		●		
Antidementia Agents	Donepezil (Aricept®)		●		⚠
	Galantamine (Razadyne®)		●		⚠
	Memantine (Namenda®)	●			

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
Antidepressants	Amitriptyline (Elavil®)			🔴	
	Amoxapine (Amoxapine®)		🟡		
	Citalopram (Celexa®)		🟡		⚠ Plavix ⚠ Clopidogrel ⊗
	Clomipramine (Anafranil®)			🔴	⚠
	Desipramine (Norpramin®)			🔴	
	Desvenlafaxine (Pristiq®)	🟢			⚠ Plavix ⚠ Clopidogrel ⊗
	Doxepin (Silenor®)			🔴	
	Duloxetine (Cymbalta®)	🟢			⚠ Plavix ⚠ Clopidogrel ⊗
	Escitalopram (Lexapro®)		🟡		⚠ Plavix ⚠ Clopidogrel ⊗
	Fluoxetine (Prozac®, Sarafem®)	🟢			⊗ Plavix ⚠ Clopidogrel ⊗
	Fluvoxamine (Luvox®)		🟡		⊗ Plavix ⊗ Clopidogrel ⊗
	Imipramine (Tofranil®)			🔴	
	Levomilnacipran (Fetzima®)	🟢			⚠ Plavix ⚠ Clopidogrel ⊗

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
	Maprotiline (Ludiomil®)		●		
	Mirtazapine (Remeron®)	●			
	Nefazodone (Serzone®)		●		⊗ Plavix ⊗ Clopidogrel ⊗
	Nortriptyline (Pamelor®)			●	
	Paroxetine (Paxil®, Brisdelle®)			●	⚠ Plavix ⚠ ⚠ Clopidogrel ⊗
	Protriptyline (Vivactil®)		●		
	Sertraline (Zoloft®)		●		⚠ Plavix ⚠ ⚠ Clopidogrel ⊗
	Trazodone (Oleptro®)	●			
	Trimipramine (Surmontil®)			●	
	Venlafaxine (Effexor®)			●	⚠ Plavix ⚠ Clopidogrel ⊗
	Vilazodone (Viibryd®)	●			⚠ Plavix ⚠ Clopidogrel ⊗
	Vortioxetine (Trintellix®)		●		⚠ Plavix ⚠ Clopidogrel ⊗

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

CLASS	DRUG*	PHARMACOGENETIC RESULTS	INTERACTING DRUGS
Antiemetics	*Aprepitant (Emend-oral®)*		
	Dolasetron (Anzemet®)		
	Dronabinol (Marinol®)		
	Fosaprepitant (Emend-IV®)		
	Fosnetupitant / Palonosetron (Akynzeo-IV®)		
	Granisetron (Sancuso®, Sustol®)		
	Metoclopramide (Reglan®)		
	Netupitant / Palonosetron (Akynzeo-oral®)		
	Ondansetron (Zofran®, Zuplenz®)		
	Palonosetron (Aloxi®)		
	Rolapitant (Varubi®)		
Antifolates	Methotrexate (Trexall®)		
Antifungals	*Amphotericin B (AmBisome®, Abelcet®)*		
	Anidulafungin (Eraxis®)		
	Caspofungin (Cancidas®)		
	Fluconazole (Diflucan®)		Plavix Clopidogrel
	Isavuconazonium (Cresemba®)		
	Itraconazole (Sporanox®)		Plavix Clopidogrel
	Micafungin (Mycamine®)		
	Posaconazole (Noxafil®)		Plavix Clopidogrel
	Voriconazole (Vfend®)		Plavix Clopidogrel

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
Anti-HIV Agents	*Dolutegravir (Tivicay®, Triumeq®)*	●			
	Doravirine (Pifeltro®)	●			
	Efavirenz (Sustiva®)	●			
	Etravirine (Edurant®)	●			⊗ Plavix ⊗ Clopidogrel
	Raltegravir (Isentress®, Dutrebis®)	●			
	Rilpivirine (Intelence®)	●			
Anti-Hyperuricemics and Anti-Gout Agents	*Colchicine (Mitigare®)*	●			⚠
	Febuxostat (Uloric®)	●			
Antimalarials	*Proguanil (Malarone®)*	●			
Antiplatelets	**Clopidogrel (Plavix®)**			●	⚠
	Prasugrel (Effient®)	●			⚠
	Ticagrelor (Brilinta®)	●			⊗ ⚠
	Vorapaxar (Zontivity®)	●			⚠

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
Antipsychotics	Aripiprazole (Abilify®, Aristada®)		🟡		
	Asenapine (Saphris®)	🟢			
	Brexpiprazole (Rexulti®)		🟡		
	Cariprazine (Vraylar®)	🟢			
	Chlorpromazine (Thorazine®)		🟡		
	Clozapine (Clozaril®)		🟡		
	Fluphenazine (Prolixin®)	🟢			
	Haloperidol (Haldol®)			🔴	
	Iloperidone (Fanapt®)		🟡		
	Loxapine (Loxitane®, Adasuve®)	🟢			
	Lurasidone (Latuda®)	🟢			
	Olanzapine (Zyprexa®)	🟢			
	Paliperidone (Invega®)	🟢			
	Perphenazine (Trilafon®)		🟡		
	Pimavanserin (Nuplazid®)	🟢			
	Pimozide (Orap®)		🟡		
	Quetiapine (Seroquel®)	🟢			
	Risperidone (Risperdal®)		🟡		
	Thioridazine (Mellaril®)			🔴	
	Thiothixene (Navane®)	🟢			
	Trifluoperazine (Stelazine®)	🟢			
	Ziprasidone (Geodon®)	🟢			
Antispasmodics for Overactive Bladder	Darifenacin (Enablex®)		🟡		
	Fesoterodine (Toviaz®)	🟢			
	Mirabegron (Myrbetriq®)	🟢			⚠
	Oxybutynin (Ditropan®)	🟢			
	Solifenacin (Vesicare®)	🟢			
	Tolterodine (Detrol®)		🟡		
	Trospium (Sanctura®)	🟢			

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
Benzodiazepines	*Alprazolam (Xanax®)*	●			
	Clobazam (Onfi®)		●		
	Clonazepam (Klonopin®)	●			
	Diazepam (Valium®)		●		
Beta Blockers	*Atenolol (Tenormin®)*	●			
	Bisoprolol (Zebeta®)	●			
	Carvedilol (Coreg®)	●			
	Labetalol (Normodyne®, Trandate®)	●			
	Metoprolol (Lopressor®)		●		
	Nebivolol (Bystolic®)	●			
	Propranolol (Inderal®)	●			⚠
	Timolol (Blocadren®)		●		
Diuretics	Torsemide (Demadex®)	●			
Fibromyalgia Agents	*Milnacipran (Savella®)*	●			⚠ Plavix ⚠ Clopidogrel ⊗
Immunomodulators	*Apremilast (Otezla®)*	●			
	Leflunomide (Arava®)		●		⚠
	Tofacitinib (Xeljanz®)	●			
Immunosuppressants	Tacrolimus (Prograf®)	●			
Meglitinides	Nateglinide (Starlix®)	●			
	Repaglinide (Prandin®, Prandimet®)		●		⊗ Plavix ⊗ Clopidogrel
Muscle Relaxants	Carisoprodol (Soma®)		●		
	Cyclobenzaprine (Flexeril®, Amrix®)	●			
	Metaxalone (Skelaxin®)	●			
	Methocarbamol (Robaxin®)	●			
	Tizanidine (Zanaflex®)	●			⚠

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
NSAIDs	Celecoxib (Celebrex®)	●			⊗ Plavix ⚠ ⊗ Clopidogrel ⊗
	Diclofenac (Voltaren®)	●			⊗ Plavix ⚠ ⊗ Clopidogrel ⊗
	Flurbiprofen (Ansaid®)	●			⊗ Plavix ⚠ ⊗ Clopidogrel ⊗
	Ibuprofen (Advil®, Motrin®)	●			⊗ Plavix ⚠ ⊗ Clopidogrel ⊗
	Indomethacin (Indocin®)	●			⊗ Plavix ⚠ ⊗ Clopidogrel ⊗
	Ketoprofen (Orudis®)	●			⊗ Plavix ⚠ ⊗ Clopidogrel ⊗
	Ketorolac (Toradol®)	●			⊗ Plavix ⚠ ⊗ Clopidogrel ⊗
	Meloxicam (Mobic®)	●			⊗ Plavix ⚠ ⊗ Clopidogrel ⊗

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
	Nabumetone (Relafen®)	●			⊗ Plavix ⚠ ⊗ Clopidogrel ⊗
	Naproxen (Aleve®)	●			⊗ Plavix ⚠ ⊗ Clopidogrel ⊗
	Piroxicam (Feldene®)	●			⊗ Plavix ⚠ ⊗ Clopidogrel ⊗
	Sulindac (Clinoril®)	●			⊗ Plavix ⚠ ⊗ Clopidogrel ⊗

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
Opioids	*Alfentanil (Alfenta®)*	●			
	Benzhydrocodone (Apadaz®)		●		
	Buprenorphine (Butrans®, Buprenex®)	●			
	Codeine (Codeine; Fioricet® with Codeine)			●	
	Dihydrocodeine (Synalgos-DC®)	●			
	Fentanyl (Actiq®)	●			
	Hydrocodone (Vicodin®)		●		
	Hydromorphone (Dilaudid®, Exalgo®)	●			
	Levorphanol (Levo Dromoran®)	●			
	Meperidine (Demerol®)	●			
	Methadone (Dolophine®)	●			⚠ Plavix ⚠ Clopidogrel
	Morphine (MS Contin®)		●		
	Oxycodone (Percocet®, Oxycontin®)	●			
	Oxymorphone (Opana®, Numorphan®)	●			
	Sufentanil (Sufenta®)	●			
	Tapentadol (Nucynta®)	●			
	Tramadol (Ultram®)			●	⚠
Other Neurological Agents	Deutetrabenazine (Austedo®)		●		
	Dextromethorphan / Quinidine (Nuedexta®)		●		⚠ ⚠
	Flibanserin (Addyi®)		●		
	Tetrabenazine (Xenazine®)		●		
	Valbenazine (Ingrezza®)		●		
Phosphodiesterase Inhibitors for Erectile Dysfunction	*Avanafil (Stendra®)*	●			
	Sildenafil (Viagra®)	●			
	Tadalafil (Cialis®)	●			
	Vardenafil (Levitra®)	●			

GENESYS Diagnostics INC.

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	⚠	⊗	INTERACTING DRUGS
Proton Pump Inhibitors	Dexlansoprazole (Dexilant®, Kapidex®)	●			
	Esomeprazole (Nexium®)	●			⊗ Plavix ⊗ Clopidogrel
	Lansoprazole (Prevacid®)	●			
	Omeprazole (Prilosec®)	●			⊗ Plavix ⊗ Clopidogrel
	Pantoprazole (Protonix®)	●			
	Rabeprazole (Aciphex®)	●			
Statins	Atorvastatin (Lipitor®)		●		
	Fluvastatin (Lescol®)		●		⚠
	Lovastatin (Mevacor®, Altoprev®, Advicor®)		●		⚠
	Pitavastatin (Livalo®)		●		
	Pravastatin (Pravachol®)		●		
	Rosuvastatin (Crestor®)		●		⚠
	Simvastatin (Zocor®)			●	⚠
Sulfonylureas	*Chlorpropamide (Diabinese®)*	●			
	Glimepiride (Amaryl®)	●			
	Glipizide (Glucotrol®)	●			
	Glyburide (Micronase®)	●			
	Tolbutamide (Orinase®)	●			

*Current patient medications are listed in bold whereas italicized drug names indicate drugs with no pharmacogenetic guidance

Dosing Guidance

Amitriptyline (Elavil®)

Increased Amitriptyline Exposure (CYP2C19: Poor Metabolizer)

ACTIONABLE

less than p>The patient's absent CYP2C19 activity is likely to result in a significantly decreased metabolism of amitriptyline to nortriptyline and a subsequent increase in amitriptyline exposure leading to side effects.less than /p> less than p>less than strong>Psychiatric Conditions:less than /strong> Consider an alternative medication. If amitriptyline is warranted, consider a 50% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.less than /p> less than p>less than strong>Neuropathic Pain:less than /strong> Amitriptyline can be prescribed according to standard recommended dosage and administration when lower doses are considered. If higher doses are warranted, consider a 50% reduction of the recommended dose and monitor patient for side effects.less than /p>

Increased Amitriptyline Exposure (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient is predicted to be a CYP2D6 poor metabolizer which is likely to result in a significantly decreased metabolism of amitriptyline to less active compounds and a subsequent increase in amitriptyline exposure leading to side effects.less than /p> less than p>less than strong>Psychiatric Conditions:less than /strong> Consider an alternative medication. If amitriptyline is warranted, consider a 50% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.less than /p> less than p>less than strong>Neuropathic Pain:less than /strong> Amitriptyline therapy can be prescribed according to standard recommended dosage and administration when lower doses are considered. If higher doses are warranted, consider a 50% reduction of the recommended dose and monitor patient for side effects.less than /p>

Amoxapine (Amoxapine®)

Possible Increased Amoxapine Exposure (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>Like other tricyclic and tetracyclic antidepressants, amoxapine is metabolized by CYP2D6. However, the overall contribution of this enzyme in the metabolism of this drug is not well documented. Decreased CYP2D6 activity may result in higher amoxapine concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased CYP2D6 function; therapy must be initiated cautiously and adjusted according to the patient's response.less than /p>

Amphetamine (Adderall®, Evekeo®)

Possible Increased Exposure to Amphetamine (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>There is little evidence documenting the exposure of amphetamine in subjects with reduced CYP2D6 activity such as CYP2D6 poor metabolizers. Although the drug's plasma concentrations may be elevated in these subjects, the clinical relevance of this change is not well documented. Consider initiating therapy with lower doses and monitor the patient more frequently during drug titration. Consider adjusting the dose based on clinical response and tolerability. An alternative therapy may also be considered in patients with decreased tolerability.less than /p>

Aripiprazole (Abilify®, Aristada®)

Increased Exposure to Aripiprazole (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient's genotype is associated with less than strong>significantlyless than /strong> increased aripiprazole exposure. Consider using a lower dose based on formulation, with careful titration is recommended until a favorable response is achieved.less than /p>less than p>less than span style="text-decoration: underline;">Daily dosingless than /span> (oral): aripiprazole dose should initially be reduced to one-half (less than strong>50%less than /strong>) of the usual dose, then adjusted to achieve a favorable clinical response. The dose of aripiprazole for CYP2D6 poor metabolizers who are administered a strong CYP3A4 inhibitor should be reduced to one-quarter (25%) of the usual dose.less than /p>less than p>less than span style="text-decoration: underline;">Single dosingless than /span> (intramuscular): avoid using less than em>Aristada Initioless than /em> when initiating treatment with less than em>Aristadaless than /em>.less than /p>less than p>less than span style="text-decoration: underline;">Monthly dosingless than /span> (intramuscular): for less than em>Abilify Maintenaless than /em>, the starting and maintenance monthly recommended dose is lower than the usually recommended dose, and should be less than strong>300 mgless than /strong>. Some patients may benefit from a reduction to 200 mg. For less than em>Aristadaless than /em>. reduce the dose to the next lower strength; no dosage adjustment is necessary in patients taking 441 mg less than em>Aristadaless than /em>. if tolerated. For less than em>Abilify Maintenaless than /em>, reduce the monthly dose to 200 mg if a strong CYP3A4 inhibitor is prescribed to CYP2D6 poor metabolizers receiving 300 mg of aripiprazole. For less than em>Aristadaless than /em>. reduce dose to 441 mg and avoid use at 662 mg or 882 mg dose if a strong CYP3A4 inhibitor is prescribed to CYP2D6 poor metabolizers for more than 14 days. No dosage adjustment is necessary in patients taking 441 mg less than em>Aristadaless than /em>. if tolerated.less than /p>less than p>less than span style="text-decoration: underline;">Every 6 weeks or two months dosing with less than em>Aristadaless than /em>less than /span> (intramuscular): reduce the dose to a lower strength of 441 mg every 4 weeks. If a strong CYP3A4 inhibitor is co-administered for more than 14 days, avoid using the 662 mg, 882 mg or 1064 mg doses and consider the lower dose strength of 441 mg every 4 weeks.less than /p>

