

PATIENT INFORMATION	SPECIMEN INFORMATION	LAB INFORMATION
Name: CARDIO DEMO1 DOB: 07/01/1966 Sex: Male Patient Id: 12341	Provider: Sam Smith, MD Specimen Id: CARDIO12341 Resulted Date: 06/02/2026 Test Type: Pharmacogenomics Specimen Type: Buccal	Name: Compass Laboratory Services Address: 1910 Nonconnah Blvd. Address 2: Suite 108 City,State,Zip: Memphis, TN 38132 Phone: 901-348-5774 Med Dir: Charles R. Handorf, MD, PhD CLIA#: 44D2026010

BLUPRINTTM Summary

There are one or more identified possible drug-drug, drug-gene or disease-drug interactions that may increase the risk of adverse effects or decreased response.

TRURISKTM Reference Key

	There are no identified major or severe drug-drug and/or drug-gene interactions.
	There are one or more identified drug-drug and/or drug-gene interactions that may require closer monitoring. See alerts section in medication profile for more information.
	There are one or more identified drug-drug and/or drug-gene interactions that may have an elevated risk of adverse drug events. See alerts section in medication profile for more information.
	There are one or more identified drug-drug and/or drug-gene interactions that may have a highly elevated risk of adverse drug events. See alerts section in medication profile for more information.

TRUTypeTM Reference Key

	Enzyme activity may be decreased
	Enzyme activity may be increased

Active Diagnoses

I50.9

PharmD Medication Action Plan/Guidance

This Medication Action Plan provides high-level clinical considerations based on potential compounded risks related to drug-drug interactions, drug-gene interactions, and phenotypic conversions that may affect medication response. It is informed in part by the BluePrintRx Pharmacy Risk Analysis and is not intended to be comprehensive. The information does not include all relevant clinical data (e.g., complete diagnoses, current labs, unreported genetic results) and has not been reviewed by the FDA. This tool is informational only and must be interpreted by a licensed healthcare provider as part of a broader clinical assessment and patient-specific decision-making process.

(ST)=Strong, (M)=Moderate, (W)=Weak, (iv)=In Vitro

	Genotype	Phenotype	Substrate	Inhibitor	Inducer	TruType	Activity
ABCB1	*1/*1	Normal	Simvastatin, Apixaban	Simvastatin-(W), Fluoxetine-(W), Amiodarone-(M)(iv)	[]	Slow	
ABCG2	G/G	Normal	Apixaban	[]	[]	Normal	
CYP1A2	*1/*1	Normal	[]	[]	[]	Normal	
CYP2B6	*1/*1	Normal	[]	Amiodarone-(W)(iv)	[]	Normal	
CYP2C19	*1/*1	Normal	[]	Fluoxetine-(ST), Amiodarone-(M)(iv)	[]	Slow	
CYP2C8	*1/*1	Normal	Amiodarone	Amiodarone-(W)	[]	Normal	
CYP2C9	*1/*2	Intermediate	Irbesartan, Meloxicam	Fluoxetine-(W), Amiodarone-(M)(iv)	[]	Slow	
CYP2D6	*1/*1	Normal	Fluoxetine, Metoprolol	Fluoxetine-(ST), Amiodarone-(M)(iv)	[]	Slow	
CYP3A4	*1/*1	Normal	Simvastatin, Amiodarone, Eplerenone, Apixaban	Fluoxetine-(W), Amiodarone-(W)	[]	Normal- slow	
CYP3A5	*1/*1	Normal	[]	[]	[]	Normal	
CYP4F2	*1/*1	Normal	[]	[]	[]	Normal	
SLC01B1	*1/*5	Intermediate	Simvastatin	Irbesartan-(W)	[]	Slower than normal	

TRURISKTM

Current Medications

HIGH RISK	HIGH-MODERATE RISK	MODERATE RISK	STANDARD RISK
Fluoxetine 100mg Irbesartan 300mg Meloxicam 5mg Metoprolol 100mg		Amiodarone 150mg Eliquis Eplerenone 25mg	Simvastatin 40mg

Fluoxetine

Fluoxetine 100mg

Renal Dosing: No Hepatic Dosing: Yes

CYP450 Substrates

Gene	Pathway	Phenotype	TruTYPE
CYP2D6	Primary	Normal	Slow
CYP2C19	Secondary	Normal	Slow
CYP2C9	Secondary	Intermediate	Slow
CYP3A4	Secondary	Normal	Normal-Slow



CYP2D6 - Pharmacokinetic Statement

Fluoxetine is a primary CYP2D6 substrate in the formation of S-norfluoxetine, an active metabolite that is equipotent as fluoxetine. Estimated CYP2D6 activity may be decreased which may increase fluoxetine exposure and decrease formation of S-norfluoxetine. Per FDA, In a study involving labeled and unlabeled enantiomers administered as a racemate, these individuals with decreased CYP2D6 (poor) metabolized S-fluoxetine at a slower rate and thus achieved higher concentrations of S-fluoxetine. Consequently, concentrations of S-norfluoxetine at steady state were lower. The metabolism of R-fluoxetine in these poor metabolizers appears normal. When compared with normal metabolizers, the total sum at steady state of the plasma concentrations of the 4 active enantiomers was not significantly greater among poor metabolizers. Thus, the net pharmacodynamic activities were essentially the same. (3) Fluoxetine is a strong CYP2D6 and CYP2C19 inhibitor and weak CYP2C9 inhibitor. Exercise caution when co-administering with medications that are CYP2D6 and/or CYP2C19 substrates due to possible reduced metabolism. Fluoxetine inhibition of CYP450 pathways may extend multiple days and even weeks after withdrawal.

