Pharmacogenomic (PGx) Panel Report

Patient's information:

Full name:	Vardenė Pavardenė
Date of Birth:	1990-01-01

Clinitian's information:

Full name:	Vardenis Pavardenis
Institution:	Vilnius Hospital

Test Information:

Patient ID:	PGX00001
Sample type:	EDTA Blood
Test type:	Nervous system PGx panel

Sample collection date:	2024-09-04
Sample received:	2024-09-05
Test report date:	2024-09-24

Clinical indications for testing, current medications:

Escitalopram standard dose not effective for treatment of generalized anxiety disorder.

1. Specified drugs review

escitalopram

Genotype:
CYP2C19:*17/*17

Phenotype:
Ultrarapid Metabolizer

CPIC guideline annotation (population: general):

Implications: CYP2C19: Increased metabolism of citalopram and escitalopram to less active compounds when compared to CYP2C19 rapid and normal metabolizers. Lower plasma concentrations decrease the probability of clinical benefit.

Recommendation: Consider a clinically appropriate alternative antidepressant not predominantly metabolized by CYP2C19. If citalopram or escitalopram are clinically appropriate, and adequate efficacy is not achieved at standard maintenance dosing, consider titrating to a higher maintenance dose. Drug-drug interactions and other patient characteristics (e.g., age, renal function, liver function) should be considered when adjusting dose or selecting an alternative therapy.

DPWG Guideline Annotation (population: unspecified):

Implications: The risk of switching to another antidepressant is increased as the gene variation leads to a reduction in the escitalopram plasma concentration.

Recommendation: Avoid escitalopram. Antidepressants that are not metabolised or that are metabolised to a lesser extent by CYP2C19 are, for example, paroxetine or fluvoxamine.

FDA PGx Association (affected subgroup: CYP2C19 ultrarapid, intermediate, or poor metabolizers)

Recommendation: May alter systemic concentrations

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors. Clinical pharmacology and therapeutics. 2015. PMID:25974703
- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clinical pharmacology and therapeutics. 2023. PMID:37032427
- Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
- Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction between CYP2C19 and CYP2D6 and SSRIs. European journal of human genetics : EJHG. 2022. PMID:34782755
- FDA Table of Pharmacogenetic Associations.

2. Farmacogenomic recommendations review

Nervous System Drugs (N)

Therapeutic subgroup	Standard precautions/No recommendation	Use With Caution	Consider alternatives
Anesthetics (N01)	articaine/epinephrine mepivacaine oxymetazoline/tetracaine	desflurane enflurane halothane isoflurane sevoflurane	
Analgesics (N02)	codeine oliceridine tramadol	methoxyflurane	
Antiepileptics (N03)	brivaracetam carbamazepine fosphenytoin lamotrigine oxcarbazepine phenytoin		
Psycholeptics (N05)	aripiprazole aripiprazole lauroxil brexpiprazole clobazam clozapine diazepam haloperidol iloperidone perphenazine pimozide quetiapine risperidone zuclopenthixol		
Psychoanaleptics (N06)	amoxapine amphetamine desipramine dextromethorphan/bupropion donepezil fluoxetine fluvoxamine galantamine nortriptyline paroxetine	atomoxetine	amitriptyline citalopram clomipramine doxepin escitalopram imipramine trimipramine

Drug Category	Standard precautions/No recommendation	Use With Caution	Consider alternatives
Psychoanaleptics (N06)	protriptyline sertraline venlafaxine viloxazine vortioxetine		
Other nervous system drugs (N07)	cevimeline deutetrabenazine dextromethorphan/quinidine lofexidine pitolisant valbenazine	tetrabenazine	

3. Detailed drug prescribing guidance

amitriptyline

Genotype:
CYP2C19:*17/*17
CYP2D6:*33/*41

Phenotype:

CYP2C19: Ultrarapid Metabolizer
CYP2D6:
Normal Metabolizer

Activity Scores:
CYP2C19: N/A
CYP2D6: 1.25

CPIC guideline annotation (population: general):

Implications: CYP2C19: Increased metabolism of tertiary amines compared to normal metabolizers; Greater conversion of tertiary amines to secondary amines may affect response or side effects. CYP2D6: Normal metabolism of TCAs.

Recommendation: Consider alternative drug not metabolized by CYP2C19; If amitriptyline is warranted, utilize therapeutic drug monitoring to guide dose adjustment. 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. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. 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.

Citations:

• Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clinical pharmacology and therapeutics. 2013. PMID:23486447
• Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clinical pharmacology and therapeutics. 2017. PMID:27997040
• Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
• FDA Table of Pharmacogenetic Associations.

citalopram

Genotype:
CYP2C19:*17/*17

Phenotype:
Ultrarapid Metabolizer

CPIC guideline annotation (population: general):

Implications: CYP2C19: Increased metabolism of citalopram and escitalopram to less active compounds when compared to CYP2C19 rapid and normal metabolizers. Lower plasma concentrations decrease the probability of clinical benefit.

Recommendation: Consider a clinically appropriate alternative antidepressant not predominantly metabolized by CYP2C19. If citalopram or escitalopram are clinically appropriate, and adequate efficacy is not achieved at standard maintenance dosing, consider titrating to a higher maintenance dose. Drug-drug interactions and other patient characteristics (e.g., age, renal function, liver function) should be considered when adjusting dose or selecting an alternative therapy.

DPWG Guideline Annotation (population: unspecified):

Implications: The gene variation increases conversion of citalopram to a weakly active metabolite. However, there is no significant effect on the plasma concentration of citalopram, the tolerance or the response.

Recommendation: No action is needed for this gene-drug interaction.

Citations:

• Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clinical pharmacology and therapeutics. 2013. PMID:23486447
• Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clinical pharmacology and therapeutics. 2017. PMID:27997040
• Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
• FDA Table of Pharmacogenetic Associations.

clomipramine

Genotype:
CYP2C19:*17/*17
CYP2D6:*33/*41

Phenotype:

CYP2C19:
Ultrarapid Metabolizer
CYP2D6:
Normal Metabolizer

Activity Scores:
CYP2C19: N/A
CYP2D6: 1.25

CPIC guideline annotation (population: general):

Implications: CYP2C19: Increased metabolism of tertiary amines compared to normal metabolizers; Greater conversion of tertiary amines to secondary amines may affect response or side effects. CYP2D6: Normal metabolism of TCAs

Recommendation: Consider alternative drug not metabolized by CYP2C19; If clomipramine is warranted, utilize therapeutic drug monitoring to guide dose adjustment. 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. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. 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.

