PharmCAT Report

Title	pharmcat_positions
Date created	February 18, 2022
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CPIC Version	v1.14

Disclaimer: PharmCAT is only able to generate recommendations based on the information provided to the software. The gene and variant information for all reported sections are interpreted directly from user-supplied data. The user recognizes they are using PharmCAT at their own risk. For a detailed disclaimer see section IV.

Sections

Genotype Summary

Genotypes called: 19 / 19

Drugs	Gene	Genotype	Allele Functionality	Phenotype	Missing Variant Input*
rosuvastatin	ABCG2	rs2231142 reference (G)/rs2231142 reference (G)	Two normal function alleles	Normal Function	No
desflurane enflurane halothane isoflurane methoxyflurane sevoflurane succinylcholine	CACNA1S	Reference/Reference	Two normal function alleles	Uncertain Susceptibility	No
ivacaftor	CFTR	No CPIC variants found	Two ivacaftor non-responsive alleles	ivacaftor non-responsive in CF patients	No
efavirenz	CYP2B6	*1/*1	Two normal function alleles	Normal Metabolizer	No

Drugs	Gene	Genotype	Allele Functionality	Phenotype	Missing Variant Input*
amitriptyline citalopram clomipramine clopidogrel dexlansoprazole doxepin escitalopram imipramine lansoprazole omeprazole pantoprazole sertraline trimipramine voriconazole	CYP2C19	*38/*38	Two normal function alleles	Normal Metabolizer	No
celecoxib flurbiprofen fluvastatin ibuprofen lornoxicam meloxicam piroxicam tenoxicam warfarin	CYP2C9	*1/*1	Two normal function alleles	Normal Metabolizer	No
amitriptyline atomoxetine clomipramine codeine desipramine doxepin fluvoxamine hydrocodone imipramine nortriptyline ondansetron paroxetine tamoxifen tramadol trimipramine tropisetron	CYP2D6‡	*1/*3	One no function allele and one normal function allele	Intermediate Metabolizer	N/A
tacrolimus	CYP3A5‡	*1/*1	Two normal function alleles	Normal Metabolizer	No
warfarin	CYP4F2	*1/*1	N/A	N/A	No
capecitabine fluorouracil	DPYD‡	Reference/Reference	Two normal function alleles	Normal Metabolizer	No
rasburicase	G6PD	B (wildtype)/B (wildtype)	Two normal function alleles	Normal	N/A
peginterferon alfa-2a peginterferon alfa-2b	IFNL3/4‡	rs12979860 reference (C)/rs12979860 reference (C)	N/A	N/A	No

Drugs	Gene	Genotype	Allele Functionality	Phenotype	Missing Variant Input*
amikacin gentamicin kanamycin paromomycin plazomicin streptomycin tobramycin	MT-RNR1	1555A>G	increased risk of aminoglycoside-induced hearing loss	increased risk of aminoglycoside-induced hearing loss	N/A
azathioprine mercaptopurine thioguanine	NUDT15	*1/*1	Two normal function alleles	Normal Metabolizer	No
desflurane enflurane halothane isoflurane methoxyflurane sevoflurane succinylcholine	RYR1	Reference/Reference	Two normal function alleles	Uncertain Susceptibility	No
atorvastatin fluvastatin lovastatin pitavastatin pravastatin rosuvastatin simvastatin	SLCO1B1	*1/*1	Two normal function alleles	Normal Function	No
azathioprine mercaptopurine thioguanine	TPMT‡	*1/*1	Two normal function alleles	Normal Metabolizer	No
atazanavir	UGT1A1‡	*1/*1	Two normal function alleles	Normal Metabolizer	No
warfarin	VKORC1‡	rs9923231 reference (C)/rs9923231 reference (C)	N/A	N/A	No

* *Indicates there are alleles not considered for the genotype calls due to missing variant information, please see Allele calls section. Alleles that could not be considered due to missing input might change the metabolizer phenotype and possible CPIC recommendation.*

† *Check the allele call details for this gene for more details about this call.*

‡ *PharmCAT reports the genotype(s) that receive the highest score during the matcher process. In case of unphased data, additional genotypes might be possible and cannot be ruled out.*

For a full list of disclaimers and limitations see the Disclaimer section.

CPIC Recommendations

amikacin

MT-RNR1: 1555A>G increased risk of aminoglycoside-induced hearing loss (from Outside Call)

Type	Annotation
Population	general
Implication for MT-RNR1	Very high risk of developing hearing loss if administered an aminoglycoside antibiotic.
Matched Diplotypes	MT-RNR1:1555A>G
Phenotype for MT-RNR1	increased risk of aminoglycoside-induced hearing loss
Recommendation	Avoid aminoglycoside anitbiotics unless the high risk of permanent hearing loss is outweighed by the severity of infection and lack of safe or effective alternative therapies.
Classification of Recommendation	Strong
Comments	If no effective alternative to an aminoglycoside antibiotic is available, evaluate for hearing loss frequently during therapy and ensure that all appropriate precautions are utilized (e.g., lowest possible dose and duration, utilization of therapeutic drug monitoring, hydration, renal function monitoring).

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for the use of aminoglycosides based on MT-RNR1 genotype. [PMID:34032273] *Clinical pharmacology and therapeutics*. 2021.

amitriptyline

CYP2C19: *38/*38 Two normal function alleles
CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Reduced metabolism of TCAs to less active compounds compared to normal metabolizers; Higher plasma concentrations of active drug will increase the probability of side effects
Implication for CYP2C19	Normal metabolism of tertiary amines
Matched Diplotypes	CYP2C19:*38/*38, CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Phenotype for CYP2C19	Normal Metabolizer

Type	Annotation
Activity Score for CYP2D6	1.0
Recommendation	Consider a 25% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.
Classification of Recommendation	Moderate
Comments	Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression. See other considerations for dosing recommendations for conditions where lower initial doses are used, such as neuropathic pain.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium Guideline (CPICÂ®) for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants: 2016 Update [PMID:27997040] *Clinical pharmacology and therapeutics*. 2016.
- Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants [PMID:23486447] *Clinical pharmacology and therapeutics*. 2013.

atazanavir

UGT1A1: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for UGT1A1	Reference UGT1A1 activity; very low likelihood of bilirubin-related discontinuation of atazanavir.
Matched Diplotypes	UGT1A1:*1/*1
Phenotype for UGT1A1	Normal Metabolizer
Recommendation	There is no need to avoid prescribing of atazanavir based on UGT1A1 genetic test result. Inform the patient that some patients stop atazanavir because of jaundice (yellow eyes and skin), but that this patientâ€™s genotype makes this unlikely (less than about a 1 in 20 chance of stopping atazanavir because of jaundice).
Classification of Recommendation	Strong

Type	Annotation
Comments	All studies correlating UGT1A1 genotypes with atazanavir adverse events have involved ritonavir boosting. However, concentration-time profiles are equivalent when boosted with either cobicistat or ritonavir (PMID 23532097), and bilirubin-related adverse events including discontinuation of atazanavir occur in a similar percentage of patients prescribed atazanavir with cobicistat or ritonavir (PMID 23532097). Associations between UGT1A1 genotype, bilirubin elevations, and atazanavir/r discontinuation therefore almost certainly translate to atazanavir/cobicistat. "reference" function refers to the UGT1A1 allele to which other alleles are compared.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for UGT1A1 and Atazanavir Prescribing [PMID:26417955] *Clinical pharmacology and therapeutics*. 2015.

atomoxetine

CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	adults
Implication for CYP2D6	Possibly higher atomoxetine concentrations as compared to normal metabolizers but questionable clinical significance. Intermediate metabolizers with an activity score of 1 may be at an increased risk of discontinuation as compared to poor metabolizers.
Matched Diplotypes	CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Activity Score for CYP2D6	1.0
Recommendation	Initiate with a dose of 40 mg/day and increase to 80 mg/day after 3 days. If no clinical response and in the absence of adverse events after 2 weeks, consider increasing dose to 100 mg/day. If no clinical response observed after 2 weeks, consider obtaining a peak plasma concentration (1 to 2 hours after dose administered). If <200 ng/mL, consider a proportional increase in dose to approach 400 ng/mL. Dosages greater than 100 mg/day may be needed to achieve target concentrations.
Classification of Recommendation	Moderate

Type	Annotation
Comments	Therapeutic range of 200 to 1000 ng/mL has been proposed (PMID 29493375). Limited data are available regarding the relationship between atomoxetine plasma concentrations and clinical response. Available information suggests that clinical response is greater in poor metabolizers (PMs) compared to non-PMs and may be related to the higher plasma concentrations 1 to 1.5 hours after dosing in PMs compared to non-PMs administered a similar dose. Furthermore, modest improvement in response, defined as reduction in ADHD-rating scale, is observed at peak concentrations greater than 400 ng/mL. Doses above 120 mg/day have not been evaluated.

Type	Annotation
Population	pediatrics
Implication for CYP2D6	Possibly higher atomoxetine concentrations as compared to normal metabolizers but questionable clinical significance. Intermediate metabolizers with an activity score of 1 may be at an increased risk of discontinuation as compared to poor metabolizers.
Matched Diplotypes	CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Activity Score for CYP2D6	1.0
Recommendation	Initiate with a dose of 0.5 mg/kg/day and increase to 1.2 mg/kg/day after 3 days. If no clinical response and in the absence of adverse events after 2 weeks, consider obtaining a peak plasma concentration (1 to 2 hours after dose administered). If < 200 ng/mL, consider a proportional increase in dose to approach 400 ng/mL.
Classification of Recommendation	Moderate
Comments	Therapeutic range of 200 to 1000 ng/mL has been proposed (PMID 29493375). Limited data are available regarding the relationship between atomoxetine plasma concentrations and clinical response. Available information suggests that clinical response is greater in poor metabolizers (PMs) compared to non-PMs and may be related to the higher plasma concentrations 1 to 1.5 hours after dosing in PMs compared to non-PMs administered a similar dose. Furthermore, modest improvement in response, defined as reduction in ADHD-rating scale, is observed at peak concentrations greater than 400 ng/mL.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 Genotype and Atomoxetine Therapy. [PMID:30801677] *Clinical pharmacology and therapeutics*. 2019.

atorvastatin

SLCO1B1: *1/*1 Two normal function alleles
rs4149056T/rs4149056T

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	population general
Implication for SLCO1B1	Typical myopathy risk and statin exposure
Matched Diplotypes	SLCO1B1:*1/*1
Phenotype for SLCO1B1	Normal Function
Recommendation	Prescribe desired starting dose and adjust doses based on disease-specific guidelines.
Classification of Recommendation	Strong
Comments	The potential for drug-drug interactions and dose limits based on renal and hepatic function and ancestry should be evaluated prior to initiating a statin.

For more information read the guideline on cpicpgx.org.

Citations:

- The Clinical Pharmacogenomics Implementation Consortium: Guideline for SLCO1B1 and Simvastatin-Induced Myopathy [PMID:22617227] *Clinical pharmacology and therapeutics*. 2012.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update [PMID:24918167] *Clinical pharmacology and therapeutics*. 2014.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1, ABCG2, and CYP2C9 and statin-associated musculoskeletal symptoms. [PMID:35152405] *Clinical pharmacology and therapeutics*. 2022.

azathioprine

NUDT15: *1/*1 Two normal function alleles
TPMT: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for TPMT	Lower concentrations of TGN metabolites, higher MeTIMP, this is the â€¯normalâ€™ pattern. Normal risk of thiopurine-related leukopenia, neutropenia, myelosuppression.
Implication for NUDT15	Normal risk of thiopurine-related leukopenia, neutropenia, myelosuppression
Matched Diplotypes	NUDT15:*1/*1, TPMT:*1/*1
Phenotype for TPMT	Normal Metabolizer
Phenotype for NUDT15	Normal Metabolizer

Type	Annotation
Recommendation	Start with normal starting dose (e.g., 2-3 mg/kg/day) and adjust doses of azathioprine based on disease-specific guidelines. Allow 2 weeks to reach steady-state after each dose adjustment (PMID 20354201, 11302950, 15606506).
Classification of Recommendation	Strong
Comments	Normal starting doses vary by race/ethnicity and treatment regimens. If standard dose is below normal recommended dose, dose reduction might not be recommended for intermediate metabolizers.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical pharmacogenetics implementation consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing [PMID:21270794] *Clinical pharmacology and therapeutics*. 2011.
- Clinical Pharmacogenetics Implementation Consortium Guidelines for Thiopurine Methyltransferase Genotype and Thiopurine Dosing: 2013 Update [PMID:23422873] *Clinical pharmacology and therapeutics*. 2013.
- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for thiopurine dosing based on TPMT and NUDT15 genotypes: 2018 update. [PMID:30447069] *Clinical pharmacology and therapeutics*. 2018.

capecitabine

DPYD: Reference/Reference Two normal function alleles

Type	Annotation
Population	general
Implication for DPYD	Normal DPD activity and "normal" risk for fluoropyrimidine toxicity
Matched Diplotypes	DPYD:Reference/Reference
Phenotype for DPYD	Normal Metabolizer
Activity Score for DPYD	2.0
Recommendation	Based on genotype, there is no indication to change dose or therapy. Use label-recommended dosage and administration.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium Guidelines for Dihydropyrimidine Dehydrogenase Genotype and Fluoropyrimidine Dosing [PMID:23988873] *Clinical pharmacology and therapeutics*. 2013.
- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Dihydropyrimidine Dehydrogenase Genotype and Fluoropyrimidine Dosing: 2017 Update [PMID:29152729] *Clinical pharmacology and therapeutics*. 2017.

celecoxib

CYP2C9: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2C9	Normal metabolism
Matched Diplotypes	CYP2C9:*1/*1
Phenotype for CYP2C9	Normal Metabolizer
Activity Score for CYP2C9	2.0
Recommendation	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C9 and Nonsteroidal Anti-inflammatory Drugs. [PMID:32189324] *Clinical pharmacology and therapeutics*. 2020.

citalopram

CYP2C19: *38/*38 Two normal function alleles

Type	Annotation
Population	general
Implication for CYP2C19	Normal metabolism
Matched Diplotypes	CYP2C19:*38/*38
Phenotype for CYP2C19	Normal Metabolizer
Recommendation	Initiate therapy with recommended starting dose
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors [PMID:25974703] *Clinical pharmacology and therapeutics*. 2015.