Atomoxetine (Strattera®)

Possible Atomoxetine Overexposure Leading to Toxicity (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The genotype result indicates that the patient is likely to have an increased risk of adverse events with a greater chance of therapeutic success following standard dosing. Consider the following dosing strategy:less than /p>less than ul>less than li>Initiate treatment at 40 mg/day.less than /li>less than li>If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider a dose increase to 80 mg/day.less than /li>less than li>If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider therapeutic drug monitoring 2-4 hours post dose. If the plasma concentration is less than 200 ng/ml consider a dose increase to a target of 400 ng/ml. Doses greater than 100 mg/day may be needed to achieve a targeted therapeutic concentration. (Therapeutic range: 200-1000 ng/ml).less than /li>less than /ul>

Atorvastatin (Lipitor®)

Increased Myopathy Risk (SLCO1B1: Poor Function)

ACTIONABLE

less than p>The patient's genotype is associated with reduced SLCO1B1 function which results in elevated atorvastatin plasma concentrations. If atorvastatin is used in this patient, consider closer monitoring of myopathy, serum creatine kinase and liver function.less than /p> less than p>If the patient has additional myopathy risk factors, consider an alternative statin that is not influenced by SLCO1B1. Other myopathy risk factors include advanced age (65 and older), uncontrolled hypothyroidism, renal impairment, high statin dose, comedications, and female sex.less than /p>

Benzhydrocodone (Apadaz®)

Possible Altered Response to Benzhydrocodone (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>Benzhydrocodone is a prodrug of hydrocodone and is converted to active hydrocodone by intestinal enzymes. Decreased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 poor metabolizers. However, there is insufficient evidence whether these patients have decreased analgesia when taking benzhydrocodone. Adequate pain relief can be achieved by increasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 may also be considered (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone).less than /p>

Brexpiprazole (Rexulti®)

Increased Exposure to Brexpiprazole (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient's genotype may be associated with an increased brexpiprazole exposure following standard dosing. The exposure to brexpiprazole in CYP2D6 poor metabolizers is 120% higher than the exposure in CYP2D6 normal metabolizers. Because the incidence of akathisia is dose-related in patients suffering from schizophrenia or major depressive disorders, less than strong>it is recommended to prescribe half of the usual doses of brexpiprazole to CYP2D6 poor metabolizers.less than /strong> Careful titration is recommended until a favorable response is achieved.less than /p>less than p>less than span style="text-decoration: underline;">Adjunctive Treatment of Major Depression Disorderless than /span>: the recommended starting doses should be reduced by half (0.25 mg or 0.5 mg once daily). The daily maintenance doses and maximum recommended dose are 0.5-1 mg and 1.5 mg, respectively.less than /p>less than p>less than span style="text-decoration: underline;">Schizophrenialess than /span>: the recommended starting dose is 0.5 mg once daily. The daily maintenance doses and maximum recommended dose are 1-2 mg and 2 mg, respectively.less than /p>less than p>less than strong>Dose adjustments with co-medicationsless than /strong>: Administer less than strong>a quarter of the usual doseless than /strong> if a strong/moderate CYP3A4 inhibitor is co-administered. Double the usual dose over 1 to 2 weeks if a strong CYP3A4 inducer is co-administered.less than /p>

Brivaracetam (Briviact®)

Possible Sensitivity to Brivaracetam (CYP2C19: Poor Metabolizer)

ACTIONABLE

less than p>Brivaracetam is primarily metabolized by hydrolysis and to a minor extent by hydroxylation, which is mediated by CYP2C19. In CYP2C19 poor metabolizers, the plasma concentration of brivaracetam is increased by 42%. Brivaracetam dose reduction may be required. Monitor the patient for any signs of adverse reaction or drug toxicity.less than /p>

Carisoprodol (Soma®)

Altered Sensitivity to Carisoprodol (CYP2C19: Poor Metabolizer)

INFORMATIVE

less than p>CYP2C19 poor metabolizers have a lower capacity to metabolize carisoprodol to meprobamate, and may therefore have an increased risk of developing concentration-dependent side effects such as drowsiness and hypotension when receiving standard doses of carisoprodol. Carisoprodol should be used with caution in patients with reduced CYP2C19 activity. Because there is insufficient data to allow calculation of dose adjustment, consider reducing the dose or using an alternative medication.less than /p>

Chlorpromazine (Thorazine®)

Increased Sensitivity to Chlorpromazine (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>Chlorpromazine is metabolized by CYP2D6, CYP3A4 and flavin-containing monooxygenases. Decreased CYP2D6 activity results in higher chlorpromazine concentrations potentially leading to higher adverse events. Consider prescribing chlorpromazine at a lower starting dose and then adjust dosage to achieve a favorable clinical response.less than /p>

Citalopram (Celexa®)

Increased Sensitivity to Citalopram (CYP2C19: Poor Metabolizer)

ACTIONABLE

less than p>At standard label-recommended dosage, citalopram plasma concentrations levels are expected to be high and adverse events may occur. Consider a 50% reduction of the recommended starting dose to help prevent concentration-dependent adverse events. Dose escalations over 20 mg/day for CYP2C19 poor metabolizers are not recommended. An alternative medication may also be considered.less than /p>

Clobazam (Onfi®)

Increased Sensitivity to Clobazam (CYP2C19: Poor Metabolizer)

ACTIONABLE

less than p>In CYP2C19 poor metabolizers, plasma levels of the active metabolite N-desmethylclobazam were 5-fold higher than those found in CYP2C19 normal metabolizers. Therefore, the starting dose should be 5 mg/day and dose titration should proceed slowly according to weight. Patients should be titrated initially to 10 mg /day (≤30 kg body weight) or 20 mg/day (>30 kg body weight). If necessary and based upon clinical response, an additional titration to the maximum doses 20 mg/day (≤30 kg body weight) or 40 mg/day (>30 kg body weight) may be started on day 21.less than /p>

Clomipramine (Anafranil®)

Increased Clomipramine Exposure (CYP2C19: Poor Metabolizer)

INFORMATIVE

less than p>The patient's absent CYP2C19 activity is likely to result in a significantly decreased metabolism of clomipramine to desmethyl clomipramine and a subsequent increase in clomipramine exposure leading to side effects.less than /p> less than p>less than strong>Psychiatric Conditions:less than /strong> Consider an alternative medication. If clomipramine is warranted, consider a 50% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.less than /p>

Increased Clomipramine Exposure (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>The patient is predicted to be a CYP2D6 poor metabolizer which is is likely to result in a significantly decreased metabolism of clomipramine to less active compounds and a subsequent increase in clomipramine exposure leading to side effects.less than /p> less than p>less than strong>Psychiatric Conditions:less than /strong> Consider an alternative medication. If clomipramine is warranted, consider a 50% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.less than /p>

Clopidogrel (Plavix®)

Clopidogrel & Apixaban

SERIOUS

Patients requiring concurrent therapy with apixaban and an antiplatelet agent should be closely monitored for signs of bleeding.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.Discontinue apixaban in patients with active bleeding.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Clopidogrel & Betrixaban

SERIOUS

Patients requiring concurrent therapy with betrixaban and an antiplatelet agent should be closely monitored for signs of bleeding.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.Discontinue betrixaban in patients with active bleeding.The anticoagulant effect of betrixaban is expected to persist for at least 72 hours after the last dose.

Clopidogrel & Celecoxib

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Clopidogrel & Citalopram

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Clopidogrel & Dabigatran Etexilate

SERIOUS

Patients requiring concurrent therapy with dabigatran and an antiplatelet agent should be closely monitored for signs of bleeding.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.Discontinue dabigatran in patients with active bleeding.

Clopidogrel & Desvenlafaxine

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Clopidogrel & Diclofenac

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Clopidogrel & Duloxetine

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Clopidogrel & Edoxaban

SERIOUS

Patients requiring concurrent therapy with edoxaban and an antiplatelet agent should be closely monitored for signs of bleeding. Edoxaban and aspirin at dosages of 100 mg or less may be coadministered.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.Discontinue edoxaban in patients with active bleeding.

Clopidogrel & Escitalopram

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Clopidogrel & Esomeprazole

SERIOUS

Evaluate patient risk for gastrointestinal(GI) bleeding. When PPIs are needed, use dexlansoprazole, lansoprazole, pantoprazole or rabeprazole as they have a lower interaction risk. Consider the use of H2 blockers (such as famotidine, nizatidine, or ranitidine) in patients with a low bleeding risk and reserve the use of PPIs for patients at higher risk of GI bleeding.US manufacturers for clopidogrel and omeprazole state concurrent use of clopidogrel esomeprazole and omeprazole should be avoided. As esomeprazole and omeprazole are irreversible inhibitors of CYP2C19, separating clopidogrel from esomeprazole or omeprazole administration times does not change the magnitude of this interaction.The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19 are poor metabolizers of this isoenzyme. Moderate CYP2C19 inhibitors, such as omeprazole, and weak CYP2C19 inhibitors, such as cimetidine, may also affect this interaction.Consider alternatives to esomeprazole, omeprazole, and cimetidine in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on esomeprazole, omeprazole, and cimetidine. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Clopidogrel & Etravirine

SERIOUS

The US manufacturer of clopidogrel states that concurrent use of inhibitors of CYP2C19, such as etravirine should be avoided. The US manufacturer of etravirine recommends alternative to clopidogrel in patients maintained on etravirine.The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19 are poor metabolizers of this isoenzyme. Moderate CYP2C19 inhibitors, such as etravirine, may also affect this interaction.Consider alternatives to etravirine in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on etravirine. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Clopidogrel & Felbamate

SERIOUS

The US manufacturer of clopidogrel states that concurrent use of inhibitors of CYP2C19, such as felbamate and stiripentol, should be avoided.The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19 are poor metabolizers of this isoenzyme.Consider alternatives to felbamate or stiripentol in patients stabilized on clopidogrel, or alternatives to clopidogrel in patients stabilized on felbamate or stiripentol. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Clopidogrel & Fluconazole

SERIOUS

The US manufacturer of clopidogrel states that concurrent use of inhibitors of CYP2C19, such as fluconazole, ketoconazole, and voriconazole should be avoided.The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19, such as fluconazole, are poor metabolizers of this isoenzyme. Voriconazole is a moderate CYP2C19 inhibitor.Ketoconazole and voriconazole are strong inhibitors of CYP3A4. Fluconazole is a moderate inhibitor of CYP3A4.Consider alternatives to fluconazole, ketoconazole, and voriconazole in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on fluconazole, ketoconazole, and voriconazole. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Clopidogrel & Fluoxetine

SERIOUS

The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19, such as fluoxetine and fluvoxamine, are poor metabolizers of this isoenzyme.Consider alternatives to fluoxetine and fluvoxamine in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on fluoxetine or fluvoxamine. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Clopidogrel & Flurbiprofen

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Clopidogrel & Fluvoxamine

SERIOUS

The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19, such as fluoxetine and fluvoxamine, are poor metabolizers of this isoenzyme.Consider alternatives to fluoxetine and fluvoxamine in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on fluoxetine or fluvoxamine. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Clopidogrel & Fondaparinux

MODERATE

Use caution when administering platelet aggregation inhibitors concurrently with anticoagulants. Careful monitoring of appropriate laboratory values for the patient's anticoagulant (e.g. PTT for heparin, anti Xa levels for low-molecular weight heparins, INR for warfarin) as well as signs and symptoms of bleeding is warranted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Clopidogrel & Ibuprofen

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Clopidogrel & Indomethacin

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Clopidogrel & Itraconazole

SERIOUS

The US manufacturer of clopidogrel does not make specific recommendations for concurrent use with strong CYP3A4 inhibitors. Patient monitoring for adequate inhibition of platelet reactivity with clopidogrel is warranted.Consider alternatives to strong CYP3A4 inhibitors in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on strong CYP3A4 inhibitors. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Clopidogrel & Ketoprofen

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Clopidogrel & Ketorolac

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Clopidogrel & Levomilnacipran

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Clopidogrel & Meloxicam

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Clopidogrel & Methadone

MODERATE

If concomitant use of levomethadone or methadone and CYP2B6 inhibitors is necessary, closely monitor the patient when a CYP2B6 inhibitor is initiated or withdrawn. The dosage of levomethadone or methadone may need to be adjusted.If concurrent therapy is deemed medically necessary, consider obtaining serum calcium, magnesium, and potassium levels and monitoring ECG at baseline and at regular intervals. Correct any electrolyte abnormalities. Instruct patients to report any irregular heartbeat, dizziness, or fainting.If concurrent use is necessary, monitor patients for unusual dizziness or lightheadedness, extreme sleepiness, slowed or difficult breathing, or unresponsiveness.If concurrent therapy is warranted, patients should be monitored for signs and symptoms of serotonin syndrome. Instruct patients to report muscle twitching, tremors, shivering and stiffness, fever, heavy sweating, heart palpitations, restlessness, confusion, agitation, trouble with coordination, or severe diarrhea.Discuss naloxone with all patients when prescribing or renewing an opioid analgesic or medicine to treat opioid use disorder (OUD). Consider prescribing naloxone to patients prescribed medicines to treat OUD or opioid analgesics (such as those taking CNS depressants) who are at increased risk of opioid overdose and when a patient has household members/close contacts at risk for accidental overdose.