DPWG Guideline Annotation (population: unspecified):

Implications: CYP2C19: The gene variation increases the risk of ineffectiveness for obsessive compulsive disorder and anxiety disorders by reducing the plasma concentration of clomipramine. The gene variation has little to no effect on the plasma concentration of clomipramine+desmethylclomipramine, which determines the efficacy for depression and side effects.

Recommendation: Indication OBSESSIVE COMPULSIVE DISORDER or ANXIETY DISORDERS: avoid clomipramine. Antidepressants that are not metabolised by CYP2C19 - or to a lesser extent - include, for example, fluoxetine, fluvoxamine and paroxetine. If it is not possible to avoid clomipramine: monitor the effect and side effects or the plasma concentrations of clomipramine and desmethylclomipramine. For obsessive compulsive disorder, the therapeutic plasma concentration of clomipramine is greater than 200 ng/mL in combination with a plasma concentration of desmethylclomipramine that is as low as possible. For anxiety disorders, the therapeutic plasma concentration of clomipramine is approximately 100 ng/mL in combination with a plasma concentration of desmethylclomipramine lower than 200 ng/mL. A sum of the plasma concentrations of clomipramine and desmethylclomipramine exceeding 600 ng/mL is considered toxic. Add a low dose of fluvoxamine if necessary, to inhibit CYP2C19 and CYP1A2 and thereby inhibit the conversion of clomipramine to desmethylclomipramine. Indication DEPRESSION: no action required

Citations:

• Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clinical pharmacology and therapeutics. 2013. PMID:23486447
• Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clinical pharmacology and therapeutics. 2017. PMID:27997040
• Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
• FDA Table of Pharmacogenetic Associations.

doxepin

Genotype:
CYP2C19:*17/*17
CYP2D6:*33/*41

Phenotype:

CYP2C19: Ultrarapid Metabolizer
CYP2D6:
Normal Metabolizer

Activity Scores:
CYP2C19: N/A
CYP2D6: 1.25

CPIC guideline annotation (population: general):

Implications: CYP2C19: Increased metabolism of tertiary amines compared to normal metabolizers; Greater conversion of tertiary amines to secondary amines may affect response or side effects. CYP2D6: Normal metabolism of TCAs

Recommendation: Consider alternative drug not metabolized by CYP2C19; If doxepin is warranted, utilize therapeutic drug monitoring to guide dose adjustment. 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. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. 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.

Citations:

• Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clinical pharmacology and therapeutics. 2013. PMID:23486447
• Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clinical pharmacology and therapeutics. 2017. PMID:27997040
• Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
• FDA Table of Pharmacogenetic Associations.

imipramine

Genotype:
CYP2C19:*17/*17
CYP2D6:*33/*41

Phenotype:

CYP2C19:
Ultrarapid Metabolizer
CYP2D6:
Normal Metabolizer

Activity Scores:
CYP2C19: N/A
CYP2D6: 1.25

CPIC guideline annotation (population: general):

Implications: CYP2C19: Increased metabolism of tertiary amines compared to normal metabolizers; Greater conversion of tertiary amines to secondary amines may affect response or side effects. CYP2D6: Normal metabolism of TCAs

Recommendation: Consider alternative drug not metabolized by CYP2C19; If imipramine is warranted, utilize therapeutic drug monitoring to guide dose adjustment. 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. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. 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.

DPWG Guideline Annotation (population: unspecified):

Implications: CYP2C19: The genetic variation decreases imipramine plasma concentrations, but not imipramine+desipramine plasma concentrations, which govern effectiveness and side effects.

Recommendation: NO action is required for this gene-drug interaction.

Citations:

• Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clinical pharmacology and therapeutics. 2013. PMID:23486447
• Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clinical pharmacology and therapeutics. 2017. PMID:27997040
• Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
• FDA Table of Pharmacogenetic Associations.

trimipramine

Genotype:
CYP2C19:*17/*17
CYP2D6:*33/*41

Phenotype:

CYP2C19: Ultrarapid Metabolizer
CYP2D6:
Normal Metabolizer

Activity Scores:
CYP2C19: N/A
CYP2D6: 1.25

CPIC guideline annotation (population: general):

Implications: CYP2C19: Increased metabolism of tertiary amines compared to normal metabolizers; Greater conversion of tertiary amines to secondary amines may affect response or side effects. CYP2D6: Normal metabolism of TCAs

Recommendation: Consider alternative drug not metabolized by CYP2C19; If trimipramine is warranted, utilize therapeutic drug monitoring to guide dose adjustment. 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. Titrate dose to observed clinical response with symptom improvement and minimal (if any) side effects. 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.

Citations:

• Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clinical pharmacology and therapeutics. 2013. PMID:23486447
• Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clinical pharmacology and therapeutics. 2017. PMID:27997040
• FDA Table of Pharmacogenetic Associations.

atomoxetine

Genotype:
CYP2D6:*33/*41

Phenotype:
Normal Metabolizer

Activity Score: 1.25

CPIC guideline annotation (population: adults):

Implications: CYP2D6: Normal metabolizers of atomoxetine have a lower likelihood of response as compared to poor metabolizers. This is associated with increased discontinuation due to lack of efficacy as compared to poor metabolizers.

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. 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.

Citations:

• Clinical Pharmacogenetics Implementation Consortium Guideline for Cytochrome P450 (CYP)2D6 Genotype and Atomoxetine Therapy. Clinical pharmacology and therapeutics. 2019. PMID:30801677
• Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
• Dutch pharmacogenetics working group (DPWG) guideline for the gene-drug interaction of CYP2D6 and COMT with atomoxetine and methylphenidate. European journal of human genetics : EJHG. 2023. PMID:36509836
• Drugs@FDA: Drug Product Strattera (Atomoxetine hydrochloride), NDA021411, Eli Lilly and Company.
• FDA Table of Pharmacogenetic Associations.

enflurane

Genotype:

CACNA1S: Reference/ Reference;
RYR1:Reference/ Reference

Phenotype:

CACNA1S:
Uncertain Susceptibility
RYR1:
Uncertain Susceptibility

CPIC guideline annotation (population: general):

Implications: 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).

Recommendation: Clinical findings, family history, further genetic testing and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants.

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. Clinical pharmacology and therapeutics. 2019. PMID:30499100

halothane

Genotype:

CACNA1S: Reference/ Reference;
RYR1:Reference/ Reference

Phenotype:

CACNA1S:
Uncertain Susceptibility
RYR1:
Uncertain Susceptibility

CPIC guideline annotation (population: general):

Implications: 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).