SLC Influx Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None

ABC Efflux Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None



CONSIDERATION FACTORS:

1 Reduced CYP450 Primary pathway(s)
5 major DDIs

CYP2D6 - Published Guidance*

CPIC:C PharmGKB:3

FDA Product Label:

Drugs Metabolized by CYP2D6: Fluoxetine is a potent inhibitor of CYP2D6 enzyme pathway.(3)
No dosing recommendations available. Monitor closely for increased response or adverse events. Monitor for prolongation of QTc interval.(8)(1)

Variability in Metabolism — A subset (about 7%) of the population has reduced activity of the drug metabolizing enzyme cytochrome P450 2D6 (CYP2D6). Such individuals are referred to as "poor metabolizers" of drugs such as debrisoquin, dextromethorphan, and the TCAs. In a study involving labeled and unlabeled enantiomers administered as a racemate, these individuals metabolized S-fluoxetine at a slower rate and thus achieved higher concentrations of S-fluoxetine.

Consequently, concentrations of S-norfluoxetine at steady state were lower. The metabolism of R-fluoxetine in these poor metabolizers appears normal. When compared with normal metabolizers, the total sum at steady state of the plasma concentrations of the 4 active enantiomers was not significantly greater among poor metabolizers. Thus, the net pharmacodynamic activities were essentially the same. Alternative, nonsaturable pathways (non-2D6) also contribute to the metabolism of fluoxetine. This explains how fluoxetine achieves a steady-state concentration rather than increasing without limit.

The FDA-approved drug label for fluoxetine and olanzapine (SYMBYAX) states that individuals who are CYP2D6 poor metabolizers metabolized S-fluoxetine at a slower rate and achieved higher concentrations.(3) Fluoxetine inhibits the activity of CYP2D6 and may make individuals with normal CYP2D6 metabolic activity resemble a poor metabolizer. Coadministration of fluoxetine with other drugs that are metabolized by CYP2D6... should be approached with caution.(3)

**Given the medications being taken by this patient, the current estimated enzyme activity (TruType) may behave more like a different phenotype than the genetic phenotype for this patient. This is the relevant CPIC guidance that is closest to the estimated phenotype/activity. Visit CPIC.org to reference CPIC guidelines for other phenotype recommendations.*

DRUG TO DRUG INTERACTIONS

Severe: 0 Major: 5 Moderate: 0 Minor: 0

Simvastatin - Major DDI

The serum concentration of Simvastatin can be increased when it is combined with Fluoxetine.

Irbesartan - Major DDI

The metabolism of Irbesartan can be decreased when combined with Fluoxetine.

Amiodarone - Major DDI

The risk or severity of QTc prolongation can be increased when Fluoxetine is combined with Amiodarone.

Metoprolol - Major DDI

The serum concentration of Metoprolol can be increased when it is combined with Fluoxetine.

Apixaban - Major DDI

The risk or severity of hemorrhage can be increased when Fluoxetine is combined with Apixaban.

TruSELECT

Alternative Medications Information for Fluoxetine

Drug Name	Pathway	TruTYPE	Inhibitor	Inducer	Hepatic or Renal Dose	DDIs	TruRISK
Bupropion	CYP2B6	Normal	CYP2D6	---	Hepatic & Renal	Severe: Metoprolol Major: 1	
Desvenlafaxine	CYP3A4	Normal	---	---	Hepatic & Renal	Severe: Amiodarone Major: 2	
Escitalopram	ABCB1 CYP2C19 CYP3A4	Slower than normal Normal Normal	CYP2D6	---	Hepatic & Renal	Severe: Amiodarone Major: 3	
Citalopram	CYP2C19 ABCB1 CYP3A4	Slower than normal Slow Normal	CYP2C19 CYP2D6 CYP1A2 ABCB1	---	Hepatic & Renal	Major: Simvastatin, Amiodarone, Metoprolol, Apixaban	
Venlafaxine	CYP2D6 ABCB1	Slower than normal Slower than normal	CYP2D6	ABCB1 ABCG2	Hepatic & Renal	Major: Amiodarone, Meloxicam	

Irbesartan

Renal Dosing: No

Hepatic Dosing: Yes

CYP450 Substrates

Gene	Pathway	Phenotype	TruTYPE
CYP2C9	Primary	Intermediate	Slow
CYP3A4	Secondary	Normal	Normal-Slow

CYP2C9 - Pharmacokinetic Statement
Use caution when administering to persons with decreased metabolism of CYP2C9 as there is an increased likelihood of increased systemic exposure. Monitor for side effects such as hypotension, fast heart rate, feeling faint and muscle cramps. Consider alternative Angiotensin II antagonist such as olmesartan or telmisartan. Caution advised when co-administering strong CYP2C9 inhibitors.

SLC Influx Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None

ABC Efflux Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None

Irbesartan 300mg

HIGH

TruRISK

CONSIDERATION FACTORS:

1 Reduced CYP450 Primary pathway(s)

1 severe DDIs

5 major DDIs

DRUG TO DRUG INTERACTIONS

Severe: 1

Major: 5

Moderate: 0

Minor: 0

Amiodarone - Severe DDI

The serum concentration of Amiodarone can be increased when it is combined with Irbesartan.

Simvastatin - Major DDI

The metabolism of Simvastatin can be decreased when combined with Irbesartan.