Clopidogrel & Milnacipran

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Clopidogrel & Nabumetone

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Clopidogrel & Naproxen

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Clopidogrel & Nefazodone

SERIOUS

The US manufacturer of clopidogrel does not make specific recommendations for concurrent use with strong CYP3A4 inhibitors. Patient monitoring for adequate inhibition of platelet reactivity with clopidogrel is warranted.Consider alternatives to strong CYP3A4 inhibitors in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on strong CYP3A4 inhibitors. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Clopidogrel & Omeprazole

SERIOUS

Evaluate patient risk for gastrointestinal(GI) bleeding. When PPIs are needed, use dexlansoprazole, lansoprazole, pantoprazole or rabeprazole as they have a lower interaction risk. Consider the use of H2 blockers (such as famotidine, nizatidine, or ranitidine) in patients with a low bleeding risk and reserve the use of PPIs for patients at higher risk of GI bleeding.US manufacturers for clopidogrel and omeprazole state concurrent use of clopidogrel esomeprazole and omeprazole should be avoided. As esomeprazole and omeprazole are irreversible inhibitors of CYP2C19, separating clopidogrel from esomeprazole or omeprazole administration times does not change the magnitude of this interaction.The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19 are poor metabolizers of this isoenzyme. Moderate CYP2C19 inhibitors, such as omeprazole, and weak CYP2C19 inhibitors, such as cimetidine, may also affect this interaction.Consider alternatives to esomeprazole, omeprazole, and cimetidine in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on esomeprazole, omeprazole, and cimetidine. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Clopidogrel & Paroxetine

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Clopidogrel & Piroxicam

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Clopidogrel & Posaconazole

SERIOUS

The US manufacturer of clopidogrel does not make specific recommendations for concurrent use with strong CYP3A4 inhibitors. Patient monitoring for adequate inhibition of platelet reactivity with clopidogrel is warranted.Consider alternatives to strong CYP3A4 inhibitors in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on strong CYP3A4 inhibitors. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Clopidogrel & Repaglinide

SEVERE

Based upon results of a published clinical trial, Health Canada and the Canadian manufacturer of repaglinide state that concurrent use of clopidogrel and repaglinide is contraindicated due to the risk for hypoglycemia from unanticipated lowering of serum glucose concentrations. Alternative antiplatelet agents (e.g. prasugrel, ticagrelor) and antidiabetic agents are not known to inhibit CYP2C8 or OATP1B1.The manufacturer of clopidogrel states that when concomitant use is required in a patient maintained on clopidogrel, initiate repaglinide at 0.5mg with each meal and titrate based on blood glucose levels. Do not exceed a total daily dose of 4mg. If concomitant use of clopidogrel is required in a patient stabilized on repaglinide, down titrate the dose of repaglinide based on blood glucose levels to not exceed a total daily dose of 4mg.If concomitant use is deemed medically necessary:- Hypoglycemic risk is greatest when clopidogrel is added to existing repaglinide therapy. Frequent monitoring of serum/blood glucose is needed to monitor patient response as the magnitude of glucose lowering varies between patients.- In patients stabilized on clopidogrel when repaglinide is initiated, increased sensitivity to the hypoglycemic effect of repaglinide would be expected. In addition, because repaglinide half-life is prolonged in the presence of clopidogrel, maximal effects of repaglinide may be delayed - slower than usual dose titration would be prudent.Separating the timing of drug administration would not be expected to decrease interaction risk as the clopidogrel metabolite (clopidogrel acyl-beta-D-glucuronide) is an irreversible inhibitor of CYP2C8.

Clopidogrel & Rivaroxaban

SERIOUS

Avoid concurrent use of rivaroxaban and clopidogrel unless the benefit is expected to outweigh the increased risk of bleeding.Avoid concurrent use of rivaroxaban and higher doses of aspirin unless the benefit is expected to outweigh the increased risk of bleeding. In the ROCKET AF trial, concomitant use of low dose aspirin (almost exclusively at less than or equal to 100 mg daily) was identified as an independent risk factor for bleeding.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Clopidogrel & Sertraline

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Clopidogrel & Sulindac

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Clopidogrel & Venlafaxine

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Clopidogrel & Vilazodone

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Clopidogrel & Voriconazole

SERIOUS

The US manufacturer of clopidogrel states that concurrent use of inhibitors of CYP2C19, such as fluconazole, ketoconazole, and voriconazole should be avoided.The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19, such as fluconazole, are poor metabolizers of this isoenzyme. Voriconazole is a moderate CYP2C19 inhibitor.Ketoconazole and voriconazole are strong inhibitors of CYP3A4. Fluconazole is a moderate inhibitor of CYP3A4.Consider alternatives to fluconazole, ketoconazole, and voriconazole in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on fluconazole, ketoconazole, and voriconazole. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Clopidogrel & Vortioxetine

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Clopidogrel & Warfarin

MODERATE

Use caution when administering platelet aggregation inhibitors concurrently with anticoagulants. Careful monitoring of appropriate laboratory values for the patient's anticoagulant (e.g. PTT for heparin, anti Xa levels for low-molecular weight heparins, INR for warfarin) as well as signs and symptoms of bleeding is warranted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Clozapine (Clozaril®)

Increased Exposure to Clozapine (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient's genotype may be associated with an increased clozapine exposure following standard dosing. Monitor for adverse effects and consider a dose reduction.less than /p>

Codeine (Codeine; Fioricet® with Codeine)

Greatly Decreased Exposure to Codeine Active Metabolite (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient genotype is associated with greatly decreased conversion of codeine to its active metabolite (morphine), which may result in decreased effectiveness.less than /p> less than p>Consider avoiding prescribing codeine and instead use alternative opioids other than tramadol, or a non-opioid analgesic such as an NSAID or a COX-2 inhibitor. Alternative opioids may include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.less than /p>

Darifenacin (Enablex®)

Possible Sensitivity to Darifenacin (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>Darifenacin exposure is increased up-to 2.6-fold in CYP2D6 poor metabolizers. Although dose adjustment may not be needed in these patients, monitor patients for increased side effects when darifenacin is prescribed at standard label-recommended dosage and administration.less than /p>

Desipramine (Norpramin®)

Increased Desipramine Exposure (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>The patient is predicted to be a CYP2D6 poor metabolizer which is likely to result in a significantly decreased metabolism of desipramine to less active compounds and a subsequent increase in desipramine exposure leading to side effects.less than /p> less than p>less than strong>Psychiatric Conditions:less than /strong> Consider an alternative medication. If desipramine is warranted, consider a 50% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.less than /p>

Deutetrabenazine (Austedo®)

Increased Sensitivity to Deutetrabenazine (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>less than strong>For treating chorea associated with Huntington's disease: less than /strong>The exposure to deutetrabenazine active metabolites alpha- and and beta-dihydrotetrabenazine is expected to be increased in CYP2D6 poor metabolizers (approximately 3-fold compared to CYP2D6 normal metabolizers) and clinically relevant QT prolongation might be expected in some patients at highest therapeutic doses. Therefore, the maximum recommended dosage of deutetrabenazine in CYP2D6 poor metabolizers is 36 mg per day. Individualization of dose with careful weekly titration is required. The first week's starting dose is 6 mg once daily then this dose should be slowly titrated at weekly intervals by 6 mg per day based on tolerability and up to a maximum recommended daily dosage of 36 mg (18 mg twice daily).less than /p>

Dextroamphetamine (Dexedrine®)

Possible Increased Exposure to Dextroamphetamine (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>There is little evidence documenting the exposure of dextroamphetamine in subjects with reduced CYP2D6 activity such as CYP2D6 poor metabolizers. Although the drug's plasma concentrations may be elevated in these subjects, the clinical relevance of this change is not well documented. Consider initiating therapy with lower doses and monitor the patient more frequently during drug titration. Consider adjusting the dose based on clinical response and tolerability. An alternative therapy may also be considered in patients with decreased tolerability.less than /p>

Dextromethorphan / Quinidine (Nuedexta®)

Altered Sensitivity to Dextromethorphan-Quinidine (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>less than strong>Patients with Pseudobulbar Affectless than /strong>: the quinidine component of dextromethorphan-quinidine is intended to inhibit CYP2D6 so that higher exposure to dextromethorphan can be achieved compared to when dextromethorphan is given alone. Quinidine does not further inhibit CYP2D6 metabolism in poor metabolizers (PMs) and this component may expose PMs to an unnecessary risk since quinidine is not adding any benefit. Prescribers should consider the potential risk for quinidine-related adverse events relative to the benefit of administering the dextromethorphan-quinidine combination product (vs. dextromethorphan alone) in known CYP2D6 poor metabolizers.less than /p>

Diazepam (Valium®)

Increased Sensitivity to Diazepam (CYP2C19: Poor Metabolizer)

INFORMATIVE

less than p>CYP2C19 poor metabolizers have a lower capacity to metabolize diazepam and its active metabolite nordiazepam. Therefore, they may experience more concentration-dependent side effects, such as increased or prolonged sedation, if treated with standard doses of diazepam. Diazepam should be used with caution in these patients, and a reduced dose or longer dosing interval may be needed.less than /p>

Donepezil (Aricept®)

Possible Altered Exposure to Donepezil (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>When compared to a normal metabolizer, a poor metabolizer has a 30% decrease in donepezil clearance. The clinical significance of this decrease is not well documented. Consider using a standard dosing regimen, be alert for adverse events, and adjust dosage in response to clinical response and tolerability. less than /p>

Doxepin (Silenor®)

Increased Doxepin Exposure (CYP2C19: Poor Metabolizer)

INFORMATIVE

less than p>The patient's absent CYP2C19 activity is likely to result in a significantly decreased metabolism of doxepin to desmethyl doxepin and a subsequent increase in doxepin exposure leading to side effects.less than /p> less than p>less than strong>Psychiatric Conditions:less than /strong> Consider an alternative medication. If doxepin is warranted, consider a 50% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.less than /p> less than p>less than strong>Insomnia:less than /strong> Doxepin can be prescribed according to the standard recommended dosage and administration.less than /p>

Increased Doxepin Exposure (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>The patient is predicted to be a CYP2D6 poor metabolizer which is likely to result in a significantly decreased metabolism of doxepin to less active compounds and a subsequent increase in doxepin exposure leading to side effects.less than /p> less than p>less than strong>Psychiatric Conditions:less than /strong> Consider an alternative medication. If doxepin is warranted, consider a 50% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.less than /p> less than p>less than strong>Insomnia:less than /strong> Doxepin can be prescribed according to the standard recommended dosage and administration.less than /p>

Dronabinol (Marinol®)

Increased Dronabinol Exposure (CYP2C9: Intermediate Metabolizer)

ACTIONABLE

less than p>The patient's genotype predicts a reduced CYP2C9 metabolic activity. Increased drug exposure may occur in this patient leading to prolonged sedation. Consider standard label-recommended dosing and close monitoring for adverse effects.less than /p>

Escitalopram (Lexapro®)

Increased Sensitivity to Escitalopram (CYP2C19: Poor Metabolizer)

ACTIONABLE

less than p>At standard label-recommended dosage, escitalopram plasma concentrations levels are expected to be high and adverse events may occur. Consider a 50% reduction of the recommended starting dose to help prevent concentration-dependent adverse events. An alternative medication may also be considered.less than /p>

Flecainide (Tambocor®)

Significantly Increased Exposure to Flecainide (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient's genotype is associated with an increased flecainide exposure following standard dosing. Consider prescribing a lower flecainide dose for therapeutic indications. When compared to a CYP2D6 normal metabolizer, a poor metabolizer may require a 50% dose reduction. Careful titration with ECG recording and monitoring of flecainide plasma concentrations are recommended until a favorable clinical response is achieved.less than /p>less than p>Dose adjustments are not required when flecainide is utilized for diagnostic uses.less than /p>

Flibanserin (Addyi®)

Increased Exposure to Flibanserin (CYP2C19: Poor Metabolizer)

ACTIONABLE

less than p>less than strong>For treating premenopausal women with acquired, generalized hypoactive sexual desire disorder (HSDD):less than /strong> Flibanserin is primarily metabolized by CYP3A4 and, to a lesser extent, by CYP2C19. CYP2C19 poor metabolizers have increased flibanserin exposure compared to CYP2C19 normal metabolizers. As this change in exposure may increase the risk of hypotension, syncope, and CNS depression, advise and monitor patient more closely for serious adverse effects.less than /p>

Fluvastatin (Lescol®)

Possible Increased Fluvastatin Exposure (CYP2C9: Intermediate Metabolizer)

INFORMATIVE

less than p>Increased fluvastatin plasma concentrations due to reduced CYP2C9 activity may occur, resulting in myopathy/hepatotoxicity. Consider monitoring the patient for treatment-related adverse effects, and adjust dose based on tolerability and response. Other adverse events and predisposing factors include advanced age (65 and older), diabetes, hypothyroidism, renal or hepatic impairments, high statin dose, CYP2C9 inhibitors, ABCG2 inhibitors, and female sex.less than /p>

Fluvoxamine (Luvox®)

Increased Sensitivity to Fluvoxamine (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>At standard label-recommended dosage, fluvoxamine levels are expected to be high and adverse events may occur. Consider a 25-50% reduction of recommended starting dose to help prevent concentration-dependent adverse events and titrate based on the clinical response and tolerability. An alternative medication may also be considered.less than /p>

Galantamine (Razadyne®)

Possible Sensitivity to Galantamine (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>A CYP2D6 poor metabolizer has a drug exposure that is approximately 50% higher than the exposure in a normal metabolizer. Although dosage adjustment is not necessary in a patient identified as a CYP2D6 poor metabolizer as the dose of drug is individually titrated to tolerability, a slower titration can be considered as it may improve tolerability.less than /p>

Haloperidol (Haldol®)

Increased Exposure to Haloperidol (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient's genotype is associated with an increased haloperidol exposure following standard dosing. Consider an alternative medication or prescribe haloperidol at 50% of the usual starting dose, then adjust dosage to achieve a favorable clinical response.less than /p>

Hydrocodone (Vicodin®)

Decreased Exposure to Hydrocodone Active Metabolite (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>The patient genotype is associated with a reduced conversion of hydrocodone to an active metabolite (hydromorphone), which may result in decreased effectiveness.less than br />less than br />Hydrocodone can be prescribed at standard label-recommended age- or weight-based dosing. If no response and opioid use is warranted, consider a non-codeine or non-tramadol opioid. Alternative opioids may include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.less than /p>

Iloperidone (Fanapt®)

Increased Sensitivity to Iloperidone (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>Iloperidoneless than strong> dose should be reduced by one-half and titrated slowly to avoid orthostatic hypotensionless than /strong>. Because iloperidone is associated with QTc prolongation, caution is warranted when prescribing the drug in patients with reduced CYP2D6 activity. If patients taking iloperidone experience symptoms that could indicate the occurrence of cardiac arrhythmias (e.g., dizziness, palpitations, or syncope), the prescriber should initiate further evaluation, including cardiac monitoring.less than /p>

Imipramine (Tofranil®)

Increased Imipramine Exposure (CYP2C19: Poor Metabolizer)

INFORMATIVE

less than p>The patient's absent CYP2C19 activity is likely to result in a significantly decreased metabolism of imipramine to desipramine and a subsequent increase in imipramine exposure leading to side effects.less than /p> less than p>less than strong>Psychiatric Conditions:less than /strong> Consider an alternative medication. If imipramine is warranted, consider a 50% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.less than /p>

Increased Imipramine Exposure (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>The patient is predicted to be a CYP2D6 poor metabolizer which is is likely to result in a significantly decreased metabolism of imipramine to less active compounds and a subsequent increase in imipramine exposure leading to side effects.less than /p> less than p>less than strong>Psychiatric Conditions:less than /strong> Consider an alternative medication. If imipramine is warranted, consider a 50% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.less than /p>

Leflunomide (Arava®)

Increased Exposure to Leflunomide (CYP2C19: Poor Metabolizer)

INFORMATIVE

less than p>Leflunomide is metabolized by CYP2C19 and CYP1A2 to its active metabolite teriflunomide. Preliminary studies indicate that patients with decreased CYP2C19 activity have a higher risk of developing gastrointestinal side effects and hepatotoxicity. There is insufficient data to calculate dose adjustment. If leflunomide is prescribed at standard dosing, monitor closely the patient's response and be alert to increased side effects.less than /p>less than p>Full blood cell count (CBC) and liver function parameters should be checked no more than 6 months before beginning treatment, and every month for the initial 6 months of therapy. Blood pressure should be checked before beginning treatment and periodically thereafter.less than /p>