Recommendation: Clinical findings, family history, further genetic testing and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants.

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. Clinical pharmacology and therapeutics. 2019. PMID:30499100

isoflurane

Genotype:

CACNA1S: Reference/ Reference;
RYR1:Reference/ Reference

Phenotype:

CACNA1S:
Uncertain Susceptibility
RYR1:
Uncertain Susceptibility

CPIC guideline annotation (population: general):

Implications: 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).

Recommendation: Clinical findings, family history, further genetic testing and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants.

FDA Label Annotation (population: unspecified):

Recommendation: CONTRAINDICATIONS...with known or suspected genetic susceptibility to malignant hyperthermia...FORANE [isoflurane] can induce malignant hyperthermia in patients with known or suspected susceptibility based on genetic factors or family history, including those with certain inherited ryanodine receptor (RYR1) or dihydropyridine receptor (CACNA1S) variants." See label for more information

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. Clinical pharmacology and therapeutics. 2019. PMID:30499100
• Drugs@FDA: Drug Product FORANE (isoflurane), NDA017624, Baxter Healthcare Corporation.

methoxyflurane

Genotype:

CACNA1S: Reference/ Reference;
RYR1:Reference/ Reference

Phenotype:

CACNA1S:
Uncertain Susceptibility
RYR1:
Uncertain Susceptibility

CPIC guideline annotation (population: general):

Implications: 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).

Recommendation: Clinical findings, family history, further genetic testing and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants.

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. Clinical pharmacology and therapeutics. 2019. PMID:30499100

sevoflurane

Genotype:

CACNA1S: Reference/ Reference;
RYR1:Reference/ Reference

Phenotype:

CACNA1S:
Uncertain Susceptibility
RYR1:
Uncertain Susceptibility

CPIC guideline annotation (population: general):

Implications: 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).

Recommendation: Clinical findings, family history, further genetic testing and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants.

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. Clinical pharmacology and therapeutics. 2019. PMID:30499100
• Drugs@FDA: Drug Product Ultane (Sevoflurane), NDA020478, AbbVie Inc.

tetrabenazine

Genotype:
CYP2D6:*33/*41

Phenotype:
Normal Metabolizer

Activity Score: 1.25

FDA Label Annotation (population: unspecified):

Recommendation: Genotyped patients who are identified as extensive (EMs) or intermediate metabolizers (IMs) of CYP2D6, who need doses of XENAZINE [tetrabenazine] above 50 mg per day, should be titrated up slowly at weekly intervals by 12.5 mg daily, to allow the identification of a tolerated dose that reduces chorea. Doses above 50 mg per day should be given in a three times a day regimen. The maximum recommended daily dose is 100 mg and the maximum recommended single dose is 37.5 mg. If adverse reactions such as akathisia, parkinsonism, depression, insomnia, anxiety or sedation occur, titration should be stopped and the dose should be reduced. If the adverse reaction does not resolve, consideration should be given to withdrawing XENAZINE [tetrabenazine] treatment or initiating other specific treatment. See label for more information.

Citations:

• Drugs@FDA: Drug Product tetrabenazine (tetrabenazine), NDA021894, Oceanside Pharmaceuticals.
• FDA Table of Pharmacogenetic Associations.

carbamazepine

Genotype:
HLA-A:*03:01/*03:21N;
HLA-B:*07:02/*56:01

Phenotype:
HLA-A:*31:01 negative
HLA-B:*15:02 negative

CPIC guideline annotation (population: CBZ-no alternatives):

Implications: HLA-A: Normal risk of carbamazepine-induced SJS/TEN, DRESS, and MPE. HLA-B: Normal risk of carbamazepine-induced SJS/TEN

Recommendation: Use carbamazepine per standard dosing guidelines. HLA-B*15:02 has a 100% negative predictive value for carbamazepine-induced SJS/TEN, and its use is currently recommended to guide use of carbamazepine and oxcarbazepine only. Because there is a much weaker association and less than 100% negative predictive value of HLA-B*15:02 for SJS/TEN associated with other aromatic anticonvulsants, using these drugs instead of carbamazepine or oxcarbazepine in the setting of a negative HLA-B*15:02 test in Southeast Asians will not result in prevention of anticonvulsant-associated SJS/TEN (PMID 25355835).

Citations:

- Clinical Pharmacogenetics Implementation Consortium guidelines for HLA-B genotype and carbamazepine dosing. Clinical pharmacology and therapeutics. 2013. PMID:23695185
- Clinical Pharmacogenetics Implementation Consortium Guideline for HLA Genotype and Use of Carbamazepine and Oxcarbazepine: 2017 Update. Clinical pharmacology and therapeutics. 2018. PMID:29392710
- Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction of CYP2C9, HLA-A and HLA-B with anti-epileptic drugs. European journal of human genetics : EJHG. 2024. PMID:38570725
- Drugs@FDA: Drug Product Tegretol (carbamazepine), NDA016608, REMEDYREPACK INC.
- FDA Table of Pharmacogenetic Associations.

codeine

Genotype:
CYP2D6:*33/*41

Phenotype:
Normal Metabolizer

Activity Score: 1.25

CPIC guideline annotation (population: general):

Implications: CYP2D6: Expected morphine formation.

Recommendation: Use codeine label recommended age- or weight-specific dosing.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) guidelines for codeine therapy in the context of cytochrome P450 2D6 (CYP2D6) genotype. Clinical pharmacology and therapeutics. 2012. PMID:22205192
- Clinical Pharmacogenetics Implementation Consortium guidelines for cytochrome P450 2D6 genotype and codeine therapy: 2014 update. Clinical pharmacology and therapeutics. 2014. PMID:24458010
- Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy. Clinical pharmacology and therapeutics. 2021. PMID:33387367
- Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
- Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction between CYP2D6 and opioids (codeine, tramadol and oxycodone). European journal of human genetics : EJHG. 2022. PMID:34267337
- Drugs@FDA: Drug Product Codeine sulfate (codeine sulfate), NDA022402, West-Ward Pharmaceuticals Corp.
- FDA Table of Pharmacogenetic Associations.

desipramine

Genotype:
CYP2D6:*33/*41

Phenotype:
Normal Metabolizer

Activity Score: 1.25

CPIC guideline annotation (population: general):
Implications: CYP2D6: Normal metabolism of TCAs

Recommendation: Initiate therapy with recommended starting dose. 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.