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clomipramine

CYP2C19: *38/*38 Two normal function alleles
CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Reduced metabolism of TCAs to less active compounds compared to normal metabolizers; Higher plasma concentrations of active drug will increase the probability of side effects
Implication for CYP2C19	Normal metabolism of tertiary amines
Matched Diplotypes	CYP2C19:*38/*38, CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Phenotype for CYP2C19	Normal Metabolizer
Activity Score for CYP2D6	1.0
Recommendation	Consider a 25% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.
Classification of Recommendation	Optional
Comments	Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression. See other considerations for dosing recommendations for conditions where lower initial doses are used, such as neuropathic pain.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium Guideline (CPICÂ®) for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants: 2016 Update [PMID:27997040] *Clinical pharmacology and therapeutics*. 2016.
- Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants [PMID:23486447] *Clinical pharmacology and therapeutics*. 2013.

clopidogrel

CYP2C19: *38/*38 Two normal function alleles

Type	Annotation
Population	CVI non-ACS non-PCI
Implication for CYP2C19	Normal clopidogrel active metabolite formation; normal on-treatment platelet reactivity
Matched Diplotypes	CYP2C19:*38/*38
Phenotype for CYP2C19	Normal Metabolizer
Recommendation	If considering clopidogrel, use at standard dose (75 mg/day)
Classification of Recommendation	Strong
Comments	For non-acute coronary syndrome (non-ACS) and non-percutaneous coronary intervention (non-PCI) cardiovascular indications. Non-ACS, non-PCI cardiovascular indications include peripheral arterial disease and stable coronary artery disease following a recent myocardial infarction outside the setting of PCI.

Type	Annotation
Population	CVI ACS PCI
Implication for CYP2C19	Normal clopidogrel active metabolite formation; normal on-treatment platelet reactivity
Matched Diplotypes	CYP2C19:*38/*38
Phenotype for CYP2C19	Normal Metabolizer
Recommendation	If considering clopidogrel, use at standard dose (75 mg/day)
Classification of Recommendation	Strong
Comments	For cardiovascular indications of acute coronary syndrome (ACS) and/or percutaneous coronary intervention (PCI). ACS and/or PCI includes patients undergoing PCI for an ACS or non-ACS (elective) indication.

Type	Annotation
Population	NVI
Implication for CYP2C19	Normal clopidogrel active metabolite formation; normal on-treatment platelet reactivity
Matched Diplotypes	CYP2C19:*38/*38
Phenotype for CYP2C19	Normal Metabolizer
Recommendation	If considering clopidogrel, use at standard dose (75 mg/day)

Type	Annotation
Classification of Recommendation	Strong
Comments	For neurovascular indications. Neurovascular disease includes acute ischemic stroke or transient ischemic attack, secondary prevention of stroke, or prevention of thromboembolic events following neurointerventional procedures such as carotid artery stenting and stent-assisted coiling of intracranial aneurysms.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium Guidelines for Cytochrome P450-2C19 (CYP2C19) Genotype and Clopidogrel Therapy [PMID:21716271] *Clinical pharmacology and therapeutics*. 2011.
- Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for cytochrome P450-2C19 (CYP2C19) genotype and clopidogrel therapy: 2013 Update [PMID:23698643] *Clinical pharmacology and therapeutics*. 2013.
- Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2C19 Genotype and Clopidogrel Therapy: 2022 Update. [PMID:35034351] *Clinical pharmacology and therapeutics*. 2022.

codeine

CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Reduced morphine formation
Matched Diplotypes	CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Activity Score for CYP2D6	1
Recommendation	Use codeine label recommended age- or weight-specific dosing. If no response and opioid use is warranted, consider a non-tramadol opioid.
Classification of Recommendation	Moderate

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for Codeine Therapy in the Context of Cytochrome P450 2D6 (CYP2D6) Genotype [PMID:22205192] *Clinical pharmacology and therapeutics*. 2011.
- Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for cytochrome P450 2D6 (CYP2D6) genotype and codeine therapy: 2014 Update [PMID:24458010] *Clinical pharmacology and therapeutics*. 2014.

- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2D6, OPRM1, and COMT genotype and select opioid therapy. [PMID:33387367] *Clinical pharmacology and therapeutics*. 2021.

desflurane

CACNA1S: Reference/Reference Two normal function alleles
RYR1: Reference/Reference Two normal function alleles

Type	Annotation
Population	general
Implication for RYR1	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Implication for CACNA1S	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Matched Diplotypes	CACNA1S:Reference/Reference, RYR1:Reference/Reference
Phenotype for RYR1	Uncertain Susceptibility
Phenotype for CACNA1S	Uncertain Susceptibility
Recommendation	Clinical findings, family history, further genetic testing and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for the use of potent volatile anesthetic agents and succinylcholine in the context of RYR1 or CACNA1S genotypes [PMID:30499100] *Clinical pharmacology and therapeutics*. 2018.

desipramine

CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general

Type	Annotation
Implication for CYP2D6	Reduced metabolism of TCAs to less active compounds compared to normal metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.
Matched Diplotypes	CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Activity Score for CYP2D6	1.0
Recommendation	Consider a 25% reduction of recommended starting dose. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. Utilize therapeutic drug monitoring to guide dose adjustments.
Classification of Recommendation	Optional
Comments	Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression. See other considerations for dosing recommendations for conditions where lower initial doses are used, such as neuropathic pain.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium Guideline (CPICÂ®) for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants: 2016 Update [PMID:27997040] *Clinical pharmacology and therapeutics*. 2016.
- Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants [PMID:23486447] *Clinical pharmacology and therapeutics*. 2013.

dexlansoprazole

CYP2C19: *38/*38 Two normal function alleles

Type	Annotation
Population	general
Implication for CYP2C19	Normal PPI metabolism; may be at increased risk of therapeutic failure compared to CYP2C19 IMs and PMs
Matched Diplotypes	CYP2C19:*38/*38
Phenotype for CYP2C19	Normal Metabolizer
Recommendation	Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.
Classification of Recommendation	Optional

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C19 and Proton Pump Inhibitor Dosing. [PMID:32770672] *Clinical pharmacology and therapeutics*. 2020.

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doxepin

CYP2C19: *38/*38 Two normal function alleles
CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Reduced metabolism of TCAs to less active compounds compared to normal metabolizers; Higher plasma concentrations of active drug will increase the probability of side effects
Implication for CYP2C19	Normal metabolism of tertiary amines
Matched Diplotypes	CYP2C19:*38/*38, CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Phenotype for CYP2C19	Normal Metabolizer
Activity Score for CYP2D6	1.0
Recommendation	Consider a 25% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.
Classification of Recommendation	Optional
Comments	Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression. See other considerations for dosing recommendations for conditions where lower initial doses are used, such as neuropathic pain.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium Guideline (CPICÂ®) for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants: 2016 Update [PMID:27997040] *Clinical pharmacology and therapeutics*. 2016.
- Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants [PMID:23486447] *Clinical pharmacology and therapeutics*. 2013.

efavirenz

CYP2B6: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	child >40kg_adult
Implication for CYP2B6	Normal efavirenz metabolism
Matched Diplotypes	CYP2B6:*1/*1
Phenotype for CYP2B6	Normal Metabolizer
Recommendation	Initiate efavirenz with standard dosing (600 mg/day)
Classification of Recommendation	Strong
Comments	The ENCORE study showed that in treatment-naÃ¯ve patients randomized to initiate efavirenz-based regimens (combined with tenofovir and emtricitabine), 400 mg/day was non-inferior to 600 mg/day regardless of CYP2B6 genotype (PMID 24522178).

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2B6 and Efavirenz-containing Antiretroviral Therapy. [PMID:31006110] *Clinical pharmacology and therapeutics*. 2019.

enflurane

CACNA1S: Reference/Reference Two normal function alleles
RYR1: Reference/Reference Two normal function alleles

Type	Annotation
Population	general
Implication for RYR1	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Implication for CACNA1S	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Matched Diplotypes	CACNA1S:Reference/Reference, RYR1:Reference/Reference

Type	Annotation
Phenotype for RYR1	Uncertain Susceptibility
Phenotype for CACNA1S	Uncertain Susceptibility
Recommendation	Clinical findings, family history, further genetic testing and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for the use of potent volatile anesthetic agents and succinylcholine in the context of RYR1 or CACNA1S genotypes [PMID:30499100] *Clinical pharmacology and therapeutics*. 2018.

escitalopram

CYP2C19: *38/*38 Two normal function alleles

Type	Annotation
Population	general
Implication for CYP2C19	Normal metabolism
Matched Diplotypes	CYP2C19:*38/*38
Phenotype for CYP2C19	Normal Metabolizer
Recommendation	Initiate therapy with recommended starting dose
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors [PMID:25974703] *Clinical pharmacology and therapeutics*. 2015.

fluorouracil

DPYD: Reference/Reference Two normal function alleles

Type	Annotation

Type	Annotation
Population	general
Implication for DPYD	Normal DPD activity and "normal" risk for fluoropyrimidine toxicity
Matched Diplotypes	DPYD:Reference/Reference
Phenotype for DPYD	Normal Metabolizer
Activity Score for DPYD	2.0
Recommendation	Based on genotype, there is no indication to change dose or therapy. Use label-recommended dosage and administration.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium Guidelines for Dihydropyrimidine Dehydrogenase Genotype and Fluoropyrimidine Dosing [PMID:23988873] *Clinical pharmacology and therapeutics*. 2013.
- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for Dihydropyrimidine Dehydrogenase Genotype and Fluoropyrimidine Dosing: 2017 Update [PMID:29152729] *Clinical pharmacology and therapeutics*. 2017.

flurbiprofen

CYP2C9: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2C9	Normal metabolism
Matched Diplotypes	CYP2C9:*1/*1
Phenotype for CYP2C9	Normal Metabolizer
Activity Score for CYP2C9	2.0
Recommendation	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C9 and Nonsteroidal Anti-inflammatory Drugs. [PMID:32189324] *Clinical pharmacology and therapeutics*. 2020.

fluvastatin

CYP2C9: *1/*1 Two normal function alleles
SLCO1B1: *1/*1 Two normal function alleles
rs4149056T/rs4149056T

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2C9	Normal exposure.
Implication for SLCO1B1	Typical myopathy risk and statin exposure.
Matched Diplotypes	CYP2C9:*1/*1, SLCO1B1:*1/*1
Phenotype for CYP2C9	Normal Metabolizer
Phenotype for SLCO1B1	Normal Function
Activity Score for CYP2C9	2.0
Recommendation	Prescribe desired starting dose and adjust doses of fluvastatin based on disease-specific guidelines.
Classification of Recommendation	Strong
Comments	The potential for drug-drug interactions and dose limits based on renal and hepatic function and ancestry should be evaluated prior to initiating a statin.

For more information read the guideline on cpicpgx.org.

Citations:

- The Clinical Pharmacogenomics Implementation Consortium: Guideline for SLCO1B1 and Simvastatin-Induced Myopathy [PMID:22617227] *Clinical pharmacology and therapeutics*. 2012.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update [PMID:24918167] *Clinical pharmacology and therapeutics*. 2014.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1, ABCG2, and CYP2C9 and statin-associated musculoskeletal symptoms. [PMID:35152405] *Clinical pharmacology and therapeutics*. 2022.

fluvoxamine

CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Reduced metabolism when compared to normal metabolizers. Higher plasma concentrations may increase the probability of side effects.
Matched Diplotypes	CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Activity Score for CYP2D6	1.0
Recommendation	Initiate therapy with recommended starting dose.
Classification of Recommendation	Moderate

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors [PMID:25974703] *Clinical pharmacology and therapeutics*. 2015.

gentamicin

MT-RNR1: 1555A>G increased risk of aminoglycoside-induced hearing loss (from Outside Call)

Type	Annotation
Population	general
Implication for MT-RNR1	Very high risk of developing hearing loss if administered an aminoglycoside antibiotic.
Matched Diplotypes	MT-RNR1:1555A>G
Phenotype for MT-RNR1	increased risk of aminoglycoside-induced hearing loss
Recommendation	Avoid aminoglycoside anitbiotics unless the high risk of permanent hearing loss is outweighed by the severity of infection and lack of safe or effective alternative therapies.
Classification of Recommendation	Strong

Type	Annotation
Comments	If no effective alternative to an aminoglycoside antibiotic is available, evaluate for hearing loss frequently during therapy and ensure that all appropriate precautions are utilized (e.g., lowest possible dose and duration, utilization of therapeutic drug monitoring, hydration, renal function monitoring).