Fluoxetine - Major DDI

The metabolism of Irbesartan can be decreased when combined with Fluoxetine.

Eplerenone - Major DDI

The risk or severity of hyperkalemia can be increased when Eplerenone is combined with Irbesartan.

Meloxicam - Major DDI

The risk or severity of renal failure, hyperkalemia, and hypertension can be increased when Irbesartan is combined with Meloxicam.

Apixaban - Major DDI

The metabolism of Apixaban can be decreased when combined with Irbesartan.

TruSELECT

Alternative Medications Information for Irbesartan

Drug Name	Pathway	TruTYPE	Inhibitor	Inducer	Hepatic or Renal Dose	DDIs	TruRISK
Olmesartan	SLCO1B1	Slower than normal	---	---	Hepatic	Major: Simvastatin, Eplerenone, Meloxicam	
Telmisartan	---	---	ABCB1 CYP2C19	---	Hepatic	Major: Simvastatin, Fluoxetine, Eplerenone, Meloxicam, Apixaban	
Candesartan	ABCB1	Slow	---	---	Hepatic & Renal	Severe: Simvastatin, Amiodarone, Apixaban Major: 3	

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Meloxicam

Meloxicam 5mg

Renal Dosing: Yes

Hepatic Dosing: Yes

CYP450 Substrates

Gene	Pathway	Phenotype	TruTYPE
CYP2C9	Primary	Intermediate	Slow
CYP3A4	Secondary	Normal	Normal-Slow



CYP2C9 - Pharmacokinetic Statement

Use discretion when prescribing NSAIDs in persons with possible reduced CYP2C9 activity. Consider initiating therapy at reduced dosages due to decreased metabolism and clearance of meloxicam or consider alternative therapy, such as, ketorolac or oxaprozin which are not metabolized by CYP2C9. Avoid the use of CYP2C9 inhibitors, such as fluoxetine, as it is likely to exacerbate the effect and increase likelihood of adverse drug events such as gastrointestinal bleeding. Monitor blood pressure and kidney function. Note: Per CPIC guidelines, meloxicam dosing guidelines are based on CYP2C9 genotype/phenotype. No dosing guidelines are provided for an adjusted phenotype or TruTYPE.

SLC Influx Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None

ABC Efflux Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None



CONSIDERATION FACTORS:

- 1 Reduced CYP450 Primary pathway(s)
- 1 severe DDIs
- 5 major DDIs

CYP2C9 - Published Guidance*

CPIC:A PharmGKB:1A

CPIC:

Meloxicam should not be used in patients that have slow or poor CYP2C9 activity. Select alternative therapy, such as, ketorolac which is not metabolized by CYP2C9.(1)

Per FDA drug label,

In patients who are known or suspected to be poor CYP2C9 metabolizers based on genotype or previous history/experience with other CYP2C9 substrates (such as warfarin or phenytoin), consider dose reduction, as these patients may have abnormally high plasma levels of meloxicam due to reduced metabolic clearance. Monitor these patients for adverse effects.(3)

TruTYPE is the estimation of CYP2C9 activity and not the innate phenotype, on which CPIC and FDA guidelines are based. TruTYPE identifies changes in enzyme activity due to concomitant medications that are inhibitors or inducers of primary metabolizing enzyme, age, disease-states, and other food/herbal products. TruTYPE has not been evaluated by the FDA and is only used as an informational resource.

**Given the medications being taken by this patient, the current estimated enzyme activity (TruType) may behave more like a different phenotype than the genetic phenotype for this patient. This is the relevant CPIC guidance that is closest to the estimated phenotype/activity. Visit CPIC.org to reference CPIC guidelines for other phenotype recommendations.*

DRUG TO DRUG INTERACTIONS

Severe: 1 Major: 5 Moderate: 0 Minor: 0

Amiodarone - Severe DDI

The metabolism of Meloxicam can be decreased when combined with Amiodarone.

Simvastatin - Major DDI

The metabolism of Meloxicam can be decreased when combined with Simvastatin.

Irbesartan - Major DDI

The risk or severity of renal failure, hyperkalemia, and hypertension can be increased when Irbesartan is combined with Meloxicam.

Eplerenone - Major DDI

The therapeutic efficacy of Eplerenone can be decreased when used in combination with Meloxicam.

Metoprolol - Major DDI

Meloxicam may decrease the antihypertensive activities of Metoprolol.

Apixaban - Major DDI

The risk or severity of bleeding and hemorrhage can be increased when Meloxicam is combined with Apixaban.

TruSELECT

Alternative Medications Information for Meloxicam

Drug Name	Pathway	TruTYPE	Inhibitor	Inducer	Hepatic or Renal Dose	DDIs	TruRISK
Oxaprozin	---	---	---	---	Hepatic & Renal	Major: Irbesartan, Eplerenone, Metoprolol, Apixaban	
Acetaminophen	ABCG2	Normal	---	---	Hepatic & Renal	Severe: Amiodarone Major: 2	
Ketorolac	---	---	---	---	Renal	Severe: Amiodarone Major: 5	
Naproxen	---	---	ABCB1	---	Renal	Severe: Amiodarone Major: 5	

Metoprolol

Metoprolol 100mg

Renal Dosing: No

Hepatic Dosing: Yes

CYP450 Substrates

Gene	Pathway	Phenotype	TruTYPE
CYP2D6	Primary	Normal	Slow



CYP2D6 - Pharmacokinetic Statement

Increased response is more likely due to increased plasma levels of metoprolol from reduced CYP2D6 activity. Side effects of beta blockers include bradycardia, syncope, cold extremities, reduced exercise tolerance, and hypotension. Consider using alternative therapy not metabolized by CYP2D6 such as atenolol or bisoprolol. If metoprolol use warranted, consider reducing starting dose to 50-75% of standard dosing.