Citations:

• Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clinical pharmacology and therapeutics. 2013. PMID:23486447
• Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clinical pharmacology and therapeutics. 2017. PMID:27997040
• FDA Table of Pharmacogenetic Associations.

fluvoxamine

Genotype:
CYP2D6:*33/*41

Phenotype:
Normal Metabolizer

Activity Score: 1.25

CPIC guideline annotation (population: general):
Implications: CYP2D6: Normal metabolism
Recommendation: Initiate therapy with recommended starting dose.

Citations:

• Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors. Clinical pharmacology and therapeutics. 2015. PMID:25974703
• Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clinical pharmacology and therapeutics. 2023. PMID:37032427
• FDA Table of Pharmacogenetic Associations.

fosphenytoin

Genotype:
CYP2C9:*1/*1;
HLA-B:*07:02/*56:01

Phenotype:
CYP2C9: Normal Metabolizer
HLA-B: *15:02 negative

Activity Scores:
CYP2C9: 2.0
HLA-B: N/A

CPIC guideline annotation (population: PHT naive):
Implications: CYP2C9: Normal phenytoin metabolism. HLA-B: n/a

Recommendation: No adjustments needed from typical dosing strategies. Subsequent doses should be adjusted according to therapeutic drug monitoring, response, and side effects. An HLA-B*15:02 negative test does not eliminate the risk of phenytoin-induced SJS/TEN and patients should be carefully monitored according to a usual standard.

Citations:

• Clinical pharmacogenetics implementation consortium guidelines for CYP2C9 and HLA-B genotypes and phenytoin dosing. Clinical pharmacology and therapeutics. 2014. PMID:25099164
• Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C9 and HLA-B Genotypes and Phenytoin Dosing: 2020 Update. Clinical pharmacology and therapeutics. 2021. PMID:32779747
• Drugs@FDA: Drug Product CEREBYX (Fosphenytoin Sodium), NDA020450, Pfizer Laboratories Div Pfizer Inc.
• FDA Table of Pharmacogenetic Associations.

nortriptyline

Genotype:
CYP2D6:*33/*41

Phenotype:
Normal Metabolizer

Activity Score: 1.25

CPIC guideline annotation (population: general):

Implications: CYP2D6: Normal metabolism of tricyclic antidepressants

Recommendation: Initiate therapy with recommended starting dose. 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.

Citations:

• Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. Clinical pharmacology and therapeutics. 2013. PMID:23486447
• Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clinical pharmacology and therapeutics. 2017. PMID:27997040
• Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
• FDA Table of Pharmacogenetic Associations.

oxcarbazepine

Genotype:
HLA-B:*07:02/*56:01

Phenotype:
*15:02 negative

CPIC guideline annotation (population: OXC naive):

Implications: HLA-B: Normal risk of oxcarbazepine-induced SJS/TEN

Recommendation: Use oxcarbazepine per standard dosing guidelines.

Citations:

• Clinical Pharmacogenetics Implementation Consortium Guideline for HLA Genotype and Use of Carbamazepine and Oxcarbazepine: 2017 Update. Clinical pharmacology and therapeutics. 2018. PMID:29392710
• Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction of CYP2C9, HLA-A and HLA-B with anti-epileptic drugs. European journal of human genetics : EJHG. 2024. PMID:38570725
• Drugs@FDA: Drug Product OXTELLAR XR (OXCARBAZEPINE), NDA202810, Supernus Pharmaceuticals, Inc.
• FDA Table of Pharmacogenetic Associations.

paroxetine

Genotype:
CYP2D6:*33/*41

Phenotype:
Normal Metabolizer

Activity Score: 1.25

CPIC guideline annotation (population: general):

Implications: CYP2D6: Normal metabolism of paroxetine to less active compounds. Paroxetine-associated phenoconversion of normal metabolizers to intermediate or poor metabolizers due to CYP2D6 autoinhibition may occur and is dose-dependent and greater at steady state concentrations.

Recommendation: Initiate therapy with recommended starting dose

Citations:

• Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors. Clinical pharmacology and therapeutics. 2015. PMID:25974703
• Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clinical pharmacology and therapeutics. 2023. PMID:37032427
• Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
• Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction between CYP2C19 and CYP2D6 and SSRIs. European journal of human genetics : EJHG. 2022. PMID:34782755
• FDA Table of Pharmacogenetic Associations.

phenytoin

Genotype:
CYP2C9:*1/*1;
HLA-B:*07:02/*56:01

Phenotype:

CYP2C9: Normal Metabolizer
HLA-B: *15:02 negative

Activity Scores:

CYP2C9: 2.0
HLA-B: N/A

CPIC guideline annotation (population: PHT naive):

Implications: CYP2C9: Normal phenytoin metabolism. HLA-B: n/a

Recommendation: No adjustments needed from typical dosing strategies. Subsequent doses should be adjusted according to therapeutic drug monitoring, response, and side effects. An HLA-B*15:02 negative test does not eliminate the risk of phenytoin-induced SJS/TEN and patients should be carefully monitored according to a usual standard.

Citations:

• Clinical pharmacogenetics implementation consortium guidelines for CYP2C9 and HLA-B genotypes and phenytoin dosing. Clinical pharmacology and therapeutics. 2014. PMID:25099164
• Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2C9 and HLA-B Genotypes and Phenytoin Dosing: 2020 Update. Clinical pharmacology and therapeutics. 2021. PMID:32779747
• Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
• Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction of CYP2C9, HLA-A and HLA-B with anti-epileptic drugs. European journal of human genetics : EJHG. 2024. PMID:38570725
• Drugs@FDA Drug Product: DILANTIN (phenytoin), NDA008762, Upjohn.
FDA Table of Pharmacogenetic Associations.

sertraline

Genotype:
CYP2B6:*1/*9;
CYP2C19:*17/*17

Phenotype:

CYP2B6: Intermediate Metabolizer
CYP2C19: Ultrarapid Metabolizer

CPIC guideline annotation (population: general):

Implications: CYP2B6: Reduced metabolism of sertraline to less active compounds when compared to CYP2B6 normal metabolizers. CYP2C19: Small increase in metabolism of sertraline to less active compounds when compared to CYP2C19 normal metabolizers.

Recommendation: Initiate therapy with recommended starting dose.

DPWG Guideline Annotation (population: unspecified):

Implications: CYP2C19: The gene variation has a negligible effect on the plasma concentration of sertraline. Moreover, no significant effect on response and side effects has been found.

Recommendation: NO action is needed for this gene-drug interaction.