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for the use of aminoglycosides based on MT-RNR1 genotype. [PMID:34032273] *Clinical pharmacology and therapeutics*. 2021.

halothane

CACNA1S: Reference/Reference Two normal function alleles
RYR1: Reference/Reference Two normal function alleles

Type	Annotation
Population	general
Implication for RYR1	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Implication for CACNA1S	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Matched Diplotypes	CACNA1S:Reference/Reference, RYR1:Reference/Reference
Phenotype for RYR1	Uncertain Susceptibility
Phenotype for CACNA1S	Uncertain Susceptibility
Recommendation	Clinical findings, family history, further genetic testing and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for the use of potent volatile anesthetic agents and succinylcholine in the context of RYR1 or CACNA1S genotypes [PMID:30499100] *Clinical pharmacology and therapeutics*. 2018.

hydrocodone

CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Minimal evidence for pharmacokinetic or clinical effect.
Matched Diplotypes	CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Activity Score for CYP2D6	1
Recommendation	Use hydrocodone label recommended age- or weight-specific dosing. If no response and opioid use is warranted, consider non-codeine or non-tramadol opioid.
Classification of Recommendation	Optional

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for Codeine Therapy in the Context of Cytochrome P450 2D6 (CYP2D6) Genotype [PMID:22205192] *Clinical pharmacology and therapeutics*. 2011.
- Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for cytochrome P450 2D6 (CYP2D6) genotype and codeine therapy: 2014 Update [PMID:24458010] *Clinical pharmacology and therapeutics*. 2014.
- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2D6, OPRM1, and COMT genotype and select opioid therapy. [PMID:33387367] *Clinical pharmacology and therapeutics*. 2021.

ibuprofen

CYP2C9: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2C9	Normal metabolism
Matched Diplotypes	CYP2C9:*1/*1
Phenotype for CYP2C9	Normal Metabolizer

Type	Annotation
Activity Score for CYP2C9	2.0
Recommendation	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C9 and Nonsteroidal Anti-inflammatory Drugs. [PMID:32189324] *Clinical pharmacology and therapeutics*. 2020.

imipramine

CYP2C19: *38/*38 Two normal function alleles
CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Reduced metabolism of TCAs to less active compounds compared to normal metabolizers; Higher plasma concentrations of active drug will increase the probability of side effects
Implication for CYP2C19	Normal metabolism of tertiary amines
Matched Diplotypes	CYP2C19:*38/*38, CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Phenotype for CYP2C19	Normal Metabolizer
Activity Score for CYP2D6	1.0
Recommendation	Consider a 25% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.
Classification of Recommendation	Optional

Type	Annotation
Comments	Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression. See other considerations for dosing recommendations for conditions where lower initial doses are used, such as neuropathic pain.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium Guideline (CPICÂ®) for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants: 2016 Update [PMID:27997040] *Clinical pharmacology and therapeutics*. 2016.
- Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants [PMID:23486447] *Clinical pharmacology and therapeutics*. 2013.

isoflurane

CACNA1S: Reference/Reference Two normal function alleles
RYR1: Reference/Reference Two normal function alleles

Type	Annotation
Population	general
Implication for RYR1	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Implication for CACNA1S	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Matched Diplotypes	CACNA1S:Reference/Reference, RYR1:Reference/Reference
Phenotype for RYR1	Uncertain Susceptibility
Phenotype for CACNA1S	Uncertain Susceptibility
Recommendation	Clinical findings, family history, further genetic testing and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for the use of potent volatile anesthetic agents and succinylcholine in the context of RYR1 or CACNA1S genotypes [PMID:30499100] *Clinical pharmacology and therapeutics*. 2018.

ivacaftor

CFTR: No CPIC variants found Two ivacaftor non-responsive alleles

Type	Annotation
Population	general
Implication for CFTR	An individual diagnosed with cystic fibrosis (CF) and negative for a CFTR variant listed in the FDA-approved drug label as being responsive to ivacaftor.
Matched Diplotypes	CFTR:No CPIC variants found
Phenotype for CFTR	ivacaftor non-responsive in CF patients
Recommendation	Ivacaftor is not recommended
Classification of Recommendation	Moderate

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for Ivacaftor Therapy in the Context of CFTR Genotype [PMID:24598717] *Clinical pharmacology and therapeutics*. 2014.

kanamycin

MT-RNR1: 1555A>G increased risk of aminoglycoside-induced hearing loss (from Outside Call)

Type	Annotation
Population	general
Implication for MT-RNR1	Very high risk of developing hearing loss if administered an aminoglycoside antibiotic.
Matched Diplotypes	MT-RNR1:1555A>G
Phenotype for MT-RNR1	increased risk of aminoglycoside-induced hearing loss
Recommendation	Avoid aminoglycoside anitbiotics unless the high risk of permanent hearing loss is outweighed by the severity of infection and lack of safe or effective alternative therapies.
Classification of Recommendation	Strong
Comments	If no effective alternative to an aminoglycoside antibiotic is available, evaluate for hearing loss frequently during therapy and ensure that all appropriate precautions are utilized (e.g., lowest possible dose and duration, utilization of therapeutic drug monitoring, hydration, renal function monitoring).

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for the use of aminoglycosides based on MT-RNR1 genotype. [PMID:34032273] *Clinical pharmacology and therapeutics*. 2021.

lansoprazole

CYP2C19: *38/*38 Two normal function alleles

Type	Annotation
Population	general
Implication for CYP2C19	Normal PPI metabolism; may be at increased risk of therapeutic failure compared to CYP2C19 IMs and PMs
Matched Diplotypes	CYP2C19:*38/*38
Phenotype for CYP2C19	Normal Metabolizer
Recommendation	Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.
Classification of Recommendation	Moderate

For more information read theguideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C19 and Proton Pump Inhibitor Dosing. [PMID:32770672] *Clinical pharmacology and therapeutics*. 2020.

lornoxicam

CYP2C9: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2C9	Normal metabolism
Matched Diplotypes	CYP2C9:*1/*1
Phenotype for CYP2C9	Normal Metabolizer

Type	Annotation
Activity Score for CYP2C9	2.0
Recommendation	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C9 and Nonsteroidal Anti-inflammatory Drugs. [PMID:32189324] *Clinical pharmacology and therapeutics*. 2020.

lovastatin

SLCO1B1: *1/*1 Two normal function alleles
rs4149056T/rs4149056T

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	population general
Implication for SLCO1B1	Typical myopathy risk and statin exposure
Matched Diplotypes	SLCO1B1:*1/*1
Phenotype for SLCO1B1	Normal Function
Recommendation	Prescribe desired starting dose and adjust doses based on disease-specific guidelines.
Classification of Recommendation	Strong
Comments	The potential for drug-drug interactions and dose limits based on renal and hepatic function and ancestry should be evaluated prior to initiating a statin.

For more information read the guideline on cpicpgx.org.

Citations:

- The Clinical Pharmacogenomics Implementation Consortium: Guideline for SLCO1B1 and Simvastatin-Induced Myopathy [PMID:22617227] *Clinical pharmacology and therapeutics*. 2012.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update [PMID:24918167] *Clinical pharmacology and therapeutics*. 2014.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1, ABCG2, and CYP2C9 and statin-

associated musculoskeletal symptoms. [PMID:35152405] *Clinical pharmacology and therapeutics*. 2022.

meloxicam

CYP2C9: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2C9	Normal metabolism
Matched Diplotypes	CYP2C9:*1/*1
Phenotype for CYP2C9	Normal Metabolizer
Activity Score for CYP2C9	2.0
Recommendation	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C9 and Nonsteroidal Anti-inflammatory Drugs. [PMID:32189324] *Clinical pharmacology and therapeutics*. 2020.

mercaptopurine

NUDT15: *1/*1 Two normal function alleles
TPMT: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general

Type	Annotation
Implication for TPMT	Lower concentrations of TGN metabolites, higher MeTIMP, this is the â€¯normalâ€™ pattern. Normal risk of thiopurine-related leukopenia, neutropenia, myelosuppression.
Implication for NUDT15	Normal risk of thiopurine-related leukopenia, neutropenia, myelosuppression
Matched Diplotypes	NUDT15:*1/*1, TPMT:*1/*1
Phenotype for TPMT	Normal Metabolizer
Phenotype for NUDT15	Normal Metabolizer
Recommendation	Start with normal starting dose (e.g., 75 mg/m2/day or 1.5 mg/kg/day) and adjust doses of mercaptopurine (and of any other myelosuppressive therapy) without any special emphasis on mercaptopurine compared to other agents. Allow at least 2 weeks to reach steady-state after each dose adjustment (PMID 20354201, 16401827, 11302950).
Classification of Recommendation	Strong
Comments	Normal starting doses vary by race/ethnicity and treatment regimens. If standard dose is below normal recommended dose, dose reduction might not be recommended for intermediate metabolizers.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical pharmacogenetics implementation consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing [PMID:21270794] *Clinical pharmacology and therapeutics*. 2011.
- Clinical Pharmacogenetics Implementation Consortium Guidelines for Thiopurine Methyltransferase Genotype and Thiopurine Dosing: 2013 Update [PMID:23422873] *Clinical pharmacology and therapeutics*. 2013.
- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for thiopurine dosing based on TPMT and NUDT15 genotypes: 2018 update. [PMID:30447069] *Clinical pharmacology and therapeutics*. 2018.

methoxyflurane

CACNA1S: Reference/Reference Two normal function alleles
RYR1: Reference/Reference Two normal function alleles

Type	Annotation
Population	general
Implication for RYR1	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Implication for CACNA1S	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Matched Diplotypes	CACNA1S:Reference/Reference, RYR1:Reference/Reference

Type	Annotation
Phenotype for RYR1	Uncertain Susceptibility
Phenotype for CACNA1S	Uncertain Susceptibility
Recommendation	Clinical findings, family history, further genetic testing and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for the use of potent volatile anesthetic agents and succinylcholine in the context of RYR1 or CACNA1S genotypes [PMID:30499100] *Clinical pharmacology and therapeutics*. 2018.

nortriptyline

CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Reduced metabolism of tricyclic antidepressants to less active compounds compared to normal metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.
Matched Diplotypes	CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Activity Score for CYP2D6	1.0
Recommendation	Consider a 25% reduction of recommended starting dose. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. Utilize therapeutic drug monitoring to guide dose adjustments.
Classification of Recommendation	Optional
Comments	Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Dosing recommendations only apply to higher initial doses of tricyclic antidepressants for treatment of conditions such as depression. See other considerations for dosing recommendations for conditions where lower initial doses are used, such as neuropathic pain.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium Guideline (CPICÂ®) for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants: 2016 Update [PMID:27997040] *Clinical pharmacology and therapeutics*. 2016.
- Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants [PMID:23486447] *Clinical pharmacology and therapeutics*. 2013.

omeprazole

CYP2C19: *38/*38 Two normal function alleles

Type	Annotation
Population	general
Implication for CYP2C19	Normal PPI metabolism; may be at increased risk of therapeutic failure compared to CYP2C19 IMs and PMs
Matched Diplotypes	CYP2C19:*38/*38
Phenotype for CYP2C19	Normal Metabolizer
Recommendation	Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.
Classification of Recommendation	Moderate

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C19 and Proton Pump Inhibitor Dosing. [PMID:32770672] *Clinical pharmacology and therapeutics*. 2020.

ondansetron

CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Very limited data available for CYP2D6 intermediate metabolizers

Type	Annotation
Matched Diplotypes	CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Activity Score for CYP2D6	1.0
Recommendation	Insufficient evidence demonstrating clinical impact based on CYP2D6 genotype. Initiate therapy with recommended starting dose.
Classification of Recommendation	No Recommendation
Comments	Drug-drug interactions and other patient characteristics (e.g., age, renal function, and liver function) should be considered when selecting alternative therapy.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 Genotype and Use of Ondansetron and Tropisetron [PMID:28002639] *Clinical pharmacology and therapeutics*. 2016.

pantoprazole

CYP2C19: *38/*38 Two normal function alleles

Type	Annotation
Population	general
Implication for CYP2C19	Normal PPI metabolism; may be at increased risk of therapeutic failure compared to CYP2C19 IMs and PMs
Matched Diplotypes	CYP2C19:*38/*38
Phenotype for CYP2C19	Normal Metabolizer
Recommendation	Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.
Classification of Recommendation	Moderate

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C19 and Proton Pump Inhibitor Dosing. [PMID:32770672] *Clinical pharmacology and therapeutics*. 2020.

paromomycin

MT-RNR1: 1555A>G increased risk of aminoglycoside-induced hearing loss (from Outside Call)

Type	Annotation
Population	general
Implication for MT-RNR1	Very high risk of developing hearing loss if administered an aminoglycoside antibiotic.
Matched Diplotypes	MT-RNR1:1555A>G
Phenotype for MT-RNR1	increased risk of aminoglycoside-induced hearing loss
Recommendation	Avoid aminoglycoside anitbiotics unless the high risk of permanent hearing loss is outweighed by the severity of infection and lack of safe or effective alternative therapies.
Classification of Recommendation	Strong
Comments	If no effective alternative to an aminoglycoside antibiotic is available, evaluate for hearing loss frequently during therapy and ensure that all appropriate precautions are utilized (e.g., lowest possible dose and duration, utilization of therapeutic drug monitoring, hydration, renal function monitoring).