SLC Influx Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None

ABC Efflux Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None



CONSIDERATION FACTORS:

1 Reduced CYP450 Primary pathway(s)
4 major DDIs

CYP2D6 - Published Guidance*

CPIC:BC

Per FDA Product Label, decreased CYP2D6 activity due to CYP2D6 inhibition or poor CYP2D6 phenotype may increase metoprolol systemic exposure and decrease cardioselectivity.(3)
Drugs that are strong inhibitors of CYP2D6 such as quinidine, fluoxetine, paroxetine, and propafenone were shown to double metoprolol concentrations.(3)
CYP2D6 is absent in about 8% of Caucasians (poor metabolizers) and about 2% of most other populations. CYP2D6 can be inhibited by several drugs. Poor metabolizers of CYP2D6 will have increased (several-fold) metoprolol blood levels, decreasing metoprolol's cardioselectivity.(3)

Per DPWG, For CYP2D6 poor and intermediate metabolizer patients, if a GRADUAL REDUCTION in HEART RATE is desired, or in the event of SYMPTOMATIC BRADYCARDIA, increase the dose in smaller steps and/or prescribe no more than 25% or 50% of the standard dose, respectively. For CYP2D6 ultra metabolizers, use the maximum dose for the relevant indication as a target dose, and if the effectiveness is still insufficient: increase the dose based on effectiveness and side effects to 2.5 times the standard dose or select an alternative drug. (6)

**Given the medications being taken by this patient, the current estimated enzyme activity (TruType) may behave more like a different phenotype than the genetic phenotype for this patient. This is the relevant CPIC guidance that is closest to the estimated phenotype/activity. Visit CPIC.org to reference CPIC guidelines for other phenotype recommendations.*

DRUG TO DRUG INTERACTIONS

Severe: 0 Major: 4 Moderate: 0 Minor: 0

Simvastatin - Major DDI

The metabolism of Simvastatin can be decreased when combined with Metoprolol.

Fluoxetine - Major DDI

The serum concentration of Metoprolol can be increased when it is combined with Fluoxetine.

Amiodarone - Major DDI

The therapeutic efficacy of Metoprolol can be increased when used in combination with Amiodarone.

Meloxicam - Major DDI

Meloxicam may decrease the antihypertensive activities of Metoprolol.

TruSELECT

Alternative Medications Information for Metoprolol

Drug Name	Pathway	TruTYPE	Inhibitor	Inducer	Hepatic or Renal Dose	DDIs	TruRISK
Acebutolol	---	---	---	---	Hepatic & Renal	Major: Simvastatin, Fluoxetine, Amiodarone, Meloxicam	

Drug Name	Pathway	TruTYPE	Inhibitor	Inducer	Hepatic or Renal Dose	DDIs	TruRISK
Atenolol	ABCB1	Slow	---	---	Renal	Major: Simvastatin, Fluoxetine, Amiodarone, Meloxicam	
Bisoprolol	ABCB1	Slow	ABCB1	---	Hepatic & Renal	Major: Simvastatin, Fluoxetine, Amiodarone, Meloxicam, Apixaban	
Labetalol	---	---	---	---	Hepatic	Major: Simvastatin, Fluoxetine, Amiodarone, Meloxicam, Apixaban	
Nadolol	---	---	---	---	Renal	Major: Fluoxetine, Amiodarone, Meloxicam	

Amiodarone

Amiodarone 150mg

Renal Dosing: No

Hepatic Dosing: Yes

CYP450 Substrates

Gene	Pathway	Phenotype	TruTYPE
CYP3A4	Primary	Normal	Normal-Slow
CYP2C8	Primary	Normal	Normal

CYP3A4 - Pharmacokinetic Statement

Amiodarone is a CYP3A4 and CYP2C8 substrate. CYP3A4 and CYP2C8 are involved in forming active metabolite, DEA which will reach similar concentrations as parent drug after several days of therapy. Estimated CYP3A4 activity may be decreased which may increase amiodarone exposure and decrease formation of DEA. In vitro, amiodarone is a weak to moderate inhibitor of most CYP450 enzymes. Extra caution advised when CYP2C8 activity is decreased. Monitor for prolongation of QTc interval.(8)

CYP2C8 - Pharmacokinetic Statement

Ingredient is a substrate and inhibitor of an identified primary CYP450 pathway. The ingredient's risk profile will not be affected however, once two or more ingredients share the same primary pathway, all ingredients will alert for estimated slower than normal activity and associated risks.

Amiodarone is a CYP3A4 and CYP2C8 substrate. Estimated CYP2C8 activity is normal. Use caution when co-administering CYP3A4 and/or CYP2C8 inhibitors or inducers. Amiodarone may inhibit multiple CYP450 enzymes (CYP2B6, 2C8, 2C9, 2D6, 3A4 and 2C19). Exercise caution when co-administering medications that are CYP450 substrates due to possible reduced activity.