Citations:

• Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and CYP2C19 Genotypes and Dosing of Selective Serotonin Reuptake Inhibitors. Clinical pharmacology and therapeutics. 2015. PMID:25974703
• Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clinical pharmacology and therapeutics. 2023. PMID:37032427
• Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
• Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction between CYP2C19 and CYP2D6 and SSRIs. European journal of human genetics : EJHG. 2022. PMID:34782755

tramadol

Genotype:
CYP2D6:*33/*41

Phenotype:
Normal Metabolizer
Activity Score: 1.25

CPIC guideline annotation (population: general):
Implications: CYP2D6: Expected O-desmethyltramadol (active metabolite) formation
Recommendation: Use tramadol label recommended age- or weight-specific dosing.

Citations:

- Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy. Clinical pharmacology and therapeutics. 2021. PMID:33387367
- Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
- Dutch Pharmacogenetics Working Group (DPWG) guideline for the gene-drug interaction between CYP2D6 and opioids (codeine, tramadol and oxycodone). European journal of human genetics : EJHG. 2022. PMID:34267337
- Drugs@FDA: Drug Product ULTRAM (tramadol hydrochloride), NDA020281, Janssen Pharmaceuticals, Inc.
- FDA Table of Pharmacogenetic Associations.

venlafaxine

Genotype:
CYP2D6:*33/*41

Phenotype:
Normal Metabolizer
Activity Score: 1.25

CPIC guideline annotation (population: general):
Implications: CYP2D6: Normal metabolism
Recommendation: Initiate therapy with recommended starting dose.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clinical pharmacology and therapeutics. 2023. PMID:37032427
- Pharmacogenetics: from bench to byte--an update of guidelines. Clinical pharmacology and therapeutics. 2011. PMID:21412232
- FDA Table of Pharmacogenetic Associations.

vortioxetine

Genotype:
CYP2D6:*33/*41

Phenotype:
Normal Metabolizer
Activity Score: 1.25

CPIC guideline annotation (population: general):
Implications: CYP2D6: Normal metabolism
Recommendation: Initiate therapy with recommended starting dose.

Citations:

- Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clinical pharmacology and therapeutics. 2023. PMID:37032427
- Drugs@FDA: Drug Product Trintellix (vortioxetine), NDA204447, Cardinal Health.
- FDA Table of Pharmacogenetic Associations.

4. Genotype and Phenotype Summary

Gene	Genotype	Allele Functionality	Phenotype
ABCG2	rs2231142 reference (G)/rs2231142 reference (G)	Two Normal function alleles	Normal Function
CACNA1S	Reference/Reference	Two Normal function alleles	Uncertain Susceptibility
CFTR	Reference/Reference	Two ivacaftor non-responsive alleles	ivacaftor non-responsive in CF patients
CYP2B6	*1/*9	One Decreased function allele and one Normal function allele	Intermediate Metabolizer
CYP2C19	*17/*17	Two Increased function alleles	Ultrarapid Metabolizer
CYP2C9	*1/*1	Two 1.0 (Normal function) alleles	Normal Metabolizer
CYP2D6	*33/*41	One 0.25 (Decreased function) allele and one 1.0 (Normal function) allele	Normal Metabolizer
CYP3A4	*1/*1	Two Normal function alleles	Normal Metabolizer
CYP3A5	*3/*3	Two No function alleles	Poor Metabolizer
CYP4F2	*1/*5	N/A	N/A
DPYD	c.85T>C (*9A)/c.85T>C (*9A)	Two 1.0 (Normal function) alleles	Normal Metabolizer
G6PD	B (reference)/B (reference)	Two IV/Normal alleles	Normal
HLA-A	*03:01/*03:21N	N/A	*31:01 negative
HLA-B	*07:02/*56:01	N/A	*15:02 negative; *57:01 negative; *58:01 negative
IFNL3/4	rs12979860 variant (T)/rs12979860 variant (T)	Two Unfavorable response allele alleles	n/a
MT-RNR1	Reference	Normal risk of aminoglycoside-induced hearing loss	normal risk of aminoglycoside-induced hearing loss
NUDT15	*1/*1	Two Normal function alleles	Normal Metabolizer
RYR1	Reference/Reference	Two Normal function alleles	Uncertain Susceptibility
SLCO1B1	*15/*20	One Increased function allele and one No function allele	Decreased Function
TPMT	*1/*1	Two Normal function alleles	Normal Metabolizer
UGT1A1	*80+*28/*80+*28	Two Decreased function alleles	Poor Metabolizer
VKORC1	rs9923231 reference (C)/rs9923231 reference (C)	N/A	N/A

5. Test Information & Disclaimers

Test Information:

Genomic DNA was isolated from blood, a DNA sequencing library was prepared, Illumina next-generation sequencing and sequencing data analysis was performed, searching for PGx gene variants and their influence in gene-drug interactions. Data analysis was performed with PyPGx[1,2,3], HISAT-genotype[4] and PharmCAT[5] applications, resulting in personalized drug prescribing recommendations, according to the Clinical Pharmacogenetics Implementation Consortium (CPIC), Dutch Pharmacogenetics Working Group (DPWG) and the United States Food and Drug Administration (FDA) guidelines.

[1]Lee, S. B., et al. (2022). ClinPharmSeq: A targeted sequencing panel for clinical pharmacogenetics implementation. PloS one, 17(7), e0272129.
[2]Lee, S. B., et al. (2019). Calling Star Alleles With Stargazer in 28 Pharmacogenes With Whole Genome Sequences. Clinical pharmacology and therapeutics, 106(6), 1328–1337.
[3]Lee, S. B., et al. (2019). Stargazer: a software tool for calling star alleles from next-generation sequencing data using CYP2D6 as a model. Genetics in medicine, 21(2), 361–372.
[4]Kim, D., Paggi, J. M., Park, C., et al. (2019). Graph-based genome alignment and genotyping with HISAT2 and HISAT-genotype. Nature biotechnology, 37(8), 907–915.
[5]Sangkuhl, K., Whirl-Carrillo, M., et al. (2020). Pharmacogenomics Clinical Annotation Tool (PharmCAT). Clinical pharmacology and therapeutics, 107(1), 203–210.

Disclaimers:

• **The Pharmacogenomics (PGx) panel report is intended solely for use by qualified healthcare professionals.** The information it contains is provided as general educational health content. It is not meant to replace professional medical advice, diagnosis, or treatment. Patients should consult a physician, pharmacist, or other healthcare professional for guidance on the appropriate use of prescribed medications.