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for the use of aminoglycosides based on MT-RNR1 genotype. [PMID:34032273] *Clinical pharmacology and therapeutics*. 2021.

paroxetine

CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Reduced metabolism when compared to normal metabolizers. Higher plasma concentrations may increase the probability of side effects.
Matched Diplotypes	CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Activity Score for CYP2D6	1.0

Type	Annotation
Recommendation	Initiate therapy with recommended starting dose
Classification of Recommendation	Moderate

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors [PMID:25974703] *Clinical pharmacology and therapeutics*. 2015.

peginterferon alfa-2a

IFNL3/4: rs12979860 reference (C)/rs12979860 reference (C) N/A

No CPIC recommendation for this allele combination.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for IFNL3 (IL28B) genotype and peginterferon alpha based regimens [PMID:24096968] *Clinical pharmacology and therapeutics*. 2013.

peginterferon alfa-2b

IFNL3/4: rs12979860 reference (C)/rs12979860 reference (C) N/A

No CPIC recommendation for this allele combination.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for IFNL3 (IL28B) genotype and peginterferon alpha based regimens [PMID:24096968] *Clinical pharmacology and therapeutics*. 2013.

piroxicam

CYP2C9: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2C9	Normal metabolism
Matched Diplotypes	CYP2C9:*1/*1
Phenotype for CYP2C9	Normal Metabolizer
Activity Score for CYP2C9	2.0
Recommendation	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C9 and Nonsteroidal Anti-inflammatory Drugs. [PMID:32189324] *Clinical pharmacology and therapeutics*. 2020.

pitavastatin

SLCO1B1: *1/*1 Two normal function alleles
rs4149056T/rs4149056T

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	population general
Implication for SLCO1B1	Typical myopathy risk and statin exposure
Matched Diplotypes	SLCO1B1:*1/*1
Phenotype for SLCO1B1	Normal Function
Recommendation	Prescribe desired starting dose and adjust doses based on disease-specific guidelines.
Classification of Recommendation	Strong
Comments	The potential for drug-drug interactions and dose limits based on renal and hepatic function and ancestry should be evaluated prior to initiating a statin.

For more information read the guideline on cpicpgx.org.

Citations:

- The Clinical Pharmacogenomics Implementation Consortium: Guideline for SLCO1B1 and Simvastatin-Induced Myopathy [PMID:22617227] *Clinical pharmacology and therapeutics*. 2012.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update [PMID:24918167] *Clinical pharmacology and therapeutics*. 2014.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1, ABCG2, and CYP2C9 and statin-associated musculoskeletal symptoms. [PMID:35152405] *Clinical pharmacology and therapeutics*. 2022.

plazomicin

MT-RNR1: 1555A>G increased risk of aminoglycoside-induced hearing loss (from Outside Call)

Type	Annotation
Population	general
Implication for MT-RNR1	Very high risk of developing hearing loss if administered an aminoglycoside antibiotic.
Matched Diplotypes	MT-RNR1:1555A>G
Phenotype for MT-RNR1	increased risk of aminoglycoside-induced hearing loss
Recommendation	Avoid aminoglycoside anitbiotics unless the high risk of permanent hearing loss is outweighed by the severity of infection and lack of safe or effective alternative therapies.
Classification of Recommendation	Strong
Comments	If no effective alternative to an aminoglycoside antibiotic is available, evaluate for hearing loss frequently during therapy and ensure that all appropriate precautions are utilized (e.g., lowest possible dose and duration, utilization of therapeutic drug monitoring, hydration, renal function monitoring).

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for the use of aminoglycosides based on MT-RNR1 genotype. [PMID:34032273] *Clinical pharmacology and therapeutics*. 2021.

pravastatin

SLCO1B1: *1/*1 Two normal function alleles
rs4149056T/rs4149056T

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	population general
Implication for SLCO1B1	Typical myopathy risk and statin exposure
Matched Diplotypes	SLCO1B1:*1/*1
Phenotype for SLCO1B1	Normal Function
Recommendation	Prescribe desired starting dose and adjust doses based on disease-specific guidelines.
Classification of Recommendation	Strong
Comments	The potential for drug-drug interactions and dose limits based on renal and hepatic function and ancestry should be evaluated prior to initiating a statin.

For more information read the guideline on cpicpgx.org.

Citations:

- The Clinical Pharmacogenomics Implementation Consortium: Guideline for SLCO1B1 and Simvastatin-Induced Myopathy [PMID:22617227] *Clinical pharmacology and therapeutics*. 2012.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update [PMID:24918167] *Clinical pharmacology and therapeutics*. 2014.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1, ABCG2, and CYP2C9 and statin-associated musculoskeletal symptoms. [PMID:35152405] *Clinical pharmacology and therapeutics*. 2022.

rasburicase

G6PD: B (wildtype)/B (wildtype) Two normal function alleles (from Outside Call)

Type	Annotation
Population	general
Implication for G6PD	Low or reduced risk of hemolytic anemia
Matched Diplotypes	G6PD:B (wildtype)/B (wildtype)
Phenotype for G6PD	Normal
Recommendation	No reason to withhold rasburicase based on G6PD status.
Classification of Recommendation	Strong
Comments	A negative or inconclusive genetic test cannot be assumed to indicate normal G6PD phenotype; an enzyme actiity test is needed to assign G6PD phenotype in such cases.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for Rasburicase Therapy in the context of G6PD Deficiency Genotype [PMID:24787449] *Clinical pharmacology and therapeutics*. 2014.

rosuvastatin

ABCG2: rs2231142 reference (G)/rs2231142 reference (G) Two normal function alleles
SLCO1B1: *1/*1 Two normal function alleles
rs4149056T/rs4149056T

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for ABCG2	Typical myopathy risk and rosuvastatin exposure
Implication for SLCO1B1	Typical myopathy risk and statin exposure
Matched Diplotypes	ABCG2:rs2231142 reference (G)/rs2231142 reference (G), SLCO1B1:*1/*1
Phenotype for ABCG2	Normal Function
Phenotype for SLCO1B1	Normal Function
Recommendation	Prescribe desired starting dose and adjust doses of rosuvastatin based on disease-specific and specific population guidelines.
Classification of Recommendation	Strong
Comments	The potential for drug-drug interactions and dose limits based on renal and hepatic function and Asian ancestry should be evaluated prior to initiating rosuvastatin.

For more information read the guideline on cpicpgx.org.

Citations:

- The Clinical Pharmacogenomics Implementation Consortium: Guideline for SLCO1B1 and Simvastatin-Induced Myopathy [PMID:22617227] *Clinical pharmacology and therapeutics*. 2012.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update [PMID:24918167] *Clinical pharmacology and therapeutics*. 2014.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1, ABCG2, and CYP2C9 and statin-associated musculoskeletal symptoms. [PMID:35152405] *Clinical pharmacology and therapeutics*. 2022.

sertraline

CYP2C19: *38/*38 Two normal function alleles

Type	Annotation
Population	general
Implication for CYP2C19	Normal metabolism
Matched Diplotypes	CYP2C19:*38/*38
Phenotype for CYP2C19	Normal Metabolizer
Recommendation	Initiate therapy with recommended starting dose
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors [PMID:25974703] *Clinical pharmacology and therapeutics*. 2015.

sevoflurane

CACNA1S: Reference/Reference Two normal function alleles
RYR1: Reference/Reference Two normal function alleles

Type	Annotation
Population	general
Implication for RYR1	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Implication for CACNA1S	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Matched Diplotypes	CACNA1S:Reference/Reference, RYR1:Reference/Reference
Phenotype for RYR1	Uncertain Susceptibility
Phenotype for CACNA1S	Uncertain Susceptibility
Recommendation	Clinical findings, family history, further genetic testing and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for the use of potent volatile anesthetic agents and succinylcholine in the context of RYR1 or CACNA1S genotypes [PMID:30499100] *Clinical pharmacology and therapeutics*. 2018.

simvastatin

SLCO1B1: *1/*1 Two normal function alleles
rs4149056T/rs4149056T

The SLCO1B1 genotype (star nomenclature) will be displayed if determinable with the provided VCF based on the SLCO1B1 star allele definition published by CPIC and recommendations are provided based on the genotype.

In case no genotype can be determined, recommendations are based on the rs4149056 genotype alone as per guideline. The minor C allele at rs4149056 defines SLCO1B1*5.

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for SLCO1B1	Typical myopathy risk and statin exposure
Matched Diplotypes	SLCO1B1:*1/*1
Phenotype for SLCO1B1	Normal Function
Recommendation	Prescribe desired starting dose and adjust doses based on disease-specific guidelines.
Classification of Recommendation	Strong
Comments	The potential for drug-drug interactions and dose limits based on renal and hepatic function and ancestry should be evaluated prior to initiating a statin.

For more information read theguideline on cpicpgx.org.

Citations:

- The Clinical Pharmacogenomics Implementation Consortium: Guideline for SLCO1B1 and Simvastatin-Induced Myopathy [PMID:22617227] *Clinical pharmacology and therapeutics*. 2012.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1 and simvastatin-induced myopathy: 2014 update [PMID:24918167] *Clinical pharmacology and therapeutics*. 2014.
- The Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for SLCO1B1, ABCG2, and CYP2C9 and statin-associated musculoskeletal symptoms. [PMID:35152405] *Clinical pharmacology and therapeutics*. 2022.

streptomycin

MT-RNR1: 1555A>G increased risk of aminoglycoside-induced hearing loss (from Outside Call)

Type	Annotation
Population	general
Implication for MT-RNR1	Very high risk of developing hearing loss if administered an aminoglycoside antibiotic.
Matched Diplotypes	MT-RNR1:1555A>G
Phenotype for MT-RNR1	increased risk of aminoglycoside-induced hearing loss
Recommendation	Avoid aminoglycoside anitbiotics unless the high risk of permanent hearing loss is outweighed by the severity of infection and lack of safe or effective alternative therapies.
Classification of Recommendation	Strong
Comments	If no effective alternative to an aminoglycoside antibiotic is available, evaluate for hearing loss frequently during therapy and ensure that all appropriate precautions are utilized (e.g., lowest possible dose and duration, utilization of therapeutic drug monitoring, hydration, renal function monitoring).

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for the use of aminoglycosides based on MT-RNR1 genotype. [PMID:34032273] *Clinical pharmacology and therapeutics*. 2021.

succinylcholine

CACNA1S: Reference/Reference Two normal function alleles
RYR1: Reference/Reference Two normal function alleles

Type	Annotation
Population	general
Implication for RYR1	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Implication for CACNA1S	These results do not eliminate the chance that this patient is susceptible to malignant hyperthermia (MH). The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown (PMID 28902675).
Matched Diplotypes	CACNA1S:Reference/Reference, RYR1:Reference/Reference
Phenotype for RYR1	Uncertain Susceptibility
Phenotype for CACNA1S	Uncertain Susceptibility
Recommendation	Clinical findings, family history, further genetic testing and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants.