Lisdexamfetamine (Vyvanse®)

Possible Increased Exposure to Lisdexamfetamine Active Metabolite (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>There is little evidence documenting the exposure of lisdexamfetamine and its active metabolite dextroamphetamine in subjects with reduced CYP2D6 activity such as CYP2D6 poor metabolizers. Although dextroamphetamine plasma concentrations may be elevated in these subjects, the clinical relevance of this change is not well documented. Consider initiating therapy with lower doses and monitor the patient more frequently during drug titration. Consider adjusting the dose based on clinical response and tolerability. An alternative therapy may also be considered in patients with decreased tolerability.less than /p>

Lofexidine (Lucemyra®)

Increased Exposure to Lofexidine (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>Lofexidine is metabolized by CYP2D6 with contributions from CYP2C19 and CYP1A2. Although the exposure of lofexidine has not been systematically evaluated in CYP2D6 poor metabolizers, it is likely that exposure would be increased similarly to those who lack CYP2D6 activity due to concomitant dosing with strong CYP2D6 inhibitors (approximately 28% increase). Consider standard dosing and less than strong>monitor closely for adverse events such as orthostatic hypotension and bradycardia.less than /strong> Dosing should be guided based on response and tolerability.less than /p>

Lovastatin (Mevacor®, Altoprev®, Advicor®)

Increased Myopathy Risk (SLCO1B1: Poor Function)

INFORMATIVE

less than p>The reduced SLCO1B1 function may result in elevated lovastatin acid plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high lovastatin doses in this patient should be avoided. If lovastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (65 and older), uncontrolled hypothyroidism, renal impairment, comedications, and female sex.less than /p>

Maprotiline (Ludiomil®)

Possible Increased Maprotiline Exposure (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>Like other tricyclic and tetracyclic antidepressants, maprotiline is metabolized by CYP2D6 as well as CYP1A2. Compared to CYP2D6 normal metabolizers, CYP2D6 poor metabolizers have higher exposure to maprotiline at therapeutic doses which may increase the risk of concentration-dependent toxicities. There are no established dosing adjustments for patients with decreased CYP2D6 function however, it is recommended to initiate maprotiline therapy at a low dosage and gradually adjust the dosing according to the patient's response. The lowest effective dosage should always be considered during maintenance therapy.less than /p>

Metoclopramide (Reglan®)

Increased Sensitivity to Metoclopramide (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>Metoclopramide is metabolized at a slower rate in CYP2D6 poor metabolizers. Slower metabolism results in significantly higher metoclopramide serum concentrations and increased risk of CNS and extrapyramidal adverse effects. Consider reducing the dose to 5 mg four times a day or 10 mg three times a day. The maximum recommended daily dose should not exceed 30 mg in these patients.less than /p>

Metoprolol (Lopressor®)

Metoprolol & Alfuzosin

MODERATE

When starting alpha-blocker therapy in patients receiving beta-blockers, consider initiating treatment with a reduced dose of the alpha-blocker.If syncope occurs, provide supportive treatment as necessary.The adverse effect is self limiting and in most cases does not recur after the initial period of therapy or during subsequent dose titration with the alpha-blocker.

Metoprolol & Amiodarone

MODERATE

Use low doses of beta-blockers initially. Only increase the dosage of the beta-blocker after ECG verification of good tolerability.Patients receiving a concurrent therapy should be closely monitored for adverse effects, such as bradycardia and hypotension. Patients experiencing this drug interaction should have their beta -adrenergic blocking drug discontinued. Supportive therapy with sympathomimetic agents may be required.

Metoprolol & Bupropion — MODERATE

Monitor patients receiving concurrent therapy with metoprolol and inhibitors of CYP2D6. The dosage of metoprolol may need to be adjusted.The effects of rolapitant, a moderate CYP2D6 inhibitor, on CYP2D6 are expected to last at least 28 days after administration.

Metoprolol & Celecoxib — MODERATE

Monitor patient's blood pressure and adjust the dose of the beta-blocker as needed.

Metoprolol & Celecoxib — MODERATE

Monitor patients receiving concurrent therapy with metoprolol and inhibitors of CYP2D6. The dosage of metoprolol may need to be adjusted.

Metoprolol & Citalopram — MODERATE

Monitor patients receiving concurrent therapy with metoprolol and inhibitors of CYP2D6. The dosage of metoprolol may need to be adjusted.Rolapitant, a moderate CYP2D6 inhibitor, effects on CYP2D6 are expected to last at least 28 days after administration.

Metoprolol & Clonidine — SERIOUS

In a patient receiving both drugs, discontinuation of the beta-blocker prior to clonidine may decrease the occurrence of rebound hypertension. If clonidine is discontinued first, rebound hypertension can be treated by restarting the clonidine or by the IV administration of phentolamine, phenoxybenzamine or prazosin. When adding either of these agents to the drug regimen of the patient, monitor blood pressure. Since labetalol has both alpha and beta activity, administration of labetalol may prevent rebound hypertension in patients undergoing clonidine withdrawal, although conflicting reports exist.

Metoprolol & Desvenlafaxine — MODERATE

Reduce the dose of CYP2D6 substrates by up to one-half when coadministered with desvenlafaxine 400 mg.Studies have shown that desvenlafaxine does not have a clinically relevant effect on CYP2D6 metabolism at the dose of 100 mg daily. CYP2D6 substrates should be dosed at the original level when coadministered with desvenlafaxine 100 mg or lower or when desvenlafaxine is discontinued.

Metoprolol & Dextromethorphan / Quinidine — MODERATE

Monitor the response of the patient and adjust the dose of the beta-blocker as needed. The benefits of mefloquine therapy in patients with preexisting cardiac disease should be weighed carefully.

Metoprolol & Diclofenac — MODERATE

Monitor patient's blood pressure and adjust the dose of the beta-blocker as needed.

Metoprolol & Donepezil — MODERATE

Concurrent use of anticholinesterases like donepezil or galantamine with beta-blockers is not recommended. Additive effects may be increased with cardioselective beta-blockers (e.g. atenolol). Monitor patients closely if concurrent use is warranted.

Metoprolol & Doxazosin — MODERATE

When starting alpha-blocker therapy in patients receiving beta-blockers, consider initiating treatment with a reduced dose of the alpha-blocker.If syncope occurs, provide supportive treatment as necessary.The adverse effect is self limiting and in most cases does not recur after the initial period of therapy or during subsequent dose titration with the alpha-blocker.

Metoprolol & Duloxetine — MODERATE

Monitor patients receiving concurrent therapy with metoprolol and inhibitors of CYP2D6. The dosage of metoprolol may need to be adjusted.Rolapitant, a moderate CYP2D6 inhibitor, effects on CYP2D6 are expected to last at least 28 days after administration.

Metoprolol & Escitalopram — MODERATE

Monitor patients receiving concurrent therapy with metoprolol and inhibitors of CYP2D6. The dosage of metoprolol may need to be adjusted.Rolapitant, a moderate CYP2D6 inhibitor, effects on CYP2D6 are expected to last at least 28 days after administration.

Metoprolol & Fluoxetine — MODERATE

Monitor patients receiving concurrent therapy with metoprolol and inhibitors of CYP2D6. The dosage of metoprolol may need to be adjusted.The effects of rolapitant, a moderate CYP2D6 inhibitor, on CYP2D6 are expected to last at least 28 days after administration.

Metoprolol & Flurbiprofen — MODERATE

Monitor patient's blood pressure and adjust the dose of the beta-blocker as needed.

Metoprolol & Galantamine — MODERATE

Concurrent use of anticholinesterases like donepezil or galantamine with beta-blockers is not recommended. Additive effects may be increased with cardioselective beta-blockers (e.g. atenolol). Monitor patients closely if concurrent use is warranted.

Metoprolol & Ibuprofen — MODERATE

Monitor patient's blood pressure and adjust the dose of the beta-blocker as needed.

Metoprolol & Indomethacin — MODERATE

Monitor patient's blood pressure and adjust the dose of the beta-blocker as needed.

Metoprolol & Ketoprofen — MODERATE

Monitor patient's blood pressure and adjust the dose of the beta-blocker as needed.

Metoprolol & Ketorolac — MODERATE

Monitor patient's blood pressure and adjust the dose of the beta-blocker as needed.

Metoprolol & Lacosamide — MODERATE

Lacosamide should be used with caution in patients on concomitant medications that affect cardiac conduction, including beta-blockers and calcium channel blockers.If concurrent use is needed, obtain an ECG before lacosamide therapy and after lacosamide dose is titrated to steady-state.Patients should be monitored closely when lacosamide is given intravenously.

Metoprolol & Meloxicam — MODERATE

Monitor patient's blood pressure and adjust the dose of the beta-blocker as needed.

Metoprolol & Mirabegron

MODERATE

Mirabegron has a long half-life of approximately 50 hours so extended monitoring over 10 to 13 days may be required to evaluate the full effect of this interaction. The manufacturer of mirabegron recommends appropriate monitoring and dose adjustment if necessary for drugs with a narrow therapeutic index. Weigh the risks versus benefits of mirabegron treatment for overactive bladder symptoms based upon the interacting medication and patient specific characteristics.

Metoprolol & Nabumetone

MODERATE

Monitor patient's blood pressure and adjust the dose of the beta-blocker as needed.

Metoprolol & Naproxen

MODERATE

Monitor patient's blood pressure and adjust the dose of the beta-blocker as needed.

Metoprolol & Paroxetine

MODERATE

Monitor patients receiving concurrent therapy with metoprolol and inhibitors of CYP2D6. The dosage of metoprolol may need to be adjusted.The effects of rolapitant, a moderate CYP2D6 inhibitor, on CYP2D6 are expected to last at least 28 days after administration.

Metoprolol & Phenobarbital

MODERATE

Caution when barbiturates are started or stopped. Adjust dosage of beta-blocker if necessary. This interaction may be avoided by using beta-blockers primarily excreted unchanged by the kidneys (e.g., atenolol, nadolol).

Metoprolol & Piroxicam

MODERATE

Monitor patient's blood pressure and adjust the dose of the beta-blocker as needed.

Metoprolol & Primidone

MODERATE

Caution when barbiturates are started or stopped. Adjust dosage of beta-blocker if necessary. This interaction may be avoided by using beta-blockers primarily excreted unchanged by the kidneys (e.g., atenolol, nadolol).

Metoprolol & Propafenone

MODERATE

Monitor cardiac function of patients receiving beta-blockers when starting or stopping propafenone. Adjust the dose of the beta-blocker accordingly.

Metoprolol & Quinidine

MODERATE

Monitor the response of the patient and adjust the dose of the beta-blocker as needed. The benefits of mefloquine therapy in patients with preexisting cardiac disease should be weighed carefully.

Metoprolol & Ranolazine

MODERATE

Monitor patients receiving concurrent therapy with metoprolol and inhibitors of CYP2D6. The dosage of metoprolol may need to be adjusted.

Metoprolol & Rolapitant

MODERATE

Monitor patients receiving concurrent therapy with metoprolol and inhibitors of CYP2D6. The dosage of metoprolol may need to be adjusted.Rolapitant, a moderate CYP2D6 inhibitor, effects on CYP2D6 are expected to last at least 28 days after administration.

Metoprolol & Sertraline

MODERATE

Monitor patients receiving concurrent therapy with metoprolol and inhibitors of CYP2D6. The dosage of metoprolol may need to be adjusted.Rolapitant, a moderate CYP2D6 inhibitor, effects on CYP2D6 are expected to last at least 28 days after administration.

Metoprolol & Sulindac

MODERATE

Monitor patient's blood pressure and adjust the dose of the beta-blocker as needed.

Metoprolol & Terazosin

MODERATE

When starting alpha-blocker therapy in patients receiving beta-blockers, consider initiating treatment with a reduced dose of the alpha-blocker.If syncope occurs, provide supportive treatment as necessary.The adverse effect is self limiting and in most cases does not recur after the initial period of therapy or during subsequent dose titration with the alpha-blocker.

Metoprolol & Tizanidine

MODERATE

Patients receiving concurrent therapy should be monitored for hypotension. The risk of hypotension may be decreased by careful titration of tizanidine dosages and monitoring for hypotension prior to dose advancement. Counsel patients about the risk of orthostatic hypotension.

Significantly Increased Exposure to Metoprolol (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient's genotype is associated with an increased metoprolol exposure following standard dosing. When compared to a normal metabolizer, a poor metabolizer may require a 75% dose reduction. If metoprolol is prescribed, be alert to adverse events (e.g., bradycardia or cold extremities).less than /p>

Mexiletine (Mexitil®)

Significantly Increased Sensitivity to Mexiletine (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>Consider prescribing a lower mexiletine dose. A slow titration with ECG recording and monitoring of mexiletine plasma concentrations are recommended until a favorable clinical response is achieved.less than /p>

Morphine (MS Contin®)

Altered Response to Morphine (COMT: High/Normal COMT Activity)

INFORMATIVE

less than p>The patient does not carry the COMT Val158Met variant. The patient may require higher doses of morphine for adequate pain control. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.less than /p>

Naltrexone (Vivitrol®, Contrave®)

Altered Response to Naltrexone (OPRM1: Normal OPRM1 Function)

INFORMATIVE

less than p>less than span style="text-decoration: underline;">Treatment of alcohol dependence:less than /span> the patient has the OPRM1 118AA wild-type genotype that is associated with a poorer outcome with naltrexone therapy. Naltrexone-treated patients not carrying the OPRM1 118A>G G allele are less likely to respond to this drug, and may have higher relapse rates than those who are carriers of this allele. This association has not been reported consistently across studies.less than /p>

Nefazodone (Serzone®)

Possible Sensitivity to Nefazodone (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>Nefazodone is metabolized by CYP3A4 to its active metabolite m-chlorophenylpiperazine and other metabolites. The m-chlorophenylpiperazine metabolite which may contribute to adverse events, is further metabolized by CYP2D6. Individuals lacking CYP2D6 activity have higher levels of m-chlorophenylpiperazine metabolite and may experience more moderate and transient side effects when starting therapy. Consider prescribing nefazodone at a lower dose and adjust dose according to the patient's tolerability and clinical response.less than /p>

Nortriptyline (Pamelor®)

Increased Nortriptyline Exposure (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient is predicted to be a CYP2D6 poor metabolizer which is likely to result in a significantly decreased metabolism of nortriptyline to less active compounds and a subsequent increase in nortriptyline exposure leading to side effects.less than /p> less than p>less than strong>Psychiatric Conditions:less than /strong> Consider an alternative medication. If nortriptyline is warranted, consider a 50% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.less than /p>

Paroxetine (Paxil®, Brisdelle®)

Possible Increased Sensitivity to Paroxetine (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>At standard label-recommended dosage, paroxetine levels are expected to be high, and adverse events may occur. Consider an alternative medication. If paroxetine is warranted, consider a 50% decrease of the initial dose and titrate based on the clinical response and tolerability.less than /p>

Perphenazine (Trilafon®)

Increased Sensitivity to Perphenazine (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>Patients with a decreased CYP2D6 function will eliminate perphenazine more slowly, which can result in higher drug concentrations and possibly more adverse events (extrapyramidal symptoms). Consider close monitoring and dose reduction to avoid toxicity.less than /p>

Phenobarbital (Luminal®)

Possible Sensitivity to Phenobarbital (CYP2C19: Poor Metabolizer)

INFORMATIVE

less than p>CYP2C19 is partly involved in the metabolism of phenobarbital, and although CYP2C19 poor metabolizers have a 20% lower clearance of phenobarbital than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, phenobarbital can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.less than /p>

Pimozide (Orap®)

Increased Exposure to Pimozide (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The pimozide concentrations observed in poor CYP2D6 metabolizers are expected to be high, and the time to achieve steady-state pimozide concentrations is expected to be long (approximately 2 weeks). Consequently, CYP2D6 poor metabolizers are at an increased risk of QT prolongation at standard doses of pimozide. In CYP2D6 poor metabolizers, pimozide doses should not exceed 4 mg/day in adults and doses should not be increased earlier than 14 days.less than /p>less than p>Cautions should be taken when pimozide is administered with other drugs that prolong QT.less than /p>

Pitavastatin (Livalo®)

Increased Myopathy Risk (SLCO1B1: Poor Function)

INFORMATIVE

less than p>The reduced SLCO1B1 function may result in elevated pitavastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pitavastatin doses in this patient should be avoided. If pitavastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (65 and older), uncontrolled hypothyroidism, renal impairment, comedications, and female sex.less than /p>

Plavix

Plavix & Apixaban

SERIOUS

Patients requiring concurrent therapy with apixaban and an antiplatelet agent should be closely monitored for signs of bleeding.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.Discontinue apixaban in patients with active bleeding.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Plavix & Betrixaban

SERIOUS

Patients requiring concurrent therapy with betrixaban and an antiplatelet agent should be closely monitored for signs of bleeding.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.Discontinue betrixaban in patients with active bleeding.The anticoagulant effect of betrixaban is expected to persist for at least 72 hours after the last dose.