• Phenotype prediction and interpretation rely on a specific set of selected variants being analyzed (Supplementary Table 1). For the cytochrome P450 genes, as well as TPMT, NUDT15, UGT1A1, and SLCO1B1, the *1 allele is defined by the absence of any variations listed in the gene definition tables. This allele is not identified by specific variants; instead, it is automatically assigned when no variations at the specified positions are found in the submitted VCF file. The same principle applies to other genes with multiple variant positions (such as CACNA1S, CFTR, DPYD, and RYR1): if no variants are detected in the VCF file, the reference sequence is assigned by default. There is always a possibility of undetected variations that could influence allele function, but if such variations go unrecognized, the *1 (or reference) allele, which assumes normal function, will be assigned by default. Structural variation star alleles that cannot be detected using VCF file data: CYP2B7-CYP2B6 hybrids: CYP2B6*29, CYP2B6*30, partial and whole gene deletions: CYP2C19*36, CYP2C19*37, CYP4F2*16, SLCO1B1*48, SLCO1B1*49. In situations where an allele is characterized by a combination of two or more variants, and each individual variant also defines an allele, the match is determined by the longer allele.

• CPIC, DPWG and FDA guidelines represent expert consensus based on available clinical evidence and peer-reviewed research at the time of writing. They are designed to assist clinicians in decision-making and highlight areas for further research. However, new evidence may have emerged after the guidelines were published. These guidelines are limited in scope and do not apply to diseases or interventions not specifically mentioned. They also do not account for individual patient differences or encompass all appropriate methods of care. Health-care providers are ultimately responsible for determining the best treatment for their patients. Following the guidelines is optional, and the decision to use them is solely at the discretion of the clinician and patient. Saidė **Genomics is not liable for any harm or damage resulting from the use of these guidelines, including any errors or omissions.**

Databases and program versions used:

DRAGEN Germline: 4.1.23 , PharmCAT: 2.14.0, PharmCAT data: 2024-07-15-21-58, HISAT-genotype: 1.3.2, PyPGx: 0.25

Test performed and confirmed by:	
Performed:	Confirmed:

Supplementary Table 1. All named alleles used for analysis.

Gene	Named Alleles
ABCG2	rs2231142 reference (G);rs2231142 variant (T)
CACNA1S	Reference;c.520C>T;c.3257G>A
CFTR	711+3A->G; 2789+5G->A; 3272-26A->G; 3849+10kbC->T; A455E; A1067T; D110E; D110H; D579G; D1152H; D1270N; E56K; E193K; E831X; F1052V; F1074L; G178R; G551D; G551S; G1069R; G1244E; G1349D; K1060T; L206W; P67L; R74W; R117C; R117H; R347H; R352Q; R1070Q; R1070W; S549N; S549R(A>C); S549R(T>G); S945L; S977F; S1251N; S1255P; ivacaftor non-responsive CFTR sequence
CYP2B6	*1;*2;*3;*4;*5;*6;*7;*8;*9;*10;*11;*12;*13;*14;*15;*17;*18;*19;*20;*21;*22;*23;*24;*25;*26;*27;*28;*31;*32;*33;*34;*35;*36;*37;*38;*39;*40;*41;*42;*43;*44;*45;*46;*47;*48;*49
CYP2C19	*1;*2;*3;*4;*5;*6;*7;*8;*9;*10;*11;*12;*13;*14;*15;*16;*17;*18;*19;*22;*23;*24;*25;*26;*28;*29;*30;*31;*32;*33;*34;*35;*38;*39
CYP2C9	*1;*2;*3;*4;*5;*6;*7;*8;*9;*10;*11;*12;*13;*14;*15;*16;*17;*18;*19;*20;*21;*22;*23;*24;*25;*26;*27;*28;*29;*30;*31;*32;*33;*34;*35;*36;*37;*38;*39;*40;*41;*42;*43;*44;*45;*46;*47;*48;*49;*50;*51;*52;*53;*54;*55;*56;*57;*58;*59;*60;*61;*62;*63;*64;*65;*66;*67;*68;*69;*70;*71;*72;*73;*74;*75;*76;*77;*78;*79;*80;*81;*82;*83;*84;*85
CYP2D6	*1;*1x2;*1x≥3;*2;*2x2;*2x≥3;*3;*3x2;*4;*4x2;*4x≥3;*5;*6;*6x2;*7;*8;*9;*9x2;*10;*10x2;*11;*12;*13;*14;*15;*17;*17x2;*18;*19;*20;*21;*22;*23;*24;*25;*26;*27;*27x2;*28;*28x2;*29;*29x2;*30;*31;*32;*33;*34;*35;*35x2;*36;*36x2;*37;*38;*39;*40;*41;*41x2;*41x3;*42;*43;*43x2;*44;*45;*45x2;*46;*47;*48;*49;*50;*51;*52;*53;*54;*55;*56;*58;*59;*60;*61;*62;*63;*64;*65;*68;*69;*70;*71;*72;*73;*74;*75;*81;*82;*83;*84;*85;*86;*87;*88;*89;*90;*91;*92;*93;*94;*95;*96;*97;*98;*99;*100;*101;*102;*103;*104;*105;*106;*107;*108;*109;*110;*111;*112;*113;*114;*115;*116;*117;*118;*119;*120;*121;*122;*123;*124;*125;*126;*127;*128;*129;*130;*131;*132;*133;*134;*135;*136;*137;*138;*139;*140;*141;*142;*143;*144;*145;*146;*146x2;*147;*148;*149;*152;*153;*154;*155;*156;*157;*158;*159;*160;*161;*162;*163
CYP3A4	*1;*2;*3;*4;*5;*6;*7;*8;*9;*10;*11;*12;*13;*14;*15;*16;*17;*18;*19;*20;*21;*22;*23;*24;*26;*28;*29;*30;*31;*32;*33;*34;*35;*37;*38;*39;*40;*41;*42;*43;*44;*45;*46;*47;*48
CYP3A5	*1;*3;*6;*7;*8;*9
CYP4F2	*1;*2;*3;*4;*5;*6;*7;*8;*9;*10;*11;*12;*13;*14;*15;*17
DPYD	Reference; c.46C>G; c.61C>T; c.62G>A; c.85T>C (*9A); c.295_298delTCAT (*7); c.313G>A; c.343A>G; c.451A>G; c.496A>G; c.498G>A; c.525G>A; c.557A>G; c.601A>C; c.632A>G; c.703C>T (*8); c.775A>G; c.868A>G; c.929T>C; c.934C>T; c.967G>A; c.1003G>T (*11); c.1024G>A; c.1057C>T; c.1108A>G; c.1129-5923C>G; c.1129-5923C>G, c.1236G>A (HapB3); c.1156G>T (*12); c.1180C>T; c.1181G>T; c.1218G>A; c.1260T>A; c.1278G>T; c.1294G>A; c.1314T>G; c.1349C>T; c.1358C>G; c.1371C>T; c.1403C>A; c.1475C>T; c.1484A>G; c.1519G>A; c.1543G>A; c.1577C>G; c.1601G>A (*4); c.1615G>A; c.1627A>G (*5); c.1679T>G (*13); c.1682G>T; c.1774C>T; c.1775G>A; c.1777G>A; c.1796T>C; c.1896T>C; c.1898delC (*3); c.1905+1G>A (*2A); c.1905C>G; c.1906A>C; c.1990G>T; c.2021G>A; c.2161G>A; c.2186C>T; c.2194G>A (*6); c.2195T>G; c.2279C>T; c.2303C>A; c.2336C>A; c.2482G>A; c.2582A>G;c.2623A>C; c.2639G>T; c.2656C>T; c.2657G>A (*9B); c.2846A>T; c.2872A>G; c.2915A>G; c.2921A>T; c.2933A>G; c.2977C>T; c.2978T>G; c.2983G>T (*10); c.3049G>A; c.3061G>C; c.3067C>A
HLA-A	*31:01
HLA-B	*15:02;*57:01;*58:01
IFNL3	rs12979860 reference (C);rs12979860 variant (T)
MT-RNR1	Reference;m.663A>G;m.669T>C;m.747A>G;m.786G>A;m.807A>C;m.807A>G;m.827A>G;m.839A>G;m.896A>G;m.930A>G;m.951G>A;m.960C>del;m.961T>G;m.961T>del;m.961T>del+Cn;m.988G>A;m.1095T>C;m.1189T>C;m.1243T>C;m.1494C>T;m.1520T>C;m.1537C>T;m.1555A>G;m.1556C>T
NUDT15	*1;*2;*3;*4;*5;*6;*7;*8;*9;*10;*11;*12;*13;*14;*15;*16;*17;*18;*19;*20
SLCO1B1	*1;*2;*3;*4;*5;*6;*7;*8;*9;*10;*11;*12;*13;*14;*15;*16;*19;*20;*23;*24;*25;*26;*27;*28;*29;*30;*31;*32;*33;*34;*36;*37;*38;*39;*40;*41;*42;*43;*44;*45;*46;*47
TPMT	*1;*2;*3A;*3B;*3C;*4;*5;*6;*7;*8;*9;*10;*11;*12;*13;*14;*15;*16;*17;*18;*19;*20;*21;*22;*23;*24;*25;*26;*27;*28;*29;*30;*31;*32;*33;*34;*35;*36;*37;*38;*39;*40;*41;*42;*43;*44
UGT1A1	*1;*6;*27;*28;*36;*37;*80;*80+*28;*80+*37
VKORC1	rs9923231 reference (C);rs9923231 variant (T)