SLC Influx Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None

ABC Efflux Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None

MODERATE
TruRISK



CONSIDERATION FACTORS:

4 severe DDIs
3 major DDIs

CYP3A4 - Published Guidance*

FDA Product Label: Warnings
Hypotension: Slow the infusion; as needed, add vasopressor drugs, positive inotropic agents, and volume expansion.
Bradycardia and AV block: Slow the infusion or discontinue.(3)

Like all antiarrhythmic agents, amiodarone may cause a worsening of existing arrhythmias or precipitate a new arrhythmia sometimes leading to fatal outcomes. Proarrhythmia, primarily torsade de pointes (TdP), has been associated with prolongation, by intravenous amiodarone, of the QTc interval to 500 ms or greater. (3)

FDA Product Label: Pharmacokinetics-PGx
Amiodarone is a substrate for CYP3A and CYP2C8, so inhibitors and inducers affect amiodarone exposure. Amiodarone inhibits p-glycoprotein and CYP1A2, CYP2C9, CYP2D6, and CYP3A, increasing exposure to other drugs.(3)

CYP2C8 - Published Guidance*

Ingredient is a substrate and inhibitor of an identified primary CYP450 pathway.

**Given the medications being taken by this patient, the current estimated enzyme activity (TruType) may behave more like a different phenotype than the genetic phenotype for this patient. This is the relevant CPIC guidance that is closest to the estimated phenotype/activity. Visit CPIC.org to reference CPIC guidelines for other phenotype recommendations.*

DRUG TO DRUG INTERACTIONS

Severe: 4 Major: 3 Moderate: 0 Minor: 0

Irbesartan - Severe DDI

The serum concentration of Amiodarone can be increased when it is combined with Irbesartan.

Eplerenone - Severe DDI

The metabolism of Eplerenone can be decreased when combined with Amiodarone.

Meloxicam - Severe DDI

The metabolism of Meloxicam can be decreased when combined with Amiodarone.

Apixaban - Severe DDI

The metabolism of Apixaban can be decreased when combined with Amiodarone.

Simvastatin - Major DDI

The serum concentration of Simvastatin can be increased when it is combined with Amiodarone.

Fluoxetine - Major DDI

The risk or severity of QTc prolongation can be increased when Fluoxetine is combined with Amiodarone.

Metoprolol - Major DDI

The therapeutic efficacy of Metoprolol can be increased when used in combination with Amiodarone.

TruSELECT

Alternative Medications Information for Amiodarone

Drug Name	Pathway	TruTYPE	Inhibitor	Inducer	Hepatic or Renal Dose	DDIs	TruRISK
Disopyramide	CYP3A4	Normal	---	---	Hepatic & Renal	Severe: Metoprolol Major: 1	
Dofetilide	CYP3A4	Normal	---	---	Hepatic & Renal	Severe: Irbesartan Major: 2	
Quinidine	ABCB1 CYP3A4	Slow Normal	CYP2D6 ABCB1	---	Renal	Severe: Simvastatin, Irbesartan, Eplerenone Major: 4	
Sotalol	---	---	---	---	Renal	Severe: Simvastatin Major: 3	
Mexiletine	CYP2D6	Slower than normal	CYP1A2	---	Hepatic & Renal	Major: Simvastatin, Fluoxetine, Metoprolol	

Renal Dosing: Yes

Hepatic Dosing: Yes

CYP450 Substrates

Gene	Pathway	Phenotype	TruTYPE
CYP3A4	Primary	Normal	Normal-Slow
CYP2C8	Secondary	Normal	Normal
CYP1A2	Secondary	Normal	Normal
CYP2C9	Secondary	Intermediate	Slow
CYP2C19	Secondary	Normal	Slow

CYP3A4 - Pharmacokinetic Statement

Apixaban is a primary CYP3A4 substrate and minor, secondary substrate for multiple CYP450 enzymes. Estimated CYP3A4 activity may be decreased which may increase systemic concentrations of apixaban. Caution advised when co-administering a strong CYP3A4 inhibitor.

SLC Influx Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None

ABC Efflux Transport

Gene	Pathway	Phenotype	TruTYPE
ABCG2	Primary	Normal	Normal
ABCB1	Primary	Normal	Slow

ABCG2 - Pharmacokinetic Statement

Patients with atrial fibrillation and the TT genotype (rs2231142) may have decreased clearance and increased concentrations of apixaban as compared to patients with the GG and GT genotypes. Other clinical and genetic factors may also influence clearance and concentrations of apixaban in patients with atrial fibrillation.(1)

**ABCB1 - Pharmacokinetic Statement**

Apixaban is an ABCB1 and ABCG2 substrate. Caution advised if ABC transport activity decreased or increased due to possible variability in apixaban exposure.

MODERATE
TruRISK**CONSIDERATION FACTORS:**

1 severe DDIs
4 major DDIs

CYP3A4 - Published Guidance*

FDA Product Label: Pharmacokinetics-PGx
Strong dual inhibitors of CYP3A4 and P-gp increase blood levels of apixaban: Reduce ELIQUIS dose to 2.5 mg or avoid concomitant use.(3)

ABCG2 - Published Guidance**PharmGKB:3**

Patients with atrial fibrillation and the TT genotype (rs2231142) may have decreased clearance and increased concentrations of apixaban as compared to patients with the GG and GT genotypes. Other clinical and genetic factors may also influence clearance and concentrations of apixaban in patients with atrial fibrillation.(1)

**Given the medications being taken by this patient, the current estimated enzyme activity (TruType) may behave more like a different phenotype than the genetic phenotype for this patient. This is the relevant CPIC guidance that is closest to the estimated phenotype/activity. Visit CPIC.org to reference CPIC guidelines for other phenotype recommendations.*

DRUG TO DRUG INTERACTIONS

Severe: 1 Major: 4 Moderate: 0 Minor: 0

Amiodarone - Severe DDI

The metabolism of Apixaban can be decreased when combined with Amiodarone.