Plavix & Celecoxib

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Plavix & Citalopram

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Plavix & Dabigatran Etexilate

SERIOUS

Patients requiring concurrent therapy with dabigatran and an antiplatelet agent should be closely monitored for signs of bleeding.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.Discontinue dabigatran in patients with active bleeding.

Plavix & Desvenlafaxine

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Plavix & Diclofenac

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Plavix & Duloxetine

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Plavix & Edoxaban

SERIOUS

Patients requiring concurrent therapy with edoxaban and an antiplatelet agent should be closely monitored for signs of bleeding. Edoxaban and aspirin at dosages of 100 mg or less may be coadministered.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.Discontinue edoxaban in patients with active bleeding.

Plavix & Escitalopram

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Plavix & Esomeprazole

SERIOUS

Evaluate patient risk for gastrointestinal(GI) bleeding. When PPIs are needed, use dexlansoprazole, lansoprazole, pantoprazole or rabeprazole as they have a lower interaction risk. Consider the use of H2 blockers (such as famotidine, nizatidine, or ranitidine) in patients with a low bleeding risk and reserve the use of PPIs for patients at higher risk of GI bleeding.US manufacturers for clopidogrel and omeprazole state concurrent use of clopidogrel esomeprazole and omeprazole should be avoided. As esomeprazole and omeprazole are irreversible inhibitors of CYP2C19, separating clopidogrel from esomeprazole or omeprazole administration times does not change the magnitude of this interaction.The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19 are poor metabolizers of this isoenzyme. Moderate CYP2C19 inhibitors, such as omeprazole, and weak CYP2C19 inhibitors, such as cimetidine, may also affect this interaction.Consider alternatives to esomeprazole, omeprazole, and cimetidine in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on esomeprazole, omeprazole, and cimetidine. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Plavix & Etravirine

SERIOUS

The US manufacturer of clopidogrel states that concurrent use of inhibitors of CYP2C19, such as etravirine should be avoided. The US manufacturer of etravirine recommends alternative to clopidogrel in patients maintained on etravirine.The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19 are poor metabolizers of this isoenzyme. Moderate CYP2C19 inhibitors, such as etravirine, may also affect this interaction.Consider alternatives to etravirine in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on etravirine. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Plavix & Felbamate

SERIOUS

The US manufacturer of clopidogrel states that concurrent use of inhibitors of CYP2C19, such as felbamate and stiripentol, should be avoided.The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19 are poor metabolizers of this isoenzyme.Consider alternatives to felbamate or stiripentol in patients stabilized on clopidogrel, or alternatives to clopidogrel in patients stabilized on felbamate or stiripentol. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Plavix & Fluconazole

SERIOUS

The US manufacturer of clopidogrel states that concurrent use of inhibitors of CYP2C19, such as fluconazole, ketoconazole, and voriconazole should be avoided.The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19, such as fluconazole, are poor metabolizers of this isoenzyme. Voriconazole is a moderate CYP2C19 inhibitor.Ketoconazole and voriconazole are strong inhibitors of CYP3A4. Fluconazole is a moderate inhibitor of CYP3A4.Consider alternatives to fluconazole, ketoconazole, and voriconazole in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on fluconazole, ketoconazole, and voriconazole. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Plavix & Fluoxetine

SERIOUS

The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19, such as fluoxetine and fluvoxamine, are poor metabolizers of this isoenzyme.Consider alternatives to fluoxetine and fluvoxamine in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on fluoxetine or fluvoxamine. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Plavix & Flurbiprofen

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Plavix & Fluvoxamine

SERIOUS

The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19, such as fluoxetine and fluvoxamine, are poor metabolizers of this isoenzyme.Consider alternatives to fluoxetine and fluvoxamine in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on fluoxetine or fluvoxamine. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Plavix & Fondaparinux

MODERATE

Use caution when administering platelet aggregation inhibitors concurrently with anticoagulants. Careful monitoring of appropriate laboratory values for the patient's anticoagulant (e.g. PTT for heparin, anti Xa levels for low-molecular weight heparins, INR for warfarin) as well as signs and symptoms of bleeding is warranted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Plavix & Ibuprofen

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Plavix & Indomethacin

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Plavix & Itraconazole

SERIOUS

The US manufacturer of clopidogrel does not make specific recommendations for concurrent use with strong CYP3A4 inhibitors. Patient monitoring for adequate inhibition of platelet reactivity with clopidogrel is warranted.Consider alternatives to strong CYP3A4 inhibitors in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on strong CYP3A4 inhibitors. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Plavix & Ketoprofen

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Plavix & Ketorolac

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Plavix & Levomilnacipran

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Plavix & Meloxicam

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Plavix & Methadone

MODERATE

If concomitant use of levomethadone or methadone and CYP2B6 inhibitors is necessary, closely monitor the patient when a CYP2B6 inhibitor is initiated or withdrawn. The dosage of levomethadone or methadone may need to be adjusted.If concurrent therapy is deemed medically necessary, consider obtaining serum calcium, magnesium, and potassium levels and monitoring ECG at baseline and at regular intervals. Correct any electrolyte abnormalities. Instruct patients to report any irregular heartbeat, dizziness, or fainting.If concurrent use is necessary, monitor patients for unusual dizziness or lightheadedness, extreme sleepiness, slowed or difficult breathing, or unresponsiveness.If concurrent therapy is warranted, patients should be monitored for signs and symptoms of serotonin syndrome. Instruct patients to report muscle twitching, tremors, shivering and stiffness, fever, heavy sweating, heart palpitations, restlessness, confusion, agitation, trouble with coordination, or severe diarrhea.Discuss naloxone with all patients when prescribing or renewing an opioid analgesic or medicine to treat opioid use disorder (OUD). Consider prescribing naloxone to patients prescribed medicines to treat OUD or opioid analgesics (such as those taking CNS depressants) who are at increased risk of opioid overdose and when a patient has household members/close contacts at risk for accidental overdose.

Plavix & Milnacipran

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Plavix & Nabumetone

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Plavix & Naproxen

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Plavix & Nefazodone

SERIOUS

The US manufacturer of clopidogrel does not make specific recommendations for concurrent use with strong CYP3A4 inhibitors. Patient monitoring for adequate inhibition of platelet reactivity with clopidogrel is warranted.Consider alternatives to strong CYP3A4 inhibitors in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on strong CYP3A4 inhibitors. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Plavix & Omeprazole

SERIOUS

Evaluate patient risk for gastrointestinal(GI) bleeding. When PPIs are needed, use dexlansoprazole, lansoprazole, pantoprazole or rabeprazole as they have a lower interaction risk. Consider the use of H2 blockers (such as famotidine, nizatidine, or ranitidine) in patients with a low bleeding risk and reserve the use of PPIs for patients at higher risk of GI bleeding.US manufacturers for clopidogrel and omeprazole state concurrent use of clopidogrel esomeprazole and omeprazole should be avoided. As esomeprazole and omeprazole are irreversible inhibitors of CYP2C19, separating clopidogrel from esomeprazole or omeprazole administration times does not change the magnitude of this interaction.The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19 are poor metabolizers of this isoenzyme. Moderate CYP2C19 inhibitors, such as omeprazole, and weak CYP2C19 inhibitors, such as cimetidine, may also affect this interaction.Consider alternatives to esomeprazole, omeprazole, and cimetidine in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on esomeprazole, omeprazole, and cimetidine. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Plavix & Paroxetine

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Plavix & Piroxicam

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Plavix & Posaconazole

SERIOUS

The US manufacturer of clopidogrel does not make specific recommendations for concurrent use with strong CYP3A4 inhibitors. Patient monitoring for adequate inhibition of platelet reactivity with clopidogrel is warranted.Consider alternatives to strong CYP3A4 inhibitors in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on strong CYP3A4 inhibitors. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Plavix & Repaglinide

SEVERE

Based upon results of a published clinical trial, Health Canada and the Canadian manufacturer of repaglinide state that concurrent use of clopidogrel and repaglinide is contraindicated due to the risk for hypoglycemia from unanticipated lowering of serum glucose concentrations. Alternative antiplatelet agents (e.g. prasugrel, ticagrelor) and antidiabetic agents are not known to inhibit CYP2C8 or OATP1B1.The manufacturer of clopidogrel states that when concomitant use is required in a patient maintained on clopidogrel, initiate repaglinide at 0.5mg with each meal and titrate based on blood glucose levels. Do not exceed a total daily dose of 4mg. If concomitant use of clopidogrel is required in a patient stabilized on repaglinide, down titrate the dose of repaglinide based on blood glucose levels to not exceed a total daily dose of 4mg.If concomitant use is deemed medically necessary:- Hypoglycemic risk is greatest when clopidogrel is added to existing repaglinide therapy. Frequent monitoring of serum/blood glucose is needed to monitor patient response as the magnitude of glucose lowering varies between patients.- In patients stabilized on clopidogrel when repaglinide is initiated, increased sensitivity to the hypoglycemic effect of repaglinide would be expected. In addition, because repaglinide half-life is prolonged in the presence of clopidogrel, maximal effects of repaglinide may be delayed - slower than usual dose titration would be prudent.Separating the timing of drug administration would not be expected to decrease interaction risk as the clopidogrel metabolite (clopidogrel acyl-beta-D-glucuronide) is an irreversible inhibitor of CYP2C8.

Plavix & Rivaroxaban

SERIOUS

Avoid concurrent use of rivaroxaban and clopidogrel unless the benefit is expected to outweigh the increased risk of bleeding.Avoid concurrent use of rivaroxaban and higher doses of aspirin unless the benefit is expected to outweigh the increased risk of bleeding. In the ROCKET AF trial, concomitant use of low dose aspirin (almost exclusively at less than or equal to 100 mg daily) was identified as an independent risk factor for bleeding.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Plavix & Sertraline

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Plavix & Sulindac

SERIOUS

Use caution when administering platelet aggregation inhibitors with NSAIDs. It would be prudent to monitor patients more closely during concurrent therapy and to use the lowest NSAID dose possible.If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The 2010 ACCF/ACG/AHA Consensus guidelines recommend the use of proton pump inhibitors (PPIs) in patients with multiple risk factors for GI bleeding who require antiplatelet therapy. However, esomeprazole and omeprazole should be avoided with clopidogrel as they are expected to reduce the effectiveness of clopidogrel. Use of other PPIs should be approached with caution, as they may reduce the effectiveness of clopidogrel.

Plavix & Venlafaxine

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Plavix & Vilazodone

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Plavix & Voriconazole

SERIOUS

The US manufacturer of clopidogrel states that concurrent use of inhibitors of CYP2C19, such as fluconazole, ketoconazole, and voriconazole should be avoided.The US manufacturer of clopidogrel states that alternatives to clopidogrel should be considered in patients who are poor metabolizers of CYP2C19. It would be prudent to assume that patients taking strong inhibitors of CYP2C19, such as fluconazole, are poor metabolizers of this isoenzyme. Voriconazole is a moderate CYP2C19 inhibitor.Ketoconazole and voriconazole are strong inhibitors of CYP3A4. Fluconazole is a moderate inhibitor of CYP3A4.Consider alternatives to fluconazole, ketoconazole, and voriconazole in patients stabilized on clopidogrel and alternatives to clopidogrel in patients stabilized on fluconazole, ketoconazole, and voriconazole. If concurrent therapy is warranted, consider appropriate testing to assure adequate inhibition of platelet reactivity.