G6PD	202G>A_376A>G_1264C>G; A;A- 202A_376G; A- 680T_376G; A- 968C_376G; Aachen; Abeno; Acrokorinthos; Alhambra; Amazonia; Amiens; Amsterdam; Anadia; Ananindeua; Andalus; Arakawa; Asahi; Asahikawa; Aures; Aveiro; B (reference); Bajo Maumere; Bangkok; Bangkok Noi; Bao Loc; Bari; Belem; Beverly Hills, Genova, Iwate, Niigata, Yamaguchi; Brighton; Buenos Aires; Cairo; Calvo Mackenna; Campinas; Canton, Taiwan-Hakka, Gifu-like, Agrigento-like; Cassano; Chatham; Chikugo; Chinese-1; Chinese-5; Cincinnati; Cleveland Corum; Clinic; Coimbra Shunde; Cosenza; Costanzo; Covao do Lobo; Crispim; Dagua; Durham; Farroupilha; Figuera da Foz; Flores; Fukaya; Fushan; Gaohe; Georgia; Gidra; Gond; Guadalajara; Guangzhou; Haikou; Hammersmith; Harilaou; Harima; Hartford; Hechi; Hermoupolis; Honiara; Ierapetra; Ilesha; Insuli; Iowa, Walter Reed, Springfield; Iwatsuki; Japan, Shinagawa; Kaiping, Anant, Dhon, Sapporo-like, Wosera; Kalyan-Kerala, Jamnaga, Rohini; Kambos; Kamiube, Keelung; Kamogawa; Kawasaki; Kozukata; Krakow; La Jolla; Lages; Lagosanto; Laibin; Lille; Liuzhou; Loma Linda; Ludhiana; Lynwood; Madrid; Mahidol; Malaga; Manhattan; Mediterranean, Dallas, Panama, Sassari, Cagliari, Birmingham; Metaponto; Mexico City; Miaoli; Minnesota, Marion, Gastonia, LeJeune; Mira d'Aire; Mizushima; Montalbano; Montpellier; Mt Sinai; Munich; Murcia Oristano; Musashino; Namouru; Nankang; Nanning; Naone; Nara; Nashville, Anaheim, Portici; Neapolis; Nice; Nilgiri; No name; North Dallas; Olomouc; Omiya; Orissa; Osaka; Palestrina; Papua; Partenope; Pawnee; Pedoplis-Ckaro; Piotrkow; Plymouth; Praha; Puerto Limon; Quing Yan; Radlowo; Rehevot; Rignano; Riley; Riverside; Roubaix; S. Antioco; Salerno Pyrgos; Santa Maria; Santiago; Santiago de Cuba, Morioka; Sao Borja; Seattle, Lodi, Modena, Ferrara II, Athens-like; Seoul; Serres; Shenzen; Shinshu; Sibari; Sierra Leone; Sinnai; Songklanagarind; Split; Stonybrook; Sugao; Sumare; Sunderland; Surabaya; Suwalki; Swansea; Taipei, Chinese-3; Telti, Kobe; Tenri; Tokyo, Fukushima; Toledo; Tomah; Tondela; Torun; Tsukui; Ube Konan; Union,Maewo, Chinese-2, Kalo; Urayasu; Utrecht; Valladolid; Vancouver; Vanua Lava; Viangchan, Jammu; Volendam; Wayne; West Virginia; Wexham; Wisconsin; Yunan
RYR1	Reference;c.38T>G;c.51_53del;c.97A>G;c.103T>C;c.119G>C;c.130C>T;c.131G>A;c.152C>A;c.178G>A;c.178G>T;c.190T>C;c.212C>A;c.251C>T;c.418G>A;c.455C>A;c.463C>A;c.467G>A;c.479A>G;c.487C>T;c.488G>A;c.488G>T;c.493G>A;c.496G>A;c.497A>G;c.526G>A;c.528G>T;c.529C>T;c.533A>C;c.533A>G;c.625G>A;c.641C>T;c.652G>A;c.677T>A;c.680A>T;c.742G>A;c.742G>C;c.946C>T;c.947G>T;c.982C>T;c.992_994dup;c.1021G>A;c.1021G>C;c.1024G>A;c.1100G>A;c.1100G>T;c.1144C>A;c.1201C>A;c.1201C>G;c.1201C>T;c.1202G>A;c.1202G>T;c.1209C>G;c.1411C>T;c.1422G>T;c.1453A>G;c.1459C>G;c.1460T>C;c.1475G>A;c.1553T>C;c.1565A>C;c.1565A>G;c.1589G>A;c.1597C>A;c.1597C