Simvastatin - Major DDI

The serum concentration of Apixaban can be increased when it is combined with Simvastatin.

Irbesartan - Major DDI

The metabolism of Apixaban can be decreased when combined with Irbesartan.

Fluoxetine - Major DDI

The risk or severity of hemorrhage can be increased when Fluoxetine is combined with Apixaban.

Meloxicam - Major DDI

The risk or severity of bleeding and hemorrhage can be increased when Meloxicam is combined with Apixaban.

TruSELECT**Alternative Medications Information for Apixaban**

Drug Name	Pathway	TruTYPE	Inhibitor	Inducer	Hepatic or Renal Dose	DDIs	TruRISK
Betrixaban	ABCB1	Slow	---	---	Hepatic & Renal	Major: Simvastatin, Fluoxetine, Amiodarone, Meloxicam	⬆
Dabigatran	ABCB1	Slow	---	---	Renal	Major: Simvastatin, Fluoxetine, Amiodarone, Meloxicam	⬆
Edoxaban	ABCB1	Slow	---	---	---	Major: Simvastatin, Fluoxetine, Amiodarone, Meloxicam	⬆

Drug Name	Pathway	TruTYPE	Inhibitor	Inducer	Hepatic or Renal Dose	DDIs	TruRISK
Rivaroxaban	ABCB1 ABCG2 CYP3A4	Slow Normal Normal-Slow	---	---	Hepatic & Renal	Severe: Amiodarone Major: 3	

Eplerenone

Eplerenone 25mg

Renal Dosing: Yes

Hepatic Dosing: No

CYP450 Substrates

Gene	Pathway	Phenotype	TruTYPE
CYP3A4	Primary	Normal	Normal-Slow

CYP3A4 - Pharmacokinetic Statement

Closely monitor for adverse effects due to possible increased exposure to eplerenone from estimated reduced CYP3A4 activity. Consider using alternative therapy not metabolized by CYP3A4 or adjusting the dose if side effects suspected. Common side effects may include hypertriglyceridemia, cough, dizziness, hyponatremia and fatigue. Strong CYP3A4 inhibitors are not recommended when using eplerenone.

SLC Influx Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None

ABC Efflux Transport

Gene	Pathway	Phenotype	TruTYPE
None	None	None	None

MODERATE
TruRISK



CONSIDERATION FACTORS:

1 severe DDIs
2 major DDIs

CYP3A4 - Published Guidance*

FDA:
Concomitant use with strong CYP3A inhibitors contraindicated.(3)

FDA Product Label: Pharmacokinetics-PGx
CYP3A Inhibitors: In post-MI HFREF patients do not exceed 25 mg once daily when used with moderate CYP3A inhibitors (e.g., verapamil, erythromycin, saquinavir, fluconazole). In patients with hypertension initiate at 25 mg once daily. For inadequate blood pressure response, dosing may be increased to a maximum of 25 mg twice daily.(3)

Per FDA Label
Eplerenone is metabolized primarily by CYP3A4. A potent inhibitor of CYP3A4 (ketoconazole) caused increased exposure of about 5-fold while less potent CYP3A4 inhibitors (erythromycin, saquinavir, verapamil, and fluconazole) gave approximately 2-fold increases. Grapefruit juice caused only a small increase (about 25%) in exposure. (See PRECAUTIONS and DOSAGE AND ADMINISTRATION.)(3)

**Given the medications being taken by this patient, the current estimated enzyme activity (TruType) may behave more like a different phenotype than the genetic phenotype for this patient. This is the relevant CPIC guidance that is closest to the estimated phenotype/activity. Visit CPIC.org to reference CPIC guidelines for other phenotype recommendations.*

DRUG TO DRUG INTERACTIONS

Severe: 1 Major: 2 Moderate: 0 Minor: 0

Amiodarone - Severe DDI

The metabolism of Eplerenone can be decreased when combined with Amiodarone.

Irbesartan - Major DDI

The risk or severity of hyperkalemia can be increased when Eplerenone is combined with Irbesartan.

Meloxicam - Major DDI

The therapeutic efficacy of Eplerenone can be decreased when used in combination with Meloxicam.

TruSELECT

Alternative Medications Information for Eplerenone

Drug Name	Pathway	TruTYPE	Inhibitor	Inducer	Hepatic or Renal Dose	DDIs	TruRISK
Amiloride	---	---	---	---	Hepatic & Renal	Major: Irbesartan, Meloxicam	⬆
Triamterene	CYP1A2	Normal	---	---	Hepatic & Renal	Severe: Amiodarone Major: 3	⬆

Renal Dosing: Yes

Hepatic Dosing: Yes

CYP450 Substrates

Gene	Pathway	Phenotype	TruTYPE
CYP3A4	Primary	Normal	Normal-Slow
CYP2D6	Secondary	Normal	Slow

CYP3A4 - Pharmacokinetic Statement

Simvastatin is a CYP3A4 substrate. Estimated CYP3A4 activity may be decreased which may increase simvastatin exposure. Serious side effects may include rhabdomyolysis and myopathy. Alternative therapies should be considered such as pitavastatin, pravastatin or rosuvastatin. Reduced SLC01B1 activity may increase the risk of myopathy when prescribing statin based therapies. Current guidelines recommend if the use of Simvastatin is warranted, reduce dosages to 20 mg/day and monitor serum Creatine Kinase levels.(3)

SLC Influx Transport

Gene	Pathway	Phenotype	TruTYPE
SLCO1B1	Primary	Intermediate	Slower than normal

**SLCO1B1 - Pharmacokinetic Statement**

Estimated SLCO1B1 activity may be decreased which may increase simvastatin systemic exposure. If side effects suspected, consider alternative therapy such as pitavastatin or pravastatin.