Type	Annotation
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for the use of potent volatile anesthetic agents and succinylcholine in the context of RYR1 or CACNA1S genotypes [PMID:30499100] *Clinical pharmacology and therapeutics*. 2018.

tacrolimus

CYP3A5: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP3A5	Lower dose-adjusted trough concentrations of tacrolimus and decreased chance of achieving target tacrolimus concentrations.
Matched Diplotypes	CYP3A5:*1/*1
Phenotype for CYP3A5	Normal Metabolizer
Recommendation	Increase starting dose 1.5 to 2 times recommended starting dose. Total starting dose should not exceed 0.3 mg/kg/day. Use therapeutic drug monitoring to guide dose adjustments.
Classification of Recommendation	Strong
Comments	This recommendation includes the use of tacrolimus in kidney, heart, lung and hematopoietic stem cell transplant patients, and liver transplant patients where the donor and recipient genotypes are identical. Further dose adjustments or selection of alternative therapy may be necessary due to other clinical factors (e.g., medication interactions, or hepatic function). Typically with other CYP enzymes, a normal metabolizer would be classified as having normal metabolism, and therefore, the drug dose would not change based on the patientâ€™s genotype. However, in the case of CYP3A5 and tacrolimus, a CYP3A5 expresser (i.e., CYP3A5 normal metabolizer or intermediate metabolizer) would require a higher recommended starting dose, and the CYP3A5 non-expresser (i.e., poor metabolizer) would require the standard recommended starting dose.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical pharmacogenetics implementation consortium (CPIC) guidelines for CYP3A5 genotype and tacrolimus dosing [PMID:25801146] *Clinical pharmacology and therapeutics*. 2015.

tamoxifen

CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Lower endoxifen concentrations compared to normal metabolizers; higher risk of breast cancer recurrence, event-free and recurrence-free survival compared to normal metabolizers.
Matched Diplotypes	CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Activity Score for CYP2D6	1.0
Recommendation	Consider hormonal therapy such as an aromatase inhibitor for postmenopausal women or aromatase inhibitor along with ovarian function suppression in premenopausal women, given that these approaches are superior to tamoxifen regardless of CYP2D6 genotype (PMID 26211827). If aromatase inhibitor use is contraindicated, consideration should be given to use a higher but FDA approved tamoxifen dose (40 mg/day)(PMID 27226358). Avoid CYP2D6 strong to weak inhibitors.
Classification of Recommendation	Optional

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and Tamoxifen Therapy. [PMID:29385237] *Clinical pharmacology and therapeutics*. 2018.

tenoxicam

CYP2C9: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2C9	Normal metabolism

Type	Annotation
Matched Diplotypes	CYP2C9:*1/*1
Phenotype for CYP2C9	Normal Metabolizer
Activity Score for CYP2C9	2.0
Recommendation	Initiate therapy with recommended starting dose. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.
Classification of Recommendation	Strong

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C9 and Nonsteroidal Anti-inflammatory Drugs. [PMID:32189324] *Clinical pharmacology and therapeutics*. 2020.

thioguanine

NUDT15: *1/*1 Two normal function alleles
TPMT: *1/*1 Two normal function alleles

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for TPMT	Lower concentrations of TGN metabolites, but note that TGN after thioguanine are 5-10X higher than TGN after mercaptopurine or azathioprine. Normal risk of thiopurine-related leukopenia, neutropenia, myelosuppression.
Implication for NUDT15	Normal risk of thiopurine-related leukopenia, neutropenia, myelosuppression
Matched Diplotypes	NUDT15:*1/*1, TPMT:*1/*1
Phenotype for TPMT	Normal Metabolizer
Phenotype for NUDT15	Normal Metabolizer
Recommendation	Start with normal starting dose (e.g., 40-60 mg/m2/day) and adjust doses of thioguanine and of other myelosuppressive therapy without any special emphasis on thioguanine. Allow 2 weeks to reach steady-state after each dose adjustment (PMID 20354201, 11037857).
Classification of Recommendation	Strong

Type	Annotation
Comments	Normal starting doses vary by race/ethnicity and treatment regimens. If standard dose is below normal recommended dose, dose reduction might not be recommended for intermediate metabolizers.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical pharmacogenetics implementation consortium guidelines for thiopurine methyltransferase genotype and thiopurine dosing [PMID:21270794] *Clinical pharmacology and therapeutics*. 2011.
- Clinical Pharmacogenetics Implementation Consortium Guidelines for Thiopurine Methyltransferase Genotype and Thiopurine Dosing: 2013 Update [PMID:23422873] *Clinical pharmacology and therapeutics*. 2013.
- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for thiopurine dosing based on TPMT and NUDT15 genotypes: 2018 update. [PMID:30447069] *Clinical pharmacology and therapeutics*. 2018.

tobramycin

MT-RNR1: 1555A>G increased risk of aminoglycoside-induced hearing loss (from Outside Call)

Type	Annotation
Population	general
Implication for MT-RNR1	Very high risk of developing hearing loss if administered an aminoglycoside antibiotic.
Matched Diplotypes	MT-RNR1:1555A>G
Phenotype for MT-RNR1	increased risk of aminoglycoside-induced hearing loss
Recommendation	Avoid aminoglycoside anitbiotics unless the high risk of permanent hearing loss is outweighed by the severity of infection and lack of safe or effective alternative therapies.
Classification of Recommendation	Strong
Comments	If no effective alternative to an aminoglycoside antibiotic is available, evaluate for hearing loss frequently during therapy and ensure that all appropriate precautions are utilized (e.g., lowest possible dose and duration, utilization of therapeutic drug monitoring, hydration, renal function monitoring).

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for the use of aminoglycosides based on MT-RNR1 genotype. [PMID:34032273] *Clinical pharmacology and therapeutics*. 2021.

tramadol

CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Reduced O-desmethyltramadol (active metabolite) formation
Matched Diplotypes	CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Activity Score for CYP2D6	1
Recommendation	Use tramadol label recommended age- or weight-specific dosing. If no response and opioid use is warranted, consider non-codeine opioid.
Classification of Recommendation	Optional

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guidelines for Codeine Therapy in the Context of Cytochrome P450 2D6 (CYP2D6) Genotype [PMID:22205192] *Clinical pharmacology and therapeutics*. 2011.
- Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for cytochrome P450 2D6 (CYP2D6) genotype and codeine therapy: 2014 Update [PMID:24458010] *Clinical pharmacology and therapeutics*. 2014.
- Clinical Pharmacogenetics Implementation Consortium (CPIC) guideline for CYP2D6, OPRM1, and COMT genotype and select opioid therapy. [PMID:33387367] *Clinical pharmacology and therapeutics*. 2021.

trimipramine

CYP2C19: *38/*38 Two normal function alleles
CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Reduced metabolism of TCAs to less active compounds compared to normal metabolizers; Higher plasma concentrations of active drug will increase the probability of side effects
Implication for CYP2C19	Normal metabolism of tertiary amines
Matched Diplotypes	CYP2C19:*38/*38, CYP2D6:*1/*3

Type	Annotation
Phenotype for CYP2D6	Intermediate Metabolizer
Phenotype for CYP2C19	Normal Metabolizer
Activity Score for CYP2D6	1.0
Recommendation	Consider a 25% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.
Classification of Recommendation	Optional
Comments	Patients may receive an initial low dose of a tricyclic, which is then increased over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose. Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression. See other considerations for dosing recommendations for conditions where lower initial doses are used, such as neuropathic pain.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium Guideline (CPICÂ®) for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants: 2016 Update [PMID:27997040] *Clinical pharmacology and therapeutics*. 2016.
- Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Tricyclic Antidepressants [PMID:23486447] *Clinical pharmacology and therapeutics*. 2013.

tropisetron

CYP2D6: *1/*3 One no function allele and one normal function allele (from Outside Call)

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

Type	Annotation
Population	general
Implication for CYP2D6	Very limited data available for CYP2D6 intermediate metabolizers
Matched Diplotypes	CYP2D6:*1/*3
Phenotype for CYP2D6	Intermediate Metabolizer
Activity Score for CYP2D6	1.0
Recommendation	Insufficient evidence demonstrating clinical impact based on CYP2D6 genotype. Initiate therapy with recommended starting dose.
Classification of Recommendation	No Recommendation

Type	Annotation
Comments	Drug-drug interactions and other patient characteristics (e.g., age, renal function, and liver function) should be considered when selecting alternative therapy.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 Genotype and Use of Ondansetron and Tropisetron [PMID:28002639] *Clinical pharmacology and therapeutics*. 2016.

voriconazole

CYP2C19: *38/*38 Two normal function alleles

Type	Annotation
Population	adults
Implication for CYP2C19	Normal voriconazole metabolism
Matched Diplotypes	CYP2C19:*38/*38
Phenotype for CYP2C19	Normal Metabolizer
Recommendation	Initiate therapy with recommended standard of care dosing
Classification of Recommendation	Strong
Comments	Further dose adjustments or selection of alternative therapy may be necessary due to other clinical factors, such as drug interactions, hepatic function, renal function, species, site of infection, therapeutic drug monitoring, and comorbidities.

Type	Annotation
Population	pediatrics
Implication for CYP2C19	Normal voriconazole metabolism
Matched Diplotypes	CYP2C19:*38/*38
Phenotype for CYP2C19	Normal Metabolizer
Recommendation	Initiate therapy with recommended standard of care dosing
Classification of Recommendation	Strong
Comments	Further dose adjustments or selection of alternative therapy may be necessary due to other clinical factors, such as drug interactions, hepatic function, renal function, species, site of infection, therapeutic drug monitoring, and comorbidities.

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPICÂ®) Guideline for CYP2C19 and Voriconazole Therapy [PMID:27981572] *Clinical pharmacology and therapeutics*. 2016.

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warfarin

CYP2C9: *1/*1 Two normal function alleles
CYP4F2: *1/*1 N/A
VKORC1: rs9923231 reference (C)/rs9923231 reference (C) N/A
rs12777823: G|G

Please follow the flow chart in figure 2 of the CPIC warfarin guideline to determine the appropriate dosing recommendation.

The *1 allele assignment is characterized by the absence of variants that are included in the underlying allele definitions by either position being reference or missing.

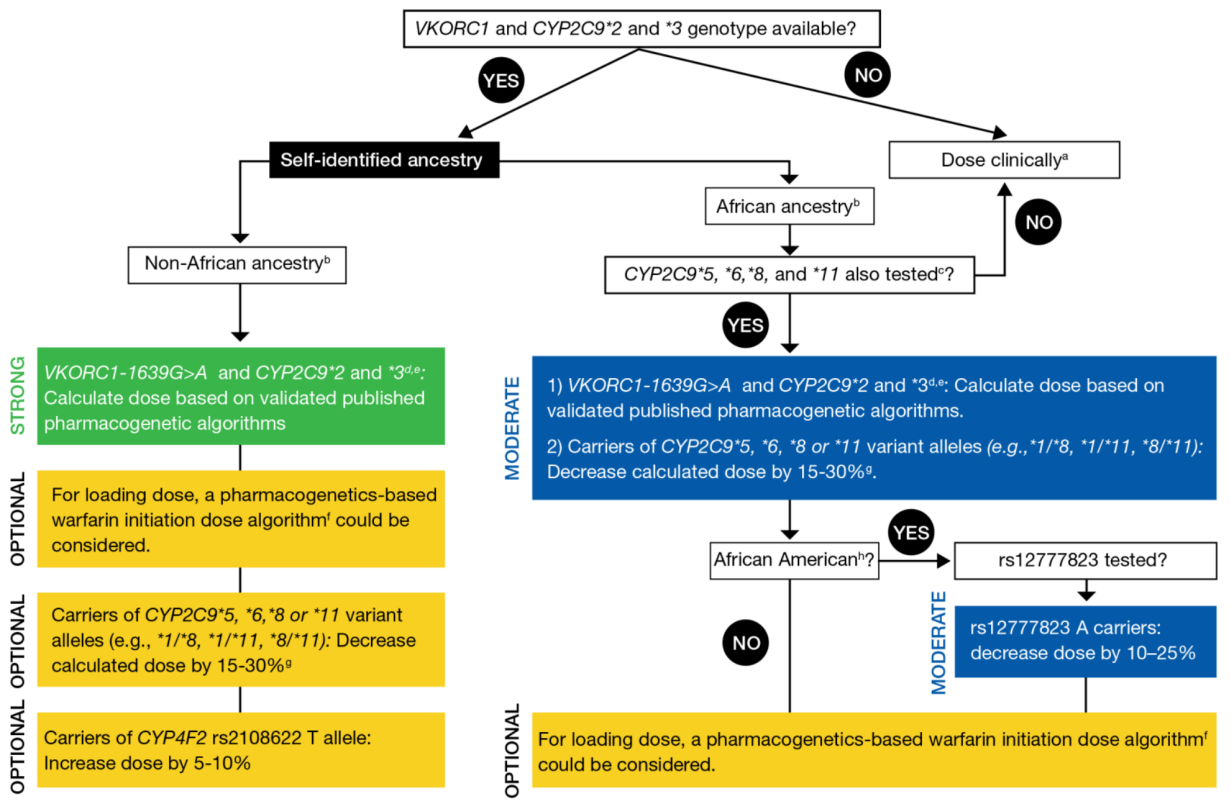

FIGURE 2. DOSING RECOMMENDATIONS FOR WARFARIN DOSING BASED ON GENOTYPE FOR ADULT PATIENTS

(a) "Dose clinically" means to dose without genetic information, which may include use of a clinical dosing algorithm or standard dose approach
(b) Data strongest for European and East Asian ancestry populations and consistent in other populations.
(c) 45-50% of individuals with self-reported African ancestry carry CYP2C9*5,*6,*8,*11, or rs12777823. IF CYP2C9*5, *6, *8, and *11 WERE NOT TESTED, DOSE WARFARIN CLINICALLY. Note: these data derive primarily from African Americans, who are largely from West Africa. It is unknown if the same associations are present for those from other parts of Africa.
(d) Most algorithms are developed for the target INR 2-3.
(e) Consider an alternative agent in individuals with genotypes associated with CYP2C9 poor metabolism (e.g., CYP2C9*3/*3, *2/*3, *3/*3) or both increased sensitivity (VKORC1 A/G or A/A) and CYP2C9 poor metabolism.
(f) See the EU-PACT trial for pharmacogenetics-based warfarin initiation (loading) dose algorithm (33) with the caveat that the loading dose PG algorithm has not been specifically tested or validated in populations of African ancestry.
(g) Larger dose reduction might be needed in variant homozygotes (i.e. 20-40%).
(h) African American refers to individuals mainly originating from West Africa.