Plavix & Vortioxetine

MODERATE

Selective serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors and agents that affect coagulation should be used concurrently with caution.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.Discontinue antiplatelet agents in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Plavix & Warfarin

MODERATE

Use caution when administering platelet aggregation inhibitors concurrently with anticoagulants. Careful monitoring of appropriate laboratory values for the patient's anticoagulant (e.g. PTT for heparin, anti Xa levels for low-molecular weight heparins, INR for warfarin) as well as signs and symptoms of bleeding is warranted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Significantly Reduced Response to Clopidogrel (CYP2C19: Poor Metabolizer)

ACTIONABLE

less than p>Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.less than /p>

Pravastatin (Pravachol®)

Increased Myopathy Risk (SLCO1B1: Poor Function)

INFORMATIVE

less than p>The reduced SLCO1B1 function may result in elevated pravastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pravastatin doses in this patient should be avoided. If pravastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (65 and older), uncontrolled hypothyroidism, renal impairment, comedications, and female sex.less than /p>

Primidone (Mysoline®)

Possible Sensitivity to Primidone (CYP2C19: Poor Metabolizer)

INFORMATIVE

less than p>CYP2C19 is partly involved in the metabolism of primidone and although CYP2C19 poor metabolizers have a 20% lower clearance of phenobarbital (active metabolite) than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, primidone can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.less than /p>

Propafenone (Rythmol®)

Increased Exposure to Propafenone (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient's genotype is associated with an increased propafenone exposure following standard dosing. Consider a 70% dose reduction in the propafenone initial dose and monitor ECG and plasma concentrations.less than /p>less than p>less than strong>Dose adjustments with co-medicationsless than /strong>: increased exposure to propafenone may lead to cardiac arrhythmias and exaggerated beta-adrenergic blocking activity. Concurrent use of propafenone in CYP2D6 poor metabolizers along with CYP3A4 inhibitors may significantly increase the plasma concentration of propafenone increasing the risk of proarrhythmia and other adverse events. Therefore, avoid simultaneous use of propafenone with a CYP3A4 inhibitor for CYP2D6 poor metabolizers.less than /p>

Protriptyline (Vivactil®)

Possible Increased Protriptyline Exposure (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>Like other tricyclic and tetracyclic antidepressants, protriptyline is metabolized by CYP2D6. Decreased CYP2D6 activity results in higher protriptyline concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased CYP2D6 function. Therefore, therapy must be initiated at a low dosage and gradually adjusted according to the patient's response. The lowest effective dosage should always be considered during maintenance therapy.less than /p>

Ranolazine (Ranexa®)

Increased Sensitivity to Ranolazine (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>Ranolazine is metabolized mainly by CYP3A4, and to a lesser extent by CYP2D6. At 500 mg twice daily, subjects lacking CYP2D6 activity (poor metabolizers) had 62% higher ranolazine exposure than subjects with normal CYP2D6 activity. The corresponding difference at 1000 mg twice daily dose was 25%.less than /p>less than p>less than strong>The risk for increased exposure leading to adverse events is higher in patients lacking CYP2D6 activity (i.e., poor metabolizers). less than /strong>The recommended initial oral dose is 375 mg twice daily. less than strong>A slower up titration and additional monitoring is recommended in these patients.less than /strong> Exposure related side effects might include nausea, vomiting, syncope, and dizziness. If a patient experiences treatment-related adverse events, down titration of the dose to 500 mg or 375 mg twice daily may be required. If symptoms do not resolve after dose reduction, treatment should be discontinued.less than /p>less than p>less than strong>Ranolazine is a QTc prolonging drug. less than /strong>Caution should be observed when treating: 1- patients with a history of congenital or a family history of long QT syndrome, 2- patients with known acquired QT interval prolongation, and 3- patients treated with drugs affecting the QTc interval. Administration of CYP3A4 inhibitors increases the exposure of ranolazine significantly. As a consequence, the QTc prolongation by ranolazine in the presence of potent CYP3A inhibitors is significantly elevated relative to when the drug is administered alone.less than /p>

Repaglinide (Prandin®, Prandimet®)

Possible Sensitivity to Repaglinide (SLCO1B1: Poor Function)

INFORMATIVE

less than p>The patient carries two copies of the the SLCO1B1 521T>C variant. This genotype is associated with reduced transporter function. Patients with this genotype are probably more susceptible to the blood glucose-lowering effect of repaglinide than those with other genotypes. Based on preliminary findings, the optimal starting dose of repaglinide may be lower in these patients. Selecting a lower starting dose may reduce the time needed to reach the correct maintenance dose, potentially with a smaller risk of hypoglycaemia. Repaglinide dose should be adjusted according to the actual blood glucose-lowering response.less than /p>

Risperidone (Risperdal®)

Increased Exposure to Risperidone (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient's genotype is associated with an increased risperidone exposure and decreased active metabolite (paliperidone) exposure following standard dosing. Consider an initial 25-35% dose reduction. If CNS adverse effects occur, consider a further dose reduction to 50% of standard dose. Dosing is individualized based on the patient's tolerability and clinical response.less than /p>

Rosuvastatin (Crestor®)

Increased Myopathy Risk (SLCO1B1 521T>C C/C)

INFORMATIVE

less than p>The reduced SLCO1B1 function may result in elevated rosuvastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high rosuvastatin doses in this patient should be avoided. If rosuvastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (65 and older), uncontrolled hypothyroidism, renal impairment, comedications, and female sex.less than /p>

Sertraline (Zoloft®)

Increased Sensitivity to Sertraline (CYP2C19: Poor Metabolizer)

INFORMATIVE

less than p>At standard label-recommended dosage, sertraline levels are expected to be high, and adverse events may occur. less than strong>Consider a 50% decrease of the initial dose and titrate based on the clinical response and tolerability.less than /strong> An alternative medication may also be considered.less than /p>

Simvastatin (Zocor®)

High Myopathy Risk (SLCO1B1: Poor Function)

ACTIONABLE

less than p>Simvastatin plasma concentrations are expected to be elevated. less than strong>Consider avoiding simvastatinless than /strong> and prescribe an alternative statin or another hypolipidemic drug, or consider prescribing simvastatin at a lower starting dose (20 mg/day). Routine creatine kinase (CK) monitoring is also advised. less than strong>The FDA recommends against the 80 mg daily dose.less than /strong> Although the association between the SLCO1B1 521T>C variant and myopathy risk is not clearly established for other statins such as atorvastatin, pitavastatin, rosuvastatin, and pravastatin, caution is advised if high doses of these statins are used in this patient. Fluvastatin plasma levels are not affected by the SLCO1B1 521T>C variant.less than /p>

Simvastatin & Amiodarone

SEVERE

The US manufacturers of lovastatin and amiodarone recommend that the dose of lovastatin not exceed 40 mg daily in patients receiving concurrent amiodarone unless the potential benefit outweighs the increased risk of myopathy.The US manufacturers of simvastatin and amiodarone recommend that the dose of simvastatin not exceed 20 mg daily in patients receiving concurrent amiodarone unless the potential benefit outweighs the increased risk of myopathy.

Simvastatin & Amiodarone

MODERATE

Use the lowest dose of atorvastatin necessary in patients receiving concurrent amiodarone therapy.The US manufacturers of amiodarone and lovastatin recommend that the dose of lovastatin not exceed 40 mg daily in patients receiving concurrent amiodarone unless the potential benefit outweighs the increased risk of myopathy.The US manufacturers of amiodarone and simvastatin recommend that the dose of simvastatin not exceed 20 mg daily in patients receiving concurrent amiodarone unless the potential benefit outweighs the increased risk of myopathy.

Simvastatin & Betrixaban

MODERATE

Assess renal function and evaluate patient for other pre-existing risk factors for bleeding prior to initiating concurrent therapy. The concurrent use of betrixaban, dabigatran, and edoxaban with lovastatin or simvastatin should be monitored closely. Consider alternate therapy such as atorvastatin, fluvastatin, pravastatin, or rosuvastatin that are not known to inhibit P-gp.Careful monitoring for signs and symptoms of bleeding is warranted during concurrent therapy. Consider regular monitoring of hemoglobin, platelet levels, and/or activated partial thromboplastin time (aPTT) or ecarin clotting time (ECT). Instruct patients to report any signs and symptoms of bleeding, such as bleeding from the eyes, gums or nose; unusual bruising; dark stools; red or dark brown urine; and/or abdominal pain or swelling.

Simvastatin & Colchicine

MODERATE

Patients receiving concurrent therapy with colchicine and HMG-CoA reductase inhibitors should be carefully monitored for myopathy or rhabdomyolysis.Patients should be instructed to report any symptoms of myopathy such as unexplained muscle aches, tenderness, weakness, or the onset of tingling/numbness in the fingers or toes.

Simvastatin & Dabigatran Etexilate

MODERATE

Assess renal function and evaluate patient for other pre-existing risk factors for bleeding prior to initiating concurrent therapy. The concurrent use of betrixaban, dabigatran, and edoxaban with lovastatin or simvastatin should be monitored closely. Consider alternate therapy such as atorvastatin, fluvastatin, pravastatin, or rosuvastatin that are not known to inhibit P-gp.Careful monitoring for signs and symptoms of bleeding is warranted during concurrent therapy. Consider regular monitoring of hemoglobin, platelet levels, and/or activated partial thromboplastin time (aPTT) or ecarin clotting time (ECT). Instruct patients to report any signs and symptoms of bleeding, such as bleeding from the eyes, gums or nose; unusual bruising; dark stools; red or dark brown urine; and/or abdominal pain or swelling.

Simvastatin & Edoxaban

MODERATE

Assess renal function and evaluate patient for other pre-existing risk factors for bleeding prior to initiating concurrent therapy. The concurrent use of betrixaban, dabigatran, and edoxaban with lovastatin or simvastatin should be monitored closely. Consider alternate therapy such as atorvastatin, fluvastatin, pravastatin, or rosuvastatin that are not known to inhibit P-gp.Careful monitoring for signs and symptoms of bleeding is warranted during concurrent therapy. Consider regular monitoring of hemoglobin, platelet levels, and/or activated partial thromboplastin time (aPTT) or ecarin clotting time (ECT). Instruct patients to report any signs and symptoms of bleeding, such as bleeding from the eyes, gums or nose; unusual bruising; dark stools; red or dark brown urine; and/or abdominal pain or swelling.

Simvastatin & Fluconazole

MODERATE

Do not use fluvastatin in doses greater than 20 mg twice daily in patients receiving fluconazole.Concurrent use of fluconazole with atorvastatin, fluvastatin, lovastatin, or simvastatin should be approached with caution. Patients should be carefully monitored for and instructed to report any signs of myopathy. Adjustment of the statin dose may be required.

Simvastatin & Itraconazole

SEVERE

Do not use lovastatin or simvastatin with itraconazole.The manufacturer of atorvastatin states the dose of atorvastatin should be limited to 20 mg in patients receiving itraconazole; however, the manufacturer of itraconazole states that all strengths of atorvastatin are contraindicated.Concurrent therapy with cerivastatin and atorvastatin, lovastatin, or simvastatin is not recommended.The US manufacturer of itraconazole states that concurrent administration with lovastatin or simvastatin is contraindicated during or two weeks after itraconazole treatment.

Simvastatin & Nefazodone

SEVERE

Do not use lovastatin or simvastatin with nefazodone.Fluvastatin and pravastatin, HMG-CoA reductase inhibitors that are not extensively metabolized by CYP P-450-3A4, may be alternatives to other HMG-CoA reductase inhibitors in patients taking nefazodone.

Simvastatin & Posaconazole

SEVERE

Strong CYP3A4 inhibitors such as ketoconazole and posaconazole are contraindicated with cerivastatin, lovastatin and simvastatin.

Simvastatin & Ranolazine

SEVERE

Do not exceed a dosage of 20 mg daily of simvastatin in patients receiving concurrent therapy with ranolazine.

Simvastatin & Ranolazine

MODERATE

Do not exceed a dosage of 20 mg daily of simvastatin in patients receiving concurrent therapy with ranolazine.Consider a reduction of lovastatin dose with concurrent ranolazine.

Simvastatin & Ticagrelor

SERIOUS

Avoid the use of doses of lovastatin and simvastatin greater than 40 mg in patients receiving ticagrelor. Monitor patients receiving concurrent therapy for signs and symptoms of myopathy.

Simvastatin & Voriconazole

SEVERE

Concurrent use of voriconazole with lovastatin or simvastatin is contraindicated. Therapy with lovastatin or simvastatin should be suspended during voriconazole therapy. In patients requiring long-term therapy with voriconazole, consider the use of pravastatin or reduced dosages of atorvastatin or fluvastatin, using the lowest dose possible Patients should be carefully monitored for and instructed to report any signs of myopathy.

Tamsulosin (Flomax®)

Increased Sensitivity to Tamsulosin (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>Tamsulosin is metabolized at a slower rate in CYP2D6 poor metabolizers, which results in significantly higher serum concentrations of tamsulosin. Therefore, this drug should be used with caution in patients known to be CYP2D6 poor metabolizers, particularly at a daily dose higher than 0.4 mg.less than /p>

Tetrabenazine (Xenazine®)

Increased Sensitivity to Tetrabenazine (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>less than strong>For treating chorea associated with Huntington's disease:less than /strong> Individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. less than strong>The maximum daily dose in CYP2D6 poor metabolizers is 50 mg with a maximum single dose of 25 mgless than /strong>. If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.less than /p>

Thioridazine (Mellaril®)

Increased Sensitivity to Thioridazine (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>Reduced cytochrome CYP2D6 activity results in elevated plasma levels of thioridazine, would be expected to augment the prolongation of the QTc interval associated with thioridazine, and may increase the risk of serious, potentially fatal, cardiac arrhythmias, such as Torsades de pointes-type arrhythmias. Such an increased risk may result also from the additive effect of coadministering thioridazine with other agents that prolong the QTc interval. Therefore, thioridazine is contraindicated in patients with reduced levels of CYP2D6 activity.less than /p>

Timolol (Blocadren®)

Increased Sensitivity to Timolol (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>Potentiated systemic beta-blockade (e.g., bradycardia) has been reported during timolol treatment by patients with decreased CYP2D6 activity. Monitor patient for treatment-related adverse effects.less than /p>

Tolterodine (Detrol®)

Possible Sensitivity to Tolterodine (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>Tolterodine is metabolized at a slower rate in CYP2D6 poor metabolizers, which results in significantly higher serum concentrations of tolterodine and negligible concentrations of its active metabolite (5-hydroxymethytolterodine). Considering the antimuscarinic potency of tolterodine and its active metabolite, and the protein binding of these compounds, tolterodine accounts for the major part of the clinical effect in poor metabolizers, and the same dosage can be applied irrespective of phenotype status.less than /p>less than p>Patients with congenital or acquired QT prolongation: the effect of tolterodine on the QT interval prolongation is greater for 8 mg/day (two times the therapeutic dose) compared to 4 mg/day, and is more pronounced in CYP2D6 poor metabolizers than normal metabolizers. This should be considered when tolterodine is prescribed to patients with a known history of QT prolongation, or patients who are taking Class IA or Class III antiarrhythmics.less than /p>

Tramadol (Ultram®)

Greatly Decreased Exposure to Tramadol Active Metabolite (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient genotype is associated with greatly decreased conversion of tramadol to its active metabolite (O-desmethyltramadol), which may result in decreased effectiveness.less than br />less than br />Consider avoiding prescribing tramadol and instead use alternative opioids other than codeine, or a non-opioid analgesic such as an NSAID or a COX-2 inhibitor. Alternative opioids may include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.less than /p>

Trimipramine (Surmontil®)

Increased Trimipramine Exposure (CYP2C19: Poor Metabolizer)

INFORMATIVE

less than p>The patient's absent CYP2C19 activity is likely to result in a significantly decreased metabolism of trimipramine to desmethyl trimipramine and a subsequent increase in trimipramine exposure leading to side effects.less than /p> less than p>less than strong>Psychiatric Conditions:less than /strong> Consider an alternative medication. If trimipramine is warranted, consider a 50% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.less than /p>

Increased Trimipramine Exposure (CYP2D6: Poor Metabolizer)

INFORMATIVE

less than p>The patient is predicted to be a CYP2D6 poor metabolizer which is likely to result in a significantly decreased metabolism of trimipramine to less active compounds and a subsequent increase in trimipramine exposure leading to side effects.less than /p> less than p>less than strong>Psychiatric Conditions:less than /strong> Consider an alternative medication. If trimipramine is warranted, consider a 50% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.less than /p>

Valbenazine (Ingrezza®)

Increased Sensitivity to Valbenazine (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The initial dose is 40 mg once daily. Based on tolerability, this dose may be maintained in CYP2D6 poor metabolizers to reduce the risk of exposure-related adverse events. Valbenazine may prolong the QT interval. The exposure to valbenazine and its major active metabolite in CYP2D6 poor metabolizers is significantly higher than the exposure in CYP2D6 normal metabolizers. Because the drug's QTc prolongation effect is concentration-dependent, it is appropriate to consider a reduced recommended dose based on the patient's tolerability. Other exposure-related adverse events include somnolence. Careful titration is recommended until a favorable response is achieved.less than /p> less than p>less than span style="text-decoration: underline;">Dose adjustments with comedications:less than /span> reduce the daily recommended dose to 40 mg if a strong CYP3A4 inhibitor is coadministered. Concomitant use with CYP3A4 inducers should be avoided.less than /p>

Venlafaxine (Effexor®)