ABC Efflux Transport

Gene	Pathway	Phenotype	TruTYPE
ABCB1	Primary	Normal	Slow

**ABCB1 - Pharmacokinetic Statement**

Simvastatin is an ABCB1 efflux transport substrate. Increased or decreased ABCB1 activity may alter simvastatin exposures. Extra caution is advised when both SLCO1B1 and ABCB1 enzyme activity is reduced due to increased risk of myopathy.

**CONSIDERATION FACTORS:**

6 major DDIs

CYP3A4 - Published Guidance*

FDA Product Label: Contraindications
Concomitant administration of strong CYP3A4 inhibitors.
Concomitant administration of gemfibrozil, cyclosporine, or danazol.(3)

FDA Product Label: Pharmacokinetics-PGx
The risk of myopathy is increased by high levels of HMG-CoA reductase inhibitory activity in plasma. Inhibitors of CYP3A4 can raise the plasma levels of HMG-CoA reductase inhibitory activity and increase the risk of myopathy.(3)

SLCO1B1 - Published Guidance**CPIC:A PharmGKB:1A**

FDA Product Label: Pharmacokinetics-PGx
Simvastatin acid is a substrate of the transport protein OATP1B1. Concomitant administration of medicinal products that are inhibitors of the transport protein OATP1B1 may lead to increased plasma concentrations of simvastatin acid and an increased risk of myopathy. For example, cyclosporine has been shown to increase the AUC of statins; although the mechanism is not fully understood, the increase in AUC for simvastatin acid is presumably due, in part, to inhibition of CYP3A4 and/or OATP1B1.(3)

CPIC:

Consider alternative therapy.(1)

**Given the medications being taken by this patient, the current estimated enzyme activity (TruType) may behave more like a different phenotype than the genetic phenotype for this patient. This is the relevant CPIC guidance that is closest to the estimated phenotype/activity. Visit CPIC.org to reference CPIC guidelines for other phenotype recommendations.*

DRUG TO DRUG INTERACTIONS

Severe: 0 Major: 6 Moderate: 0 Minor: 0

Irbesartan - Major DDI

The metabolism of Simvastatin can be decreased when combined with Irbesartan.

Fluoxetine - Major DDI

The serum concentration of Simvastatin can be increased when it is combined with Fluoxetine.

Amiodarone - Major DDI

The serum concentration of Simvastatin can be increased when it is combined with Amiodarone.

Metoprolol - Major DDI

The metabolism of Simvastatin can be decreased when combined with Metoprolol.

Meloxicam - Major DDI

The metabolism of Meloxicam can be decreased when combined with Simvastatin.

Apixaban - Major DDI

The serum concentration of Apixaban can be increased when it is combined with Simvastatin.

TruSELECT

Alternative Medications Information for Simvastatin

Drug Name	Pathway	TruTYPE	Inhibitor	Inducer	Hepatic or Renal Dose	DDIs	TruRISK
Atorvastatin	ABCB1 ABCG2 SLCO1B1 CYP3A4	Slow Normal Slower than normal Normal-Slow	ABCB1	---	Hepatic	Major: Irbesartan, Amiodarone, Apixaban	⬆
Lovastatin	SLCO1B1 ABCB1 CYP3A4	Slower than normal Slower than normal Normal-Slow	---	CYP4F2	Hepatic & Renal	Major: Irbesartan, Amiodarone	⬆
Pitavastatin	SLCO1B1	Slower than normal	---	---	Hepatic & Renal	Major: Amiodarone	⬆
Pravastatin	ABCB1 SLCO1B1 ABCG2	Slower than normal Slower than normal Normal	---	---	Hepatic & Renal	Major: Amiodarone, Apixaban	⬆
Rosuvastatin	SLCO1B1 ABCG2	Slower than normal Normal	---	---	Hepatic & Renal	Major: Irbesartan, Fluoxetine, Amiodarone	⬆

Pharmacogenetic Testing Results

Gene	Genotype	Phenotype
ABCB1	*1/*1	Normal
ABCG2	G/G	Normal
APOE	E3/E4	Increased Risk
COMT	A/A	Reduced Activity
CYP1A2	*1/*1	Normal
CYP2B6	*1/*1	Normal
CYP2C19	*1/*1	Normal
CYP2C8	*1/*1	Normal
CYP2C9	*1/*2	Intermediate
CYP2D6	*1/*1	Normal
CYP3A4	*1/*1	Normal
CYP3A5	*1/*1	Normal
CYP4F2	*1/*1	Normal
DPYD	*1/*1	Normal
DRD2;ANKK1	G/G	Decreased Risk
Factor II	G/G	No increased risk
Factor V	C/C	No increased risk
HTR1A	C/G	Increased Response
MTHFR1298	G/T	Increased risk
MTHFR677	G/A	Normal risk
NUDT15	*1/*1	Normal
OPRM1	A/A	Normal response to opioid therapy is expected
SLCO1B1	*1/*5	Increased Risk of Simvastatin-Associated Myopathy
TPMT	*1/*1	Normal
VKORC1	*1/*2	Intermediate Sensitivity

Access QuickSelect Report Common Alternatives for the High Risk Drugs



Scan the QR Code to the left to access the Sozos QuickSelect Report for this patient. The QuickSelect report provides a list of common alternative medications to the High TruRISK drugs actively being taken and what the risk level would be if that single medication were to replace the current medication patient is taking.