The CPIC warfarin guideline only considers a single SNV in VKORC1 (rs9923231), which is found in the highest frequency in Caucasians and extremely low frequency in those of African descent. While other functional variants in VKORC1 have been observed in much higher frequencies in some populations, there are currently no CPIC recommendations for how to use these other variants in warfarin dosing. An alternate name for rs9923231 is -1639G>A (note that VKORC1 is on the negative chromosomal strand, so displayed alleles are complemented).

For more information read the guideline on cpicpgx.org.

Citations:

- Clinical Pharmacogenetics Implementation Consortium Guidelines for CYP2C9 and VKORC1 Genotypes and Warfarin Dosing [PMID:21900891] *Clinical pharmacology and therapeutics*. 2011.
- Clinical pharmacogenetics implementation consortium (cpic) guideline for pharmacogenetics-guided warfarin dosing: 2017 update [PMID:28198005] *Clinical pharmacology and therapeutics*. 2017.

Allele Matching Details

ABCG2 allele match data

Genotype matched

- rs2231142 reference (G)/rs2231142 reference (G)

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr4:88131171	rs2231142	G|G	G	rs2231142 variant (T)	

CACNA1S allele match data

Genotype matched

- Reference/Reference

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr1:201060815	rs1800559	C|C	C	c.3257G>A	
chr1:201091993	rs772226819	G|G	G	c.520C>T	

CFTR allele match data

Genotype matched

- No CPIC variants found

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr7:117509035	rs397508256	G|G	G	E56K	
chr7:117509069	rs368505753	C|C	C	P67L	
chr7:117509089	rs115545701	C|C	C	R74W	
chr7:117530953	rs113993958	G|G	G	D110H	
chr7:117530955	rs397508537	C|C	C	D110E	
chr7:117530974	rs77834169	C|C	C	R117C	
chr7:117530975	rs78655421	G|G	G	R117H	
chr7:117534318	rs80282562	G|G	G	G178R	
chr7:117534363	rs397508759	G|G	G	E193K	
chr7:117534368	rs397508761	A|A	A	711+3A->G	
chr7:117535285	rs121908752	T|T	T	L206W	
chr7:117540270	rs77932196	G|G	G	R347H	
chr7:117540285	rs121908753	G|G	G	R352Q	
chr7:117548795	rs74551128	C|C	C	A455E	
chr7:117587799	rs121908757	A|A	A	S549R(A>C)	
chr7:117587800	rs121908755	G|G	G	S549N	
chr7:117587801	rs121909005	T|T	T	S549R(T>G)	
chr7:117587805	rs121909013	G|G	G	G551S	

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr7:117587806	rs75527207	G|G	G	G551D	
chr7:117590409	rs397508288	A|A	A	D579G	
chr7:117594930	rs397508387	G|G	G	E831X	
chr7:117602868	rs80224560	G|G	G	2789+5G->A	
chr7:117603708	rs397508442	C|C	C	S945L	
chr7:117606695	rs141033578	C|C	C	S977F	
chr7:117611555	rs76151804	A|A	A	3272-26A->G	
chr7:117611595	rs150212784	T|T	T	F1052V	
chr7:117611620	rs397508513	A|A	A	K1060T	
chr7:117611640	rs121909020	G|G	G	A1067T	
chr7:117611646	rs200321110	G|G	G	G1069R	
chr7:117611649	rs202179988	C|C	C	R1070W	
chr7:117611650	rs78769542	G|G	G	R1070Q	
chr7:117611663	rs186045772	T|T	T	F1074L	
chr7:117614699	rs75541969	G|G	G	D1152H	
chr7:117639961	rs75039782	C|C	C	3849+10kbC->T	
chr7:117642451	rs267606723	G|G	G	G1244E	
chr7:117642472	rs74503330	G|G	G	S1251N	
chr7:117642483	rs121909041	T|T	T	S1255P	
chr7:117642528	rs11971167	G|G	G	D1270N	
chr7:117664770	rs193922525	G|G	G	G1349D	

CYP2B6 allele match data

Genotype matched

- *1/*1

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr19:40991224	rs34223104	T|T	T	*22 *34 *35 *36	
chr19:40991367	rs34883432	A|A	A	*10	
chr19:40991369	rs8192709	C|C	C	*2 *10	
chr19:40991381	rs33973337	A|A	A	*17	
chr19:40991388	rs33980385	A|A	A	*17	
chr19:40991390	rs33926104	C|C	C	*17	
chr19:40991391	rs34284776	G|G	G	*17	
chr19:40991441	rs35303484	A|A	A	*11	
chr19:41004015	rs281864907	T|T	T	*38	
chr19:41004125	rs36060847	G|G	G	*12	
chr19:41004158	rs186335453	G|G	G	*35	
chr19:41004303	rs139801276	T|T	T	*35	
chr19:41004377	rs12721655	A|A	A	*8 *13	
chr19:41004381	rs35773040	G|G	G	*14	
chr19:41004406	rs145884402	G|G	G	*35	
chr19:41006919	rs3826711	C|C	C	*26	
chr19:41006923	rs36056539	C|C	C	*20	
chr19:41006936	rs3745274	G|G	G	*6 *7 *9 *13 *19 *20 *26 *34 *36 *37 *38	
chr19:41006968	rs373489637	T|T	T	*37	
chr19:41007013	rs36079186	T|T	T	*27 *35	
chr19:41009350	rs45482602	C|C	C	*3	
chr19:41009358	rs2279343	A|A	A	*4 *6 *7 *13 *18 *19 *20 *26 *34 *36 *37 *38	
chr19:41010006	rs139029625	G|G	G	*35	
chr19:41010088	rs34698757	C|C	C	*28	
chr19:41010108	rs193922917	C|C	C	*31	
chr19:41012316	rs28399499	T|T	T	*18	
chr19:41012339	rs34826503	C|C	C	*19	

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr19:41012465	rs34097093	C|C	C	*28	
chr19:41012693	rs35979566	T|T	T	*15	
chr19:41012740	rs193922918	G|G	G	*32	
chr19:41012803	rs35010098	C|C	C	*21	
chr19:41016726	rs3211369	A|A	A	*23	
chr19:41016778	rs564083989	G|G	G	*24	
chr19:41016805		A|A	A	*25	
chr19:41016810	rs3211371	C|C	C	*5 *7 *33 *34	

CYP2C19 allele match data

Genotype matched

- *38/*38

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr10:94761900	rs12248560	C|C	C	*4 *17	
chr10:94762706	rs28399504	A|A	A	*4	
chr10:94762712	rs367543002	C|C	C	*34	
chr10:94762715	rs367543003	T|T	T	*34	
chr10:94762755	rs55752064	T|T	T	*14	
chr10:94762760	rs17882687	A|A	A	*15 *28 *35 *39	
chr10:94762788	rs1564656981	A|A	A	*29	
chr10:94762856	rs1564657013	A|A	A	*19	
chr10:94775106	rs145328984	C|C	C	*30	
chr10:94775121	rs1564660997	C|C	C	*31	
chr10:94775160	rs118203756	G|G	G	*23	

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr10:94775185	rs1288601658	A|A	A	*32	
chr10:94775367	rs12769205	A|A	A	*2 *35	
chr10:94775416	rs41291556	T|T	T	*8	
chr10:94775423	rs17885179	A|A	A	*39	
chr10:94775453	rs72552267	G|G	G	*6	
chr10:94775489	rs17884712	G|G	G	*9	
chr10:94775507	rs58973490	G|G	G	*2 *11	
chr10:94780574	rs140278421	G|G	G	*22	
chr10:94780579	rs370803989	G|G	G	*33	
chr10:94780653	rs4986893	G|G	G	*3	
chr10:94781858	rs6413438	C|C	C	*10	
chr10:94781859	rs4244285	G|G	G	*2	
chr10:94781944	rs375781227	G|G	G	*26	
chr10:94781999	rs72558186	T|T	T	*7	
chr10:94842861	rs138142612	G|G	G	*18	
chr10:94842866	rs3758581	A|A	A	*2 *3 *4 *5 *6 *8 *9 *10 *11 *12 *13 *14 *15 *17 *18 *19 *22 *23 *24 *25 *26 *28 *29 *31 *32 *33 *35 *39	
chr10:94842879	rs118203757	G|G	G	*24	
chr10:94842995	rs113934938	G|G	G	*28	
chr10:94849995	rs17879685	C|C	C	*13	
chr10:94852738	rs56337013	C|C	C	*5	
chr10:94852765	rs192154563	C|C	C	*16	
chr10:94852785	rs118203759	C|C	C	*25	
chr10:94852914	rs55640102	A|A	A	*12	

CYP2C9 allele match data

Genotype matched

- *1/*1

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr10:94938683	rs114071557	A|A	A	*36	
chr10:94938737	rs67807361	C|C	C	*7	
chr10:94938771	rs142240658	C|C	C	*21	
chr10:94938803	rs2031308986	A|A	A	*22	
chr10:94938828	rs564813580	A|A	A	*37	
chr10:94941897	rs371055887	G|G	G	*20	
chr10:94941915		G|G	G	*23	
chr10:94941958	rs72558187	T|T	T	*13	
chr10:94941976		G|G	G	*38	
chr10:94941982	rs762239445	G|G	G	*39	
chr10:94942018		T|T	T	*40	
chr10:94942205	rs1304490498	CAATGGAAAGA|CAATGGAAAGA	CAATGGAAAGA	*25	
chr10:94942216	rs774607211	A|A	A	*41	
chr10:94942230	rs767576260	C|C	C	*43	
chr10:94942231	rs12414460	G|G	G	*42	
chr10:94942233	rs375805362	C|C	C	*62	
chr10:94942234	rs72558189	G|G	G	*14 *35	
chr10:94942249	rs200965026	C|C	C	*26 *44	
chr10:94942254	rs199523631	C|C	C	*45	
chr10:94942255	rs200183364	G|G	G	*33	
chr10:94942290	rs1799853	C|C	C	*2 *35 *61	
chr10:94942291	rs141489852	G|G	G	*63	
chr10:94942305	rs754487195	G|G	G	*46	

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr10:94942306	rs1289704600	C|C	C	*72	
chr10:94942308	rs17847037	C|C	C	*73	
chr10:94942309	rs7900194	G|G	G	*8 *27	
chr10:94947439		G|G	G	*74	
chr10:94947782	rs72558190	C|C	C	*15	
chr10:94947785	rs774550549	C|C	C	*47	
chr10:94947869		A|A	A	*69	
chr10:94947907		A|A	A	*57	
chr10:94947917	rs1326630788	T|T	T	*48	
chr10:94947938	rs2031531005	A|A	A	*28	
chr10:94949129		A|A	A	*49	
chr10:94949144		C|C	C	*50	
chr10:94949217	rs2256871	A|A	A	*9	
chr10:94949280	rs9332130	A|A	A	*10 *71	
chr10:94949281	rs9332131	GA|GA	GA	*6	
chr10:94972119	rs182132442	C|C	C	*29	
chr10:94972123		C|C	C	*64	
chr10:94972134		A|A	A	*51	
chr10:94972179	rs72558192	A|A	A	*16	
chr10:94972180	rs988617574	C|C	C	*52	
chr10:94972233	rs1237225311	C|C	C	*53	
chr10:94981199		G|G	G	*65	
chr10:94981201	rs57505750	T|T	T	*31	
chr10:94981224	rs28371685	C|C	C	*11	
chr10:94981225	rs367826293	G|G	G	*34	
chr10:94981230	rs1274535931	C|C	C	*58	
chr10:94981250	rs750820937	C|C	C	*54	

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr10:94981281	rs749060448	G|G	G	*24	
chr10:94981296	rs1057910	A|A	A	*3 *18 *68	
chr10:94981297	rs56165452	T|T	T	*4	
chr10:94981301	rs28371686	C|C	C	*5	
chr10:94981302	rs1250577724	C|C	C	*55	
chr10:94981305	rs578144976	C|C	C	*66	
chr10:94981365		C|C	C	*17	
chr10:94981371	rs542577750	G|G	G	*68	
chr10:94986042	rs764211126	A|A	A	*56	
chr10:94986073	rs72558193	A|A	A	*18	
chr10:94986136	rs1254213342	A|A	A	*75	
chr10:94988852	rs776908257	C|C	C	*67	
chr10:94988855		A|A	A	*59	
chr10:94988880		G|G	G	*70	
chr10:94988917	rs769942899	G|G	G	*19	
chr10:94988925	rs202201137	A|A	A	*61	
chr10:94988955	rs767284820	T|T	T	*60	
chr10:94988984	rs781583846	G|G	G	*30	
chr10:94989020	rs9332239	C|C	C	*12 *71	
chr10:94989023	rs868182778	G|G	G	*32	

Other Positions of Interest

Position in VCF	RSID	Call in VCF
chr10:94645745	rs12777823	G|G

CYP2D6 allele match data

Genotype reported

- *1/*3

Phasing status: Unavailable for calls made outside PharmCAT

The call for CYP2D6 comes from an outside data source which does not supply position-level detail. For specific disclaimers and limitations, see the original genotyping source.