Significantly Increased Exposure to Venlafaxine (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>The patient has a decreased CYP2D6 activity which may result in elevated plasma concentrations of venlafaxine at standard doses. Consider an alternative medication or consider prescribing venlafaxine at a reduced dose and be extra alert for adverse events; adjust the dose based on tolerability and therapeutic monitoring.less than /p>less than p>If therapeutic drug monitoring is utilized, the sum of venlafaxine and O-desmethylvenlafaxine (an active metabolite) plasma concentrations should be used for efficacy. While the sum of the parent and the active metabolite are informative for efficacy, a higher parent (venlafaxine) concentration may be associated with higher side effects, including QT prolongation.less than /p>

Voriconazole (Vfend®)

Increased Sensitivity to Voriconazole (CYP2C19: Poor Metabolizer)

ACTIONABLE

less than p>Voriconazole plasma concentrations are expected to be high if a standard dose is used, which may increase the risk of adverse events (hepatotoxicity, visual disturbances/halucinations and neurologic disorders). Consider an alternative medication that is not dependent on CYP2C19 metabolism, such as isavuconazole, liposomal amphotericin B or posaconazole. If voriconazole is warranted, consider a decreased dose and careful therapeutic drug monitoring.less than /p>

Vortioxetine (Trintellix®)

Increased Sensitivity to Vortioxetine (CYP2D6: Poor Metabolizer)

ACTIONABLE

less than p>CYP2D6 is the primary enzyme catalyzing the metabolism of vortioxetine to its major, pharmacologically inactive carboxylic acid metabolite. CYP2D6 poor metabolizers have approximately twice the vortioxetine plasma concentrations of normal metabolizers. less than strong>Vortioxetine starting dose should be reduced by one-half. The maximum recommended dose is 10 mg/day in known CYP2D6 poor metabolizers.less than /strong> Consider 5 mg/day for patients who do not tolerate higher doses.less than /p>

Warfarin (Coumadin®)

Dosing Adjustments are Expected (CYP2C9 *1/*5; VKORC1 -1639G>A G/A)

ACTIONABLE

less than p>When initiating warfarin treatment for indications with a target INR of 2-3, consider using pharmacogenetic algorithms/calculators (available at www.warfarindosing.org) to estimate dosing requirements:less than /p> less than p>less than strong>Caucasians and Asians:less than /strong> Use the patient's demographics and other clinical factors along with CYP2C9 and VKORC1 genotypes to calculate the expected therapeutic dose. Consider an additional 15-30% decrease to the calculated dose.less than /p> less than p>less than strong>Africans and African Americans:less than /strong> Use the patient's demographics and other clinical factors along with CYP2C9 and VKORC1 genotypes to calculate the expected therapeutic dose. Consider an additional 15-30% decrease to the calculated dose.less than /p> less than p>The provided recommendations in Africans and African Americans apply only when all the following CYP2C9 alleles are tested: *5, *6, *8, *11.less than /p>

Warfarin & Amiodarone

SERIOUS

The US manufacturer of amiodarone states that amiodarone will almost always potentiate the anticoagulant response in patients receiving coumarin anticoagulants. They recommend decreasing the anticoagulant dosage by 1/3 to 1/2 when amiodarone therapy is initiated. Although amiodarone has a long half -life, significant increases in the INR/prothrombin time may start in 3 to 4 days. Monitor INR closely and adjust anticoagulant dose until stabile.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Apixaban

SERIOUS

The long-term use of concurrent therapy with Direct Oral Anticoagulants (DOACs) and other anticoagulants is generally considered contraindicated. However, overlap may be necessary when switching therapy from one agent to another in order to prevent thrombotic events. Manufacturer recommendations concerning overlap (if any) and timing of discontinuation versus initiation vary depending upon which agent is being discontinued and initiated. Refer to current prescribing information for both agents for additional details.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue apixaban in patients with active bleeding.Concurrent use of apixaban and heparins (including low-molecular weight), factor Xa inhibiting oligosaccharides, GPIIb/IIIa receptor antagonists, thienopyridines, dipyridamole, dextran, vitamin K antagonists, and other oral anticoagulants increases risk of bleeding and is not recommended.When converting from warfarin to apixaban, discontinue warfarin and begin apixaban when the international normalized ratio (INR) is below 2.0.Apixaban affects INR, therefore concurrent administration with warfarin when converting from apixaban to warfarin is not useful in determining target warfarin dose. If continuous anticoagulation is warranted, discontinue apixaban and begin both warfarin and a parenteral anticoagulant when next dose of apixaban is due. Once INR is within range, discontinue the parenteral anticoagulant.When converting between apixaban and anticoagulants other than warfarin, discontinue current anticoagulant and begin new one when next dose is due.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Warfarin & Aprepitant

SERIOUS

The manufacturers of aprepitant recommend careful monitoring of INR values in the 2 week period, particularly at 7-10 days, following initiation of the 3 day course of aprepitant therapy with each chemotherapy cycle.

Warfarin & Betrixaban

SERIOUS

The long-term use of concurrent therapy with Direct Oral Anticoagulants (DOACs) and other anticoagulants is generally considered contraindicated.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue betrixaban in patients with active bleeding.Concurrent use of betrixaban and heparins (including low-molecular weight), factor Xa inhibiting oligosaccharides, GPIIb/IIIa receptor antagonists, thienopyridines, dipyridamole, dextran, vitamin K antagonists, and other oral anticoagulants increases risk of bleeding and is not recommended.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The anticoagulant effect of betrixaban is expected to persist for at least 72 hours after the last dose.

Warfarin & Carbamazepine

MODERATE

Monitor anticoagulation parameters when starting or stopping carbamazepine in a patient receiving warfarin. Adjust the dose of warfarin accordingly.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Celecoxib

SERIOUS

If concurrent therapy with anticoagulants and NSAIDs is warranted, patients should be closely monitored for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Citalopram

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Clomipramine

MODERATE

If concurrent therapy is warranted, monitor patients for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose, or discontinuing either drug.

Warfarin & Dabigatran Etexilate

SERIOUS

The long-term use of concurrent therapy with Direct Oral Anticoagulants (DOACs) and other anticoagulants is generally considered contraindicated. However, overlap may be necessary when switching therapy from one agent to another in order to prevent thrombotic events. Manufacturer recommendations concerning overlap (if any) and timing of discontinuation versus initiation vary depending upon which agent is being discontinued and initiated. Refer to current prescribing information for both agents for additional details.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, decreased blood pressure and/or fecal occult blood and promptly evaluate patients with any symptoms. Discontinue dabigatran in patients with active bleeding.The UK manufacturer of dabigatran states the use of dabigatran concomitantly used with other anticoagulants, platelet inhibitors, or dextran is contraindicated unless switching treatment to or from dabigatran.When converting from warfarin to dabigatran, discontinue warfarin and begin dabigatran when the patient's INR is below 2.0.When converting from dabigatran to warfarin, start warfarin: -----3 days before discontinuing dabigatran in patients with CrCl greater than 50 ml/min, -----2 days before discontinuing dabigatran in patients with CrCl of 31 ml/min to 50 ml/min, -----1 day before discontinuing dabigatran in patients with CrCl of 15 ml/min to 30 ml/min.There is no recommendation available for converting dabigatran to warfarin in patients with CrCl less than 15 ml/min.When converting from parenteral anticoagulant to dabigatran, administer dabigatran 0-2 hours before the next dose of the parenteral drug is due.When converting from dabigatran to a parenteral anticoagulant, begin parenteral anticoagulant: -----12 hours after last dose of dabigatran in patients with CrCl greater than or equal to 30ml/min, -----24 hours after last dose of dabigatran in patients with CrCl less than 30 ml/min.

Warfarin & Desvenlafaxine

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Dextromethorphan / Quinidine

MODERATE

Excessive hypoprothrombinemia and hemorrhage has been reported in patients receiving warfarin 6 to 10 days after starting quinidine. Monitor INR and adjust anticoagulant dose to assure efficacy and safety of anticoagulation.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Warfarin & Diclofenac

SERIOUS

If concurrent therapy with anticoagulants and NSAIDs is warranted, patients should be closely monitored for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Dronabinol

MODERATE

Monitor INRs frequently until stable in patients who start CBD and/or THC or have the dose adjusted.A Health Canada Product InfoWatch regarding the use of cannabis and warfarin advises healthcare professionals to ask patients about their use of cannabis, particularly if patients are being treated with warfarin, due to the potential for increased INR values.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.Discontinue anticoagulation in patients with active pathologic bleeding.

Warfarin & Duloxetine

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Edoxaban

SERIOUS

The long-term use of concurrent therapy with Direct Oral Anticoagulants (DOACs) and other anticoagulants is generally considered contraindicated. However, overlap may be necessary when switching therapy from one agent to another in order to prevent thrombotic events. Manufacturer recommendations concerning overlap (if any) and timing of discontinuation versus initiation vary depending upon which agent is being discontinued and initiated. Refer to current prescribing information for both agents for additional details.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue edoxaban in patients with active bleeding.Edoxaban manufacturer recommendations when converting from another anticoagulant to edoxaban:- When converting from warfarin or other vitamin K antagonists, discontinue warfarin and start edoxaban when the INR is < or = to 2.5- When converting from other (non-vitamin K antagonist) oral anticoagulants, discontinue current oral anticoagulant and start edoxaban at the time of the next scheduled dose of the other oral anticoagulant.- When converting from a low molecular weight heparin (LMWH), start edoxaban at the time of the next scheduled administration of LMWH.- When converting from unfractionated heparin, discontinue the infusion and start edoxaban 4 hours later.Edoxaban manufacturer recommendations when converting from edoxaban to another anticoagulant:- When converting from edoxaban to warfarin, for patients taking 60 mg of edoxaban, reduce the dose to 30 mg and begin warfarin concomitantly. For patients receiving 30 mg of edoxaban, reduce the dose to 15 mg and begin warfarin concomitantly. INR must be measured at least weekly and just prior to the daily dose of edoxaban to minimize the effects of edoxaban on INR measurement. Once a stable INR = or > 2.0 is achieved, edoxaban should be discontinued and the warfarin continued.- A second edoxaban to warfarin conversion option:Discontinue edoxaban and administer a parenteral anticoagulant and warfarin at the time of the next scheduled edoxaban dose. Once a stable INR = or > 2.0 is achieved the parenteral anticoagulant should be discontinued and the warfarin continued.- When converting from edoxaban to another DOAC, discontinue edoxaban and begin the other oral anticoagulant at the time of the next scheduled dose of edoxaban.- When converting from edoxaban to parenteral anticoagulation, start the parenteral anticoagulant at the time of the next dose of edoxaban.

Warfarin & Escitalopram

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Fluconazole

SERIOUS

In patients receiving warfarin when fluconazole, voriconazole, miconazole or ketoconazole is started, anticipate the need for a dose reduction. Check the baseline INR then closely monitor and adjust the dose of warfarin until the INR has stabilized on the combination. After the azole therapy is discontinued, close monitoring is again needed as the INR may fall after removal of the inhibitor. Although the interaction risk between warfarin and itraconazole is not as clear, it would be prudent to closely monitor patients on this combination as well.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Fluoxetine

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Flurbiprofen

SERIOUS

If concurrent therapy with anticoagulants and NSAIDs is warranted, patients should be closely monitored for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Fluvastatin

MODERATE

Patients should be monitored for changes in prothrombin time when a HMG Co-A reductase inhibitor is added to or discontinued from warfarin therapy, or if the dosage of the HMG Co-A reductase inhibitor is adjusted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Fluvoxamine

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Fondaparinux

MODERATE

The manufacturer recommends baseline and periodic platelet counts and hematocrits for the entire duration of heparin administration.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or blood pressure and promptly evaluate patients with any symptoms. Discontinue heparin in patients with active pathological bleeding unless the benefits outweigh the potential risk.Partial thromboplastin time (aPTT) or whole-blood clotting time (WBC) may be monitored to assess coagulation status.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Warfarin & Fosaprepitant

SERIOUS

The manufacturers of aprepitant recommend careful monitoring of INR values in the 2 week period, particularly at 7-10 days, following initiation of the 3 day course of aprepitant therapy with each chemotherapy cycle.

Warfarin & Fosphenytoin

SERIOUS

The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug. Monitor INR and adjust the anticoagulant dose accordingly. Extended monitoring may be needed as an initial increase in the INR may be followed by a fall in the INR due to phenytoin induction of warfarin metabolism. Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.Patients receiving acenocoumarol or dicoumarol and a hydantoin should also have hydantoin levels monitored and adjusted when anticoagulant therapy is initiated. Monitor the patient for signs of hydantoin toxicity (e.g. nystagmus, ataxia, dysarthria, tremor, hyperreflexia, lethargy, slurred speech, blurred vision, nausea, and vomiting).

Warfarin & Ibuprofen

SERIOUS

If concurrent therapy with anticoagulants and NSAIDs is warranted, patients should be closely monitored for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Indomethacin

SERIOUS

If concurrent therapy with anticoagulants and NSAIDs is warranted, patients should be closely monitored for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Itraconazole

SERIOUS

In patients receiving warfarin when fluconazole, voriconazole, miconazole or ketoconazole is started, anticipate the need for a dose reduction. Check the baseline INR then closely monitor and adjust the dose of warfarin until the INR has stabilized on the combination. After the azole therapy is discontinued, close monitoring is again needed as the INR may fall after removal of the inhibitor. Although the interaction risk between warfarin and itraconazole is not as clear, it would be prudent to closely monitor patients on this combination as well.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Ketoprofen

SERIOUS

If concurrent therapy with anticoagulants and NSAIDs is warranted, patients should be closely monitored for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Ketorolac

SERIOUS

The Australian and UK manufacturers of ketorolac state that the use of ketorolac in patients on anticoagulants, including low-dose heparin, is contraindicated.The US manufacturer of ketorolac states that concurrent therapy with anticoagulants should be undertaken with extreme caution after carefully weighing the benefits of concurrent therapy against the risks and that patients receiving concurrent therapy should be closely monitored.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Leflunomide

MODERATE

Monitor INR response closely in patients maintained on warfarin when initiating, titrating, and discontinuing leflunomide. Patients maintained on leflunomide may require lower initial dosages of warfarin.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Levomilnacipran

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Lovastatin

MODERATE

Patients should be monitored for changes in prothrombin time when a HMG Co-A reductase inhibitor is added to or discontinued from warfarin therapy, or if the dosage of the HMG Co-A reductase inhibitor is adjusted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Meloxicam

SERIOUS

If concurrent therapy with anticoagulants and NSAIDs is warranted, patients should be closely monitored for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Milnacipran

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Nabumetone

SERIOUS

If concurrent therapy with anticoagulants and NSAIDs is warranted, patients should be closely monitored for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Naproxen

SERIOUS

If concurrent therapy with anticoagulants and NSAIDs is warranted, patients should be closely monitored for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Paroxetine

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Phenobarbital

SERIOUS

If possible, avoid the concurrent use of these agents. If a barbiturate is initiated or discontinued in a patient maintained on anticoagulant therapy, monitor prothrombin times and adjust the dose of the anticoagulant as needed.For hypnotic indications, benzodiazepines and diphenhydramine may be alternatives to barbiturates in patients stabilized on anticoagulant therapy.