QuickPATH Reference

Anti-Platelet (Clopidogrel)

CYP2C19

Avoid- Estimated CYP2C19 activity is slower than normal or Poor. Clinical recommendations are that clopidogrel should be avoided or used with caution in patients that are intermediate or poor CYP2C19 phenotypes due to loss of antiplatelet activity. Please reference product label dosing guidelines for patients with decreased CYP2C19 activity.

Anticoagulant (Warfarin)

Anticoagulant (Warfarin)

CYP2C9

Genotype: *1/*2
Phenotype: Intermediate
TruType: Slow

VKORC1

Genotype: *1/*2
Phenotype: Intermediate Sensitivity

Reference

Three Ranges of Expected Maintenance COUMADIN Daily Doses Based on CYP2C9 and VKORC1 Genotypes*

VKORC1	CYP2C9					
	*1/*1	*1/*2	*1/*3	*2/*2	*2/*3	*3/*3
CC	5-7 mg	5-7 mg	3-4 mg	3-4 mg	3-4 mg	0.5-2 mg
CT	5-7 mg	3-4 mg	3-4 mg	3-4 mg	0.5-2 mg	0.5-2 mg
TT	3-4 mg	3-4 mg	0.5-2 mg	0.5-2 mg	0.5-2 mg	0.5-2 mg

*Ranges are derived from multiple published clinical studies. VKORC1 - 1639G>A (rs9923231) variant is used in this table. Other co-inherited VKORC1 variants may also be important determinants of warfarin dose.

Hypercholesterolemia (Statin)

CYP3A4

Normal- Estimated CYP3A4 metabolism is estimated to be in the normal range.

SLCO1B1

Caution Advised- Estimated SLCO1B1 may be slower than normal which may increase risk of myopathy associated events in certain statins (simvastatin, atorvastatin, fluvastatin, lovastatin)

Heart Failure/Hypertension (Beta Blocker)

CYP2D6

Caution Advised-Estimated CYP2D6 activity may be slower than normal. Beta blockers (metoprolol, carvedilol, nadolol, nebivolol) may have an increased risk of adverse events and may need a lower dosage if side effects suspected. Please reference product label dosing guidelines for patients suspected of reduced CYP2D6 activity.

Atrial Fibrillation/Ventricular Tachycardia (Anti-Arrhythmics)

CYP2D6

Caution Advised- Estimated CYP2D6 activity may be slower than normal. Some anti-arrhythmic medications (dronedaron, propafenone, amiodarone, flecainide, mexiletine, disopyramide) are CYP2D6 primary substrates which may increase risk of adverse events if pathways have reduced activity.

CYP3A4

Normal-Estimated CYP3A4 activity is in the normal range. Some anti-arrhythmic medications (dronedaron, propafenone, amiodarone, flecainide, mexiletine, disopyramide) are CYP3A4 primary substrates which may increase risk of adverse events if pathways have reduced activity.

Hypertension (ARBs)

CYP2C9

Caution Advised-- Estimated CYP2C9 activity may be slower than normal. Certain ARBs are CYP2C9 substrates (irbesartan, losartan, valsartan). Decreased CYP2C9 activity may increase systemic concentrations of ARBs.

Depression/Anxiety (SSRIs, SNRIs, Tricyclics)

CYP2C19

Caution Advised-Estimated CYP2C19 activity may be slower than normal which may increase exposure of certain psychiatric medications (amitriptyline, nortriptyline, escitalopram, citalopram, sertraline, etc.).

CYP2D6

Caution Advised-Estimated CYP2D6 activity may be slower than normal which may increase exposure of certain psychiatric medications (amitriptyline, nortriptyline, fluoxetine, paroxetine, etc.).

Pain Management (Opioids)

CYP2D6

Caution Advised-Estimated CYP2D6 activity may be slower than normal which may decrease response in certain opioids (hydrocodone, oxycodone, codeine).

Diabetes (Sulfonylureas)	
CYP2C9	Caution Advised- Estimated CYP2C9 activity may be slower than normal. Certain glucose lowering agents are CYP2C9 substrates (glyburide, glipizide). Decreased CYP2C9 activity may increase systemic concentrations of medication which may increase risk of hypoglycemia.

**QuickPath Reference looks only at CYP450 interaction risk by medication class. There may be Drug to Drug or Drug to Disease risks not identified unless a new report is generated. TruTYPE is not FDA approved and is informational only. Only a qualified health care professional should interpret findings.

Disclaimers & Definitions

TRUTYPE

TruTYPE is an informational resource that identifies possible enzyme activity changes due to genetics, inhibitors, inducers, age, dosage, and disease-states per FDA Product Label that may affect absorption, distribution, metabolism, and/or elimination of a medication.

TRURISK

TruRISK is an informational resource that identifies one or more major and/or severe pharmacokinetic, pharmacodynamic, and disease-drug interactions that may be present based on information from FDA Product Label and DrugBank Interaction Database.

LAB DEVELOPED TESTS

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Refer to the REFERENCE GUIDE below for more information.

Reference Guide



Scan the QR Code to the left or click below to access the References for Genetic Risk Statements & Published Guidance along with definitions and disclaimers.

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