No variant data available.

CYP2D6 genotypes are called by a separate algorithm from other genes in the PharmCAT report. Please refer to the PharmCAT wiki for more information.

CYP3A5 allele match data

Genotype matched

- *1/*1

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr7:99652770	rs41303343	T|T	T	*7	
chr7:99660516	rs28383479	C|C	C	*9	
chr7:99665212	rs10264272	C|C	C	*6	
chr7:99672916	rs776746	T|T	T	*3	
chr7:99676198	rs55817950	G|G	G	*8	

CYP4F2 allele match data

Genotype matched

- *1/*1

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr19:15879621	rs2108622	C|C	C	*3	
chr19:15897578	rs3093105	A|A	A	*2	

DPYD allele match data

Genotype matched

- Reference/Reference

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr1:97078987	rs114096998	G|G	G	c.3067C>A	
chr1:97078993	rs148799944	C|C	C	c.3061G>C	
chr1:97079005	rs140114515	C|C	C	c.3049G>A	
chr1:97079071	rs1801268	C|C	C	c.2983G>T (*10)	
chr1:97079076	rs139459586	A|A	A	c.2978T>G	
chr1:97079077	rs202144771	G|G	G	c.2977C>T	
chr1:97079121	rs72547601	T|T	T	c.2933A>G	
chr1:97079133	rs72547602	T|T	T	c.2921A>T	
chr1:97079139	rs145529148	T|T	T	c.2915A>G	
chr1:97082365	rs141044036	T|T	T	c.2872A>G	
chr1:97082391	rs67376798	T|T	T	c.2846A>T	
chr1:97098598	rs1801267	C|C	C	c.2657G>A (*9B)	
chr1:97098599	rs147545709	G|G	G	c.2656C>T	
chr1:97098616	rs55674432	C|C	C	c.2639G>T	
chr1:97098632	rs201035051	T|T	T	c.2623A>C	
chr1:97193109	rs60139309	T|T	T	c.2582A>G	
chr1:97193209	rs200687447	C|C	C	c.2482G>A	
chr1:97234958	rs199634007	G|G	G	c.2336C>A	
chr1:97234991	rs56005131	G|G	G	c.2303C>A	
chr1:97305279	rs112766203	G|G	G	c.2279C>T	
chr1:97305363	rs60511679	A|A	A	c.2195T>G	
chr1:97305364	rs1801160	C|C	C	c.2194G>A (*6)	
chr1:97305372	rs146529561	G|G	G	c.2186C>T	

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr1:97306195	rs145548112	C|C	C	c.2161G>A	
chr1:97373598	rs137999090	C|C	C	c.2021G>A	
chr1:97373629	rs138545885	C|C	C	c.1990G>T	
chr1:97382461	rs55971861	T|T	T	c.1906A>C	
chr1:97450058	rs3918290	C|C	C	c.1905+1G>A (*2A)	
chr1:97450059	rs3918289	G|G	G	c.1905C>G	
chr1:97450065	rs72549303	TG|TG	TG	c.1898delC (*3)	
chr1:97450068	rs17376848	A|A	A	c.1896T>C	
chr1:97450168	rs147601618	A|A	A	c.1796T>C	
chr1:97450187	rs145773863	C|C	C	c.1777G>A	
chr1:97450189	rs138616379	C|C	C	c.1775G>A	
chr1:97450190	rs59086055	G|G	G	c.1774C>T	
chr1:97515784	rs201615754	C|C	C	c.1682G>T	
chr1:97515787	rs55886062	A|A	A	c.1679T>G (*13)	
chr1:97515839	rs1801159	T|T	T	c.1627A>G (*5)	
chr1:97515851	rs142619737	C|C	C	c.1615G>A	
chr1:97515865	rs1801158	C|C	C	c.1601G>A (*4)	
chr1:97515889	rs190951787	G|G	G	c.1577C>G	
chr1:97515923	rs148994843	C|C	C	c.1543G>A	
chr1:97549565	rs138391898	C|C	C	c.1519G>A	
chr1:97549600	rs111858276	T|T	T	c.1484A>G	
chr1:97549609	rs72549304	G|G	G	c.1475C>T	
chr1:97549681	rs199549923	G|G	G	c.1403C>A	
chr1:97549713	rs57918000	G|G	G	c.1371C>T	
chr1:97549726	rs144395748	G|G	G	c.1358C>G	
chr1:97549735	rs72975710	G|G	G	c.1349C>T	
chr1:97573785	rs186169810	A|A	A	c.1314T>G	

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr1:97573805	rs142512579	C|C	C	c.1294G>A	
chr1:97573821	rs764666241	C|C	C	c.1278G>T	
chr1:97573839	rs200064537	A|A	A	c.1260T>A	
chr1:97573863	rs56038477	C|C	C	c.1129-5923C>G, c.1236G>A (HapB3)	
chr1:97573881	rs61622928	C|C	C	c.1218G>A	
chr1:97573918	rs143815742	C|C	C	c.1181G>T	
chr1:97573919	rs140602333	G|G	G	c.1180C>T	
chr1:97573943	rs78060119	C|C	C	c.1156G>T (*12)	
chr1:97579893	rs75017182	G|G	G	c.1129-5923C>G, c.1236G>A (HapB3)	
chr1:97593238	rs72549305	T|T	T	c.1108A>G	
chr1:97593289	rs143154602	G|G	G	c.1057C>T	
chr1:97593322	rs183385770	C|C	C	c.1024G>A	
chr1:97593343	rs72549306	C|C	C	c.1003G>T (*11)	
chr1:97593379	rs201018345	C|C	C	c.967G>A	
chr1:97595083	rs145112791	G|G	G	c.934C>T	
chr1:97595088	rs150437414	A|A	A	c.929T>C	
chr1:97595149	rs146356975	T|T	T	c.868A>G	
chr1:97679170	rs45589337	T|T	T	c.775A>G	
chr1:97691776	rs1801266	G|G	G	c.703C>T (*8)	
chr1:97699399	rs72549307	T|T	T	c.632A>G	
chr1:97699430	rs72549308	T|T	T	c.601A>C	
chr1:97699474	rs115232898	T|T	T	c.557A>G	
chr1:97699506	rs6670886	C|C	C	c.525G>A	
chr1:97699533	rs139834141	C|C	C	c.498G>A	
chr1:97699535	rs2297595	T|T	T	c.496A>G	
chr1:97721542	rs200562975	T|T	T	c.451A>G	
chr1:97721650	rs141462178	T|T	T	c.343A>G	

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr1:97740400	rs150385342	C|C	C	c.313G>A	
chr1:97740410	rs72549309	GATGA|GATGA	GATGA	c.295_298delTCAT (*7)	
chr1:97883329	rs1801265	A|A	A	c.85T>C (*9A)	
chr1:97883352	rs80081766	C|C	C	c.62G>A	
chr1:97883353	rs72549310	G|G	G	c.61C>T	
chr1:97883368	rs150036960	G|G	G	c.46C>G	

G6PD allele match data

Genotype reported

- B (wildtype)/B (wildtype)

Phasing status: Unavailable for calls made outside PharmCAT

The call for G6PD comes from an outside data source which does not supply position-level detail. For specific disclaimers and limitations, see the original genotyping source.

No variant data available.

IFNL3/4 allele match data

Genotype matched

- rs12979860 reference (C)/rs12979860 reference (C)

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr19:39248147	rs12979860	C|C	C	rs12979860 variant (T)	

MT-RNR1 allele match data

Genotype reported

- 1555A>G

Phasing status: Unavailable for calls made outside PharmCAT

The call for MT-RNR1 comes from an outside data source which does not supply position-level detail. For specific disclaimers and

limitations, see the original genotyping source.

No variant data available.

NUDT15 allele match data

Genotype matched

- *1/*1

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr13:48037748	rs769369441	T|T	T	*10	
chr13:48037749		G|G	G	*19	
chr13:48037782	rs746071566	AGGAGTC|AGGAGTC	AGGAGTC	*2 *6 *9	
chr13:48037798	rs186364861	G|G	G	*5	
chr13:48037825	rs777311140	C|C	C	*14	
chr13:48037834	rs1202487323	C|C	C	*16	
chr13:48037847	rs766023281	G|G	G	*7	
chr13:48037849		A|A	A	*8	
chr13:48037885	rs1950545307	G|G	G	*11	
chr13:48037902	rs149436418	C|C	C	*12	
chr13:48040977	rs1457579126	GA|GA	GA	*18	
chr13:48041103	rs761191455	T|T	T	*13	
chr13:48041113	rs1368252918	G|G	G	*17	
chr13:48045690	rs768324690	C|C	C	*20	
chr13:48045719	rs116855232	C|C	C	*2 *3	
chr13:48045720	rs147390019	G|G	G	*4	
chr13:48045771	rs139551410	T|T	T	*15	

RYR1 allele match data

Genotype matched

- Reference/Reference

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr19:38440802	rs193922747	T|T	T	c.103T>C	
chr19:38440829	rs193922748	C|C	C	c.130C>T	
chr19:38444211	rs118192161	C|C	C	c.487C>T	
chr19:38444212	rs193922753	G|G	G	c.488G>T	
chr19:38446710	rs1801086	G|G	G	c.742G>A c.742G>C	
chr19:38448673	rs193922762	C|C	C	c.982C>T	
chr19:38448712	rs121918592	G|G	G	c.1021G>A c.1021G>C	
chr19:38451842	rs193922764	C|C	C	c.1201C>T	
chr19:38451850	rs118192116	C|C	C	c.1209C>G	
chr19:38455359	rs118192162	A|A	A	c.1565A>C	
chr19:38455463	rs111888148	G|G	G	c.1589G>A	
chr19:38455471	rs193922768	C|C	C	c.1597C>T	
chr19:38455472	rs144336148	G|G	G	c.1598G>A	
chr19:38455528	rs193922770	C|C	C	c.1654C>T	
chr19:38457545	rs118192172	C|C	C	c.1840C>T	
chr19:38457546	rs193922772	G|G	G	c.1841G>T	
chr19:38494564	rs118192175	C|C	C	c.6487C>T	
chr19:38494565	rs118192163	G|G	G	c.6488G>A	
chr19:38494579	rs118192176	G|G	G	c.6502G>A	
chr19:38496283	rs118192177	C|C	C	c.6617C>G c.6617C>T	
chr19:38499223	rs112563513	G|G	G	c.7007G>A	
chr19:38499644	rs121918596	TGGA|TGGA	TGGA	c.7042_7044delGAG	
chr19:38499655	rs193922802	G|G	G	c.7048G>A	

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr19:38499670	rs193922803	C|C	C	c.7063C>T	
chr19:38499731	rs193922807	G|G	G	c.7124G>C	
chr19:38499975	rs193922809	G|G	G	c.7282G>A	
chr19:38499993	rs121918593	G|G	G	c.7300G>A	
chr19:38499997	rs28933396	G|G	G	c.7304G>A	
chr19:38500636	rs118192124	C|C	C	c.7354C>T	
chr19:38500642	rs193922816	C|C	C	c.7360C>T	
chr19:38500643	rs118192122	G|G	G	c.7361G>A	
chr19:38500654	rs28933397	C|C	C	c.7372C>T	
chr19:38500655	rs121918594	G|G	G	c.7373G>A	
chr19:38500898	rs118192178	C|C	C	c.7522C>G c.7522C>T	
chr19:38500899	rs193922818	G|G	G	c.7523G>A	
chr19:38512321	rs193922832	G|G	G	c.9310G>A	
chr19:38543832	rs193922843	G|G	G	c.11969G>T	
chr19:38580004	rs118192167	A|A	A	c.14387A>G	
chr19:38580094	rs121918595	C|C	C	c.14477C>T	
chr19:38580114	rs193922876	C|C	C	c.14497C>T	
chr19:38580370	rs193922878	C|C	C	c.14512C>G	
chr19:38580403	rs118192168	G|G	G	c.14545G>A	
chr19:38580440	rs63749869	G|G	G	c.14582G>A	
chr19:38584989	rs118192170	T|T	T	c.14693T>C	