Warfarin & Phenytoin

SERIOUS

The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug. Monitor INR and adjust the anticoagulant dose accordingly. Extended monitoring may be needed as an initial increase in the INR may be followed by a fall in the INR due to phenytoin induction of warfarin metabolism. Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.Patients receiving acenocoumarol or dicoumarol and a hydantoin should also have hydantoin levels monitored and adjusted when anticoagulant therapy is initiated. Monitor the patient for signs of hydantoin toxicity (e.g. nystagmus, ataxia, dysarthria, tremor, hyperreflexia, lethargy, slurred speech, blurred vision, nausea, and vomiting).

Warfarin & Piroxicam

SERIOUS

If concurrent therapy with anticoagulants and NSAIDs is warranted, patients should be closely monitored for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Prasugrel

MODERATE

Use caution when administering platelet aggregation inhibitors concurrently with anticoagulants. Careful monitoring of appropriate laboratory values for the patient's anticoagulant (e.g. PTT for heparin, anti Xa levels for low-molecular weight heparins, INR for warfarin) as well as signs and symptoms of bleeding is warranted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Primidone

SERIOUS

If possible, avoid the concurrent use of these agents. If a barbiturate is initiated or discontinued in a patient maintained on anticoagulant therapy, monitor prothrombin times and adjust the dose of the anticoagulant as needed.For hypnotic indications, benzodiazepines and diphenhydramine may be alternatives to barbiturates in patients stabilized on anticoagulant therapy.

Warfarin & Propafenone

MODERATE

The dosage of warfarin may need to be adjusted when propafenone is initiated or discontinued. The patient INR should be monitored for changes in the effects of warfarin.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Warfarin & Propranolol

MODERATE

Monitor the INR when propranolol is added to or discontinued from warfarin therapy, particularly when higher doses of propranolol (> 80 mg/dose) are prescribed.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Quinidine

MODERATE

Excessive hypoprothrombinemia and hemorrhage has been reported in patients receiving warfarin 6 to 10 days after starting quinidine. Monitor INR and adjust anticoagulant dose to assure efficacy and safety of anticoagulation.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.

Warfarin & Rivaroxaban

SERIOUS

The long-term use of concurrent therapy with Direct Oral Anticoagulants (DOACs) and other anticoagulants is generally considered contraindicated. However, overlap may be necessary when switching therapy from one agent to another in order to prevent thrombotic events. Manufacturer recommendations concerning overlap (if any) and timing of discontinuation versus initiation vary depending upon which agent is being discontinued and initiated. Refer to current prescribing information for both agents for additional details.Monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue rivaroxaban in patients with active bleeding.Avoid concurrent use of rivaroxaban and anticoagulants other than periods of therapeutic transition between agents or if benefit outweighs increased risk of bleeds.When converting from warfarin to rivaroxaban, discontinue warfarin and begin rivaroxaban once international normalized ratio (INR) is below 3.0.When converting from rivaroxaban to warfarin, rivaroxaban affects INR, therefore concurrent administration with warfarin is not useful in determining target warfarin dose. If continuous anticoagulation is warranted, discontinue rivaroxaban and begin both warfarin and a parenteral anticoagulant when next dose of rivaroxaban is due. Once INR is within range, discontinue the parenteral anticoagulant.When converting from rivaroxaban to anticoagulants other than warfarin and switching to an anticoagulant with rapid onset, discontinue rivaroxaban and begin new anticoagulant when next dose of rivaroxaban is due.When converting to rivaroxaban from anticoagulants other than warfarin, discontinue current anticoagulant and begin rivaroxaban between 0-2 hours before next evening dose of the drug is due. For patients receiving continuous infusion of unfractionated heparin, simultaneously stop the infusion and administer rivaroxaban.

Warfarin & Rosuvastatin

MODERATE

Patients should be monitored for changes in prothrombin time when a HMG Co-A reductase inhibitor is added to or discontinued from warfarin therapy, or if the dosage of the HMG Co-A reductase inhibitor is adjusted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Sertraline

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Simvastatin

MODERATE

Patients should be monitored for changes in prothrombin time when a HMG Co-A reductase inhibitor is added to or discontinued from warfarin therapy, or if the dosage of the HMG Co-A reductase inhibitor is adjusted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Sulindac

SERIOUS

If concurrent therapy with anticoagulants and NSAIDs is warranted, patients should be closely monitored for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Ticagrelor

MODERATE

Use caution when administering platelet aggregation inhibitors concurrently with anticoagulants. Careful monitoring of appropriate laboratory values for the patient's anticoagulant (e.g. PTT for heparin, anti Xa levels for low-molecular weight heparins, INR for warfarin) as well as signs and symptoms of bleeding is warranted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Tramadol

MODERATE

Patients maintained on warfarin who begin therapy with propoxyphene or tramadol containing medication should be monitored closely for signs of increased warfarin effects. The dosage of warfarin may need to be adjusted or a different opioid may need to be used.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Valproic Acid

MODERATE

Monitor INR response closely in patient maintained on warfarin when initiating, increasing or discontinuing valproic acid. Patients maintained on valproic acid may require lower initial doses of warfarin.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Venlafaxine

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Vilazodone

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Vorapaxar

MODERATE

Use caution when administering platelet aggregation inhibitors concurrently with anticoagulants. Careful monitoring of appropriate laboratory values for the patient's anticoagulant (e.g. PTT for heparin, anti Xa levels for low-molecular weight heparins, INR for warfarin) as well as signs and symptoms of bleeding is warranted.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Voriconazole

SERIOUS

In patients receiving warfarin when fluconazole, voriconazole, miconazole or ketoconazole is started, anticipate the need for a dose reduction. Check the baseline INR then closely monitor and adjust the dose of warfarin until the INR has stabilized on the combination. After the azole therapy is discontinued, close monitoring is again needed as the INR may fall after removal of the inhibitor. Although the interaction risk between warfarin and itraconazole is not as clear, it would be prudent to closely monitor patients on this combination as well.If concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin, hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Warfarin & Vortioxetine

SERIOUS

For the combination of fluvoxamine and warfarin: when possible change to a SSRI which does not inhibit warfarin metabolism (e.g. citalopram or paroxetine). For patients who require this combination, monitor for an increase in INR when fluvoxamine is started or the dose is increased. The warfarin dose may need to be reduced.For all anticoagulant/SSRI or SNRI combinations, if concurrent therapy is warranted, monitor patients receiving concurrent therapy for signs of blood loss, including decreased hemoglobin and/or hematocrit, fecal occult blood, and/or decreased blood pressure and promptly evaluate patients with any symptoms.When applicable, perform agent-specific laboratory test (e.g. INR, aPTT) to monitor efficacy and safety of anticoagulation. Discontinue anticoagulation in patients with active pathologic bleeding.Instruct patients to report any signs and symptoms of bleeding, such as unusual bleeding from the gums or nose; unusual bruising; red or black, tarry stools; red, pink or dark brown urine; acute abdominal or joint pain and/or swelling.The time of highest risk for a coumarin-type drug interaction is when the precipitant drug is initiated or discontinued. Contact the prescriber before initiating, altering the dose or discontinuing either drug.

Zonisamide (Zonegran®)

Possible Sensitivity to Zonisamide (CYP2C19: Poor Metabolizer)

INFORMATIVE

less than p>CYP2C19 is partly involved in the metabolism of zonisamide, and although preliminary studies show that CYP2C19 poor metabolizers have a slightly lower (30%) zonisamide clearance than normal metabolizers, no significant change in the clinical outcome has been reported with this antiepileptic drug. Therefore, zonisamide can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.less than /p>

GENESYS Diagnostics INC.

PATIENT INFORMATION	SPECIMEN DETAILS	ORDERED BY
NAME: Carl Cardio	**SPECIMEN TYPE:** Buccal Swab	
ACC #: 1039	**COLLECTION DATE:**	
DOB: 1/1/1900	**RECEIVED DATE:**	
SEX: Male	**REPORT DATE:** 10/16/2021	

Test Details

Gene	Genotype	Phenotype	Clinical Consequences
Apolipoprotein E	ε2/ε2	Altered APOE function	5% of patients with this genotype develop type III hyperlipoproteinemia and subsequent premature cardiovascular disease
COMT	Val158Met G/G	High/Normal COMT Activity	Consistent with a normal catechol O-methyltransferase (COMT) function.
CYP1A2	*1A/*1A	Normal Metabolizer- Possible Inducibility	Consistent with a typical CYP1A2 activity in absence of inducing substances. Rapid metabolism may occur in presence of inducers such as barbiturates, cruciferous vegetables, carbamazepine, rifampin and smoking.
CYP2B6	*1/*1	Normal Metabolizer	Consistent with a typical CYP2B6 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2C19	*2/*2	Poor Metabolizer	Consistent with a significant deficiency in CYP2C19 enzyme activity. Exercise caution if CYP2C19 drug substrates are prescribed.
CYP2C9	*1/*5	Intermediate Metabolizer	Consistent with a moderate deficiency in CYP2C9 enzyme activity.
CYP2D6	*4M/*4M XN	Poor Metabolizer	Consistent with a significant deficiency in CYP2D6 enzyme activity. Exercise caution if CYP2D6 drug substrates are prescribed.
CYP3A4	*1/*1	Normal Metabolizer	Consistent with a typical CYP3A4 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
CYP3A5	*3/*3	Poor Metabolizer	Consistent with an absence of CYP3A5 enzyme expression (Non-Expresser). This phenotype is the most common in the general population.
F2 F5	rs1799963 GG rs6025 TT	Increased Risk of Thrombosis	The patient's genotypes for F5 c.1601G>A variant (also known as Factor V Leiden) and F2 c.*97G>A variant (also known as Factor II 20210G>A) predict an increased risk for thrombosis. Consider avoiding estrogen-containing preparations. A short course of prophylactic anticoagulation may be considered in high-risk settings such as surgery.
MTHFR	c.665C>T GG	Normal MTHFR Activity	The patient does not carry the MTHFR c.665C>T variant, and the patient's MTHFR activity is normal. This is not associated with an increased risk of hyperhomocysteinemia.
MTHFR	c.1286A>C TT c.665C>T GG	No Increased Risk of Hyperhomocysteinemia	The patient does not carry the MTHFR c.665C>T or c.1286A>C variant. Therefore, the patient has normal MTHFR function, and no elevation of plasma homocysteine levels is expected.
OPRM1	A118G A/A	Normal OPRM1 Function	Consistent with a normal OPRM1 receptor signaling efficiency induced by exogenous opioids. This is associated with a good analgesia following standard opioid doses and a poor response to naltrexone.
SLCO1B1	521T>C C/C	Poor Function	Consistent with a severely decreased SLCO1B1 transporter function. Exercise caution when certain SLCO1B1 drug substrates are prescribed.
VKORC1	-1639G>A G/A	Intermediate Warfarin Sensitivity	Consistent with a moderately decreased VKORC1 expression. Exercise caution with coumarin anticoagulants.

Alleles Tested: Apolipoprotein E ε2, ε4, (ε3 is reference); **COMT** Val158Met; **CYP1A2** *1C, *1D, *1F, *1K, *1L, *1V, *1W; **CYP2B6** *6, *9; **CYP2C19** *2, *3, *4A, *4B, *6, *7, *8, *9, *10, *17; **CYP2C9** *2, *3, *4, *5, *6, *8, *11, *27; **CYP2D6** *2, *3, *4, *4M, *6, *7, *9, *10, *12, *14, *17, *29, *41, *114, *5 (gene deletion), XN (gene duplication); **CYP3A4** *2, *3, *12, *17, *22; **CYP3A5** *2, *3, *6, *7, *8, *9; **Factor II** rs1799963; **Factor V Leiden** rs6025; **MTHFR** c.1286A>C, c.665C>T; **OPRM1** A118G; **SLCO1B1** 521T>C; **VKORC1** -1639G>A

PATIENT INFORMATION		SPECIMEN DETAILS		ORDERED BY
NAME:	Carl Cardio	**SPECIMEN TYPE:**	Buccal Swab	
ACC #:	1039	**COLLECTION DATE:**		
DOB:	1/1/1900	**RECEIVED DATE:**		
SEX:	Male	**REPORT DATE:**	10/16/2021	

Limitation: This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Absence of a detectable gene mutation does not rule out the possibility that a patient has different phenotypes due to the presence of an undetected polymorphism or due to other factors such as drug-drug interactions, comorbidities and lifestyle habits. Technical limitations include the possibility of laboratory error and inaccuracy of the test due to unknown rare variants.

Methodology: Bead array and e-sensor based assays detect listed alleles and most rare variants with known clinical significance and analytical sensitivity and specificity >99%.

Lab Disclaimer: Genesys Diagnostics Inc. has validated the Genotype Test. The performance characteristics of this test were determined by Genesys Diagnostics Inc. This test is an FDA modified and Lab Developed Test.

Translational Software Disclaimer: The information presented on this report is provided as general educational health information. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of the medications prescribed.

The pharmacogenetic assay involves use of reporting software and genotype-phenotype associations performed by Translational Software (www.translationalsoftware.com). The software has not been evaluated by the Food and Drug Administration. The software, and the report generated by the software, is not intended to diagnose, treat, cure, or prevent any disease. A qualified designee within the lab uses Translational Software to generate and subsequently review the report. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

Drug interaction data is provided by First Databank (FDB) and FDB is entirely responsible for its accuracy. The drug interaction report is solely intended to be used by a medical professional. The drug interaction report is based on patient-reported medications and does not account for other factors, such as smoking history, tobacco use, diet and other underlying chronic conditions such as diabetes or heart disease. Unreported medications, herbal medications, over-the-counter supplements and other non-FDA-approved medications are not considered in the drug interaction report, but may cause drug interactions. The treating medical professional bears the ultimate responsibility for all treatment decisions made in regards to the patient, including any decisions based on the drug interaction report.

Report was signed out electronically by Life Technologies Demo on 7/29/2014.

PATIENT INFORMATION	SPECIMEN DETAILS	ORDERED BY
NAME: Carl Cardio	**SPECIMEN TYPE:** Buccal Swab	
ACC #: 1039	**COLLECTION DATE:**	
DOB: 1/1/1900	**RECEIVED DATE:**	
SEX: Male	**REPORT DATE:** 10/16/2021	

Patient Information Card

This is a summary genetic report for your patient to share with other healthcare providers. The card can be cut out along the dashed line and carried with the patient.

REPORT DETAILS

Name: Carl Cardio
DOB: 1/1/1900
ACC #: 1039

Pharmacogenetic Test Summary

Apolipoprotein E	ε2/ε2	Altered APOE function
COMT	Val158Met G/G	High/Normal COMT Activity
CYP1A2	*1A/*1A	Normal Metabolizer- Possible Inducibility
CYP2B6	*1/*1	Normal Metabolizer
CYP2C19	*2/*2	Poor Metabolizer
CYP2C9	*1/*5	Intermediate Metabolizer
CYP2D6	*4M/*4M XN	Poor Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*3/*3	Poor Metabolizer
Factor II	rs1799963 GG	Normal Thrombosis Risk
Factor V Leiden	rs6025 TT	High Thrombosis Risk
MTHFR	c.665C>T GG	Normal MTHFR Activity
MTHFR	c.1286A>C TT	Normal MTHFR Activity
OPRM1	A118G A/A	Normal OPRM1 Function
SLCO1B1	521T>C C/C	Poor Function
VKORC1	-1639G>A G/G	Low Warfarin Sensitivity

For a complete report contact Genesys Diagnostics
www.gdilabs.com