SLCO1B1 allele match data

Genotype matched

- *1/*1
- rs4149056T/rs4149056T

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr12:21172734	rs139257324	C|C	C	*33	
chr12:21172776	rs373327528	G|G	G	*23	
chr12:21172782	rs56101265	T|T	T	*2 *12	
chr12:21174595	rs56061388	T|T	T	*3 *13	
chr12:21176804	rs2306283	A|A	A	*14 *15 *20 *24 *25 *27 *28 *29 *30 *31 *32 *33 *37 *39 *42 *43 *44 *46 *47	
chr12:21176868	rs2306282	A|A	A	*16	
chr12:21176871		G|G	G	*38	
chr12:21176879	rs11045819	C|C	C	*4 *14 *25 *32 *43	
chr12:21176883	rs72559745	A|A	A	*3 *13	
chr12:21176898	rs77271279	G|G	G	*41	
chr12:21178612	rs141467543	A|A	A	*42	
chr12:21178615	rs4149056	T|T	T	*5 *15 *40 *46 *47	
chr12:21178957	rs79135870	A|A	A	*30	
chr12:21196951	rs11045852	A|A	A	*24 *25 *28 *32 *33 *43 *44	
chr12:21196975	rs183501729	C|C	C	*39	
chr12:21196976	rs11045853	G|G	G	*25 *28 *33	
chr12:21200544	rs72559747	C|C	C	*47	
chr12:21200595	rs55901008	T|T	T	*6	
chr12:21202553	rs1228465562	T|T	T	*36	
chr12:21202555	rs59113707	C|C	C	*27	
chr12:21202649	rs56387224	A|A	A	*7	
chr12:21202664	rs142965323	G|G	G	*26	
chr12:21205921	rs72559748	A|A	A	*8	
chr12:21205999	rs59502379	G|G	G	*9 *31	
chr12:21206031	rs74064213	A|A	A	*43 *44	
chr12:21222355	rs71581941	C|C	C	*45 *46	

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr12:21239042	rs34671512	A|A	A	*19 *20 *40	
chr12:21239077	rs56199088	A|A	A	*10 *12	
chr12:21239113	rs55737008	A|A	A	*11 *13	
chr12:21239145	rs200995543	C|C	C	*34	
chr12:21239158	rs140790673	C|C	C	*29	

TPMT allele match data

Genotype matched

- *1/*1

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr6:18130687	rs1142345	T|T	T	*3A *3C *41	
chr6:18130694	rs150900439	T|T	T	*20	
chr6:18130725	rs72552736	A|A	A	*7	
chr6:18130729	rs139392616	C|C	C	*40	
chr6:18130758	rs398122996	A|A	A	*37	
chr6:18130762	rs56161402	C|C	C	*8	
chr6:18130772	rs377085266	A|A	A	*25	
chr6:18130781	rs1800584	C|C	C	*4	
chr6:18132136	rs72556347	A|A	A	*26	
chr6:18132147	rs79901429	A|A	A	*31	
chr6:18132163		C|C	C	*36	
chr6:18133845	rs75543815	T|T	T	*6	
chr6:18133847	rs6921269	C|C	C	*24	
chr6:18133870	rs772832951	A|A	A	*38	

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr6:18133884	rs74423290	G|G	G	*23	
chr6:18133887	rs201695576	T|T	T	*44	
chr6:18133890	rs9333570	C|C	C	*15	
chr6:18138969	rs144041067	C|C	C	*16 *22	
chr6:18138970	rs112339338	G|G	G	*33	
chr6:18138997	rs1800460	C|C	C	*3A *3B	
chr6:18139027	rs72552737	C|C	C	*10	
chr6:18139689	rs72552738	C|C	C	*11	
chr6:18139710	rs200220210	G|G	G	*12	
chr6:18143597		T|T	T	*19	
chr6:18143606	rs151149760	T|T	T	*9	
chr6:18143613		C|C	C	*28	
chr6:18143622	rs115106679	C|C	C	*32	
chr6:18143643		A|A	A	*27	
chr6:18143700	rs753545734	C|C	C	*43	
chr6:18143718	rs111901354	G|G	G	*34	
chr6:18143724	rs1800462	C|C	C	*2	
chr6:18143728	rs1256618794	C|C	C	*43	
chr6:18147838	rs281874771	G|G	G	*39	
chr6:18147845	rs777686348	C|C	C	*18	
chr6:18147851	rs200591577	G|G	G	*21	
chr6:18147856		A|A	A	*35	
chr6:18147910	rs72552740	A|A	A	*5	
chr6:18149004		G|G	G	*17	
chr6:18149022	rs750424422	C|C	C	*30	
chr6:18149032	rs759836180	C|C	C	*42	
chr6:18149045	rs72552742	T|T	T	*13	

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr6:18149126	rs267607275	A|A	A	*29	
chr6:18149127	rs9333569	T|T	T	*14	

UGT1A1 allele match data

Genotype matched

- *1/*1

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr2:233759924	rs887829	C|C	C	*80 *80+*28 *80+*37	
chr2:233760233	rs3064744	CAT|CAT	CAT	*28 *36 *37 *80+*28 *80+*37	
chr2:233760498	rs4148323	G|G	G	*6	
chr2:233760973	rs35350960	C|C	C	*27	

VKORC1 allele match data

Genotype matched

- rs9923231 reference (C)/rs9923231 reference (C)

Phasing status: Phased

Calls at Positions

Position in VCF	RSID	Call in VCF	Reference	Related Alleles	Warnings
chr16:31096368	rs9923231	C|C	C	rs9923231 variant (T)	

Disclaimers and Other Information

Liability: PhamCAT assumes no responsibility for any injury to person or damage to persons or property arising out of, or related to any use of PharmCAT, or for any errors or omissions. The user recognizes that PharmCAT is a research tool and that they are using PharmCAT at their own risk.

A. Allele and Genotype Determination

1. PharmCAT uses gene allele definitions included in the CPIC database, with exceptions as noted in Gene Definition Exceptions document. For allele definitions and the positions used in PharmCAT, see the gene definition tables.

2. PharmCAT results are dependent on the supplied vcf calls for the queried positions (for technical information about PharmCAT input formatting and requirements, please go to pharmcat.org). PharmCAT does not assume any reference calls for positions missing from the submitted vcf file; all missing queried positions are not considered in the allele determination process. See the gene definition tables for more information about what positions are queried in the vcf file. Missing positions might alter the assigned genotype, subsequent phenotype prediction and CPIC recommendation. If the supplied vcf file is missing positions, those positions will be noted in Section 3: Allele Calls for each gene of this report. For the most reliable allele determination, reference calls as well as variant calls in the vcf file for every queried position must be provided by the user.

3. For cytochrome P450 genes, TPMT, NUDT15, UGT1A1, and SLCO1B1, the *1 allele is defined by the absence of variation specified in the gene definition tables. This allele cannot be identified by variants; rather, *1 is assigned by default when no variation for the queried positions is reported in the submitted vcf file. The same is true for all other genes with multiple variant positions in the definition table (CACNA1S, CFTR, DPYD, RYR1): the reference sequence is the default result when variants are not reported in the vcf file. It is always possible un-interrogated variation can occur which could potentially affect allele function, but because it is undetected, the assignment would be defaulted to a *1 (or reference) allele and normal function.

4. For all genes, variation reported in the vcf file but NOT included in the gene definition table will not be considered during allele assignment. There is a possibility that any such variation results in a reduced or no activity allele which could lead to inaccurate phenotype and CPIC recommendation, similar to the situation in point 3, above.

5. Nucleotide base calls are displayed on the positive chromosomal strand regardless of the gene strand; further information is provided under Gene-specific warnings in Section 3: Allele Calls.

6. PharmCAT matches variants to genotypes assuming unphased data (unless phased data is provided in the vcf file and noted as such, see pharmcat.org for details). The assumption is that defined alleles exist in trans configuration, i.e. on opposite chromosomes, with exceptions noted in Section 3: Allele Calls under "Gene-specific warnings." However, in cases where an allele is defined by a combination of two or more variants, where each variant alone also defines an allele, the match is based on the longer allele. For example, TPMT*3B is defined by one SNP, *3C is defined by another SNP, and *3A is defined by the combination of those two SNPs. In the case of unphased data that is heterozygous for both SNPs, the *1/*3A genotype is returned though the possibility of *3B/*3C cannot be ruled out.

   Below cases are summarized for which two calls with different scores are possible when provided unphased data and heterozygous calls for the variants that define the two alleles. The genotype with the higher score (longer allele) will be used to determine allele functionality, phenotype, and recommendation but the genotype with the lower score cannot be ruled out.

Table 1: Cases for which there is an overlap in the allele definitions.

Gene	Genotype (Higher Score)	Metabolizer phenotype	Genotype (Lower Score)	Metabolizer phenotype
UGT1A1	*1/*80+*28	Intermediate	*28/*80	Indeterminate
UGT1A1	*1/*80+*37	Intermediate	*37/*80	Indeterminate
TPMT	*1/*3A	Intermediate	*3B/*3C	Poor
NUDT15	*1/*2	Intermediate	*3/*6	Possible Intermediate
CYP2C9	*1/*71	N/A	*10/*22	Indeterminate
CYP2B6	*1/*36	Intermediate	*6/*22	Intermediate
CYP2B6	*1/*34	Intermediate	*33/*36	Indeterminate
CYP2B6	*1/*6	Intermediate	*4/*9	Intermediate
CYP2B6	*1/*7	Intermediate	*5/*6	Intermediate
CYP2B6	*1/*13	Intermediate	*6/*8	Intermediate

Gene	Genotype (Higher Score)	Metabolizer phenotype	Genotype (Lower Score)	Metabolizer phenotype
SLCO1B1	*1/*46	Decreased function	*15/*45	Indeterminate
SLCO1B1	*1/*20	Normal Function	*19/*37	Indeterminate
SLCO1B1	*1/*12	Indeterminate	*2/*10	Indeterminate
SLCO1B1	*1/*13	Indeterminate	*3/*11	Indeterminate
SLCO1B1	*1/*14	Normal Function	*4/*37	Indeterminate
SLCO1B1	*1/*15	Decreased function	*5/*37	Decreased function
SLCO1B1	*1/*25	Indeterminate	*4/*28	Indeterminate
SLCO1B1	*1/*31	Decreased function	*9/*37	Indeterminate
SLCO1B1	*1/*32	Indeterminate	*4/*24	Indeterminate
SLCO1B1	*1/*40	Indeterminate	*5/*19	Indeterminate
SLCO1B1	*1/*43	Indeterminate	*4/*44	Indeterminate

Table 2: Cases for which there is an overlap in the allele definitions because the definition of the non-*1 allele in the genotype with the higher score allows for reference or variant at the position that defines the first allele listed in the genotype with the lower score. Both genotypes cannot be ruled out with unphased data if the position that overlaps between the respectives alleles is heterozygous (0/1) in addition to heterozyous calls for the other variants that define the non-*1 allele in the genotype with the higher score.

Gene	Genotype (Higher Score)	Metabolizer phenotype	Genotype (Lower Score)	Metabolizer phenotype
CYP2C19	*1/*4	Intermediate	*17/*4	Intermediate
CYP2C19	*1/*2	Intermediate	*11/*2	Intermediate
CYP2C19	*1/*35	Intermediate	*15/*35	Intermediate
CYP3A5	*1/*3	Intermediate	*2/*3	Indeterminate
CYP3A5	*1/*3	Intermediate	*4/*3	Indeterminate
CYP3A5	*1/*3	Intermediate	*5/*3	Indeterminate
CYP3A5	*1/*3	Intermediate	*9/*3	Indeterminate
CYP2B6	*1/*18	Intermediate	*4/*18	Indeterminate

B. CPIC Allele Function, Phenotype and Recommendation

1. All content is sourced from the CPIC database.

C. PharmCAT Exceptions to the CPIC Guideline Gene List

1. PharmCAT does not determine CYP2D6, G6PD, MT-RNR1, or HLA genotypes from the vcf file, but genotypes for CYP2D6, G6PD, and MT-RNR1 can be provided to PharmCAT from an outside source and the corresponding phenotype and prescribing

recommendations will be included in the generated report.
2. HLAs are currently not included in PharmCAT.

D. CPIC Guideline Disclaimers and Caveats

1. A version of the following quoted disclaimer is part of each CPIC guideline and applies to the CPIC recommendations as used in PharmCAT. For the full description of potential benefits and risks, additional considerations (general and specific to gene-drug pairs), limitations, information about respective gene nomenclature systems, potential drug-drug interactions and clinical factors to consider, please see individual CPIC guidelines (cpicpgx.org).
    1. "CPIC guidelines reflect expert consensus based on clinical evidence and peer-reviewed literature available at the time they are written and are intended only to assist clinicians in decision making and to identify questions for further research. New evidence may have emerged since the time a guideline was submitted for publication. Guidelines are limited in scope and are not applicable to interventions or diseases not specifically identified. Guidelines do not account for all individual variations among patients and cannot be considered inclusive of all proper methods of care or exclusive of other treatments. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to any guidelines is voluntary, with the ultimate determination regarding its application to be made solely by the clinician and the patient. CPIC assumes no responsibility for any injury to persons or damage to persons or property arising out of or related to any use of CPIC's guidelines, or for any errors or omissions." (PMID: 27997040)
    2. "Caveats: appropriate use and/or potential misuse of genetic tests. The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy." (PMID: 27997040)
2. CPIC guidelines reflect the alleles/genotypes known and considered by the guideline authors for inclusion by the time of publication, however they may be updated online at cpicpgx.org and in the CPIC database in between publications. Additional alleles and/or more extensive allele definitions might exist by the representative gene nomenclatures for various genes.
3. CPIC is a registered service mark of the U.S. Department of Health & Human Services (HHS).

E. PharmGKB Disclaimers and Caveats

1. PharmGKB is a registered service mark of the U.S. Department of Health & Human Services (HHS).