>T;c.1598G>A;c.1615T>C;c.1615T>G;c.1630G>T;c.1654C>T;c.1834G>C;c.1840C>T;c.1841G>T;c.2050G>C;c.2122G>A;c.2447C>T;c.2537C>T;c.2654G>A;c.2797G>A;c.2924G>A;c.2996G>A;c.3095G>A;c.3127C>T;c.3166G>A;c.3166G>C;c.3172G>A;c.3224G>A;c.3418C>T;c.3527C>T;c.3656A>C;c.3667G>A;c.4024A>G;c.4178A>G;c.4400A>G;c.4711A>G;c.4747C>T;c.4763C>T;c.4775C>T;c.5024T>C;c.5033A>G;c.5036G>A;c.5132A>G;c.5183C>T;c.5186T>G;c.5317C>T;c.5341T>C;c.5360C>T;c.5440A>G;c.5441T>A;c.5890C>T;c.6037A>C;c.6178G>T;c.6302T>A;c.6304G>C;c.6349G>C;c.6377G>A;c.6387C>G;c.6388G>A;c.6478G>A;c.6487C>T;c.6488G>A;c.6488G>C;c.6488G>T;c.6502G>A;c.6544A>T;c.6548G>A;c.6599C>T;c.6612C>G;c.6617C>G;c.6617C>T;c.6628G>T;c.6635T>A;c.6640G>A;c.6670C>T;c.6671G>A;c.6710G>A;c.6742C>T;c.6743G>A;c.6757C>T;c.6838G>A;c.6847A>C;c.6961A>G;c.7007G>A;c.7018T>C;c.7025A>G;c.7032G>C;c.7035C>A;c.7036G>A;c.7042_7044delGAG;c.7043A>G;c.7048G>A;c.7060G>A;c.7063C>T;c.7073T>A;c.7075C>T;c.7076G>A;c.7084G>A;c.7085A>G;c.7089C>G;c.7090T>G;c.7097C>G;c.7099G>A;c.7112A>G;c.7123G>A;c.7124G>C;c.7199A>G;c.7210G>A;c.7282G>A;c.7291G>A;c.7291G>T;c.7292A>T;c.7300G>A;c.7304G>A;c.7304G>T;c.7307G>A;c.7310C>T;c.7317G>C;c.7354C>T;c.7355G>A;c.7355G>C;c.7358T>C;c.7360C>T;c.7361G>A;c.7372C>T;c.7373G>A;c.7373G>T;c.7385C>T;c.7487C>T;c.7522C>G;c.7522C>T;c.7523G>A;c.7528T>C;c.7760A>G;c.7771C>G;c.7771C>T;c.7777C>G;c.7778G>A;c.7787C>T;c.7816T>A;c.7879G>A;c.7879G>C;c.8005G>A;c.8026C>T;c.8054C>T;c.8188G>C;c.8189A>G;c.8198G>A;c.8290G>A;c.8327C>T;c.8360C>G;c.8518C>T;c.8527T>C;c.8600T>A;c.8638G>A;c.8654C>G;c.8729C>T;c.8926C>T;c.9152G>A;c.9268G>A;c.9310G>A;c.9356G>A;c.9499C>T;c.9635A>G;c.9649T>C;c.9652G>A;c.9676G>C;c.9758T>C;c.9797T>C;c.9848G>A;c.9850T>A;c.9868G>A;c.10042C>T;c.10043G>A;c.10097G>A;c.10100A>G;c.10229C>A;c.10237A>T;c.10252A>G;c.10556C>T;c.10616G>A;c.10747G>C;c.10750G>C;c.10891G>T;c.11086G>C;c.11120G>T;c.11126C>T;c.11132C>T;c.11266C>G;c.11314C>T;c.11315G>A;c.11416G>A;c.11518G>A;c.11708G>A;c.11723A>T;c.11748T>G;c.11798A>G;c.11813G>A;c.11947C>T;c.11953T>C;c.11958C>G;c.11969G>T;c.12028G>A;c.12064A>G;c.12115A>T;c.12121C>T;c.12149C>A;c.12242C>T;c.12310G>C;c.12355A>T;c.12383C>T;c.12398A>G;c.12406C>A;c.12413T>C;c.12532G>A;c.12533G>T;c.12553G>A;c.12689T>G;c.12700G>C;c.12700G>T;c.12848A>T;c.12881C>T;c.12884C>T;c.13505A>G;c.13513G>C;c.13672C>T;c.13673G>A;c.13702C>G;c.13760C>T;c.13913G>A;c.13918A>G;c.13934G>A;c.13990T>C;c.13994_13995delTCinsCT;c.14002C>T;c.14051T>C;c.14126C>T;c.14168G>A;c.14186A>C;c.14197T>G;c.14201G>A;c.14209C>T;c.14210G>A;c.14270G>A;c.14364+1G>T;c.14387A>G;c.14422_14423delinsAA;c.14424C>A;c.14449A>T;c.14458G>A;c.14458G>T;c.14471T>C;c.14477C>T;c.14497C>T;c.14509C>G;c.14512C>G;c.14524G>A;c.14539G>C;c.14545G>A;c.14558C>T;c.14567C>G;c.14581C>T;c.14582G>A;c.14627A>G;c.14639T>C;c.14678G>A;c.14680G>A;c.14693T>C;c.14782A>G;c.14803G>A;c.14813T>C;c.14814C>G;c.14817C>A;c.14818G>A;c.14825G>T;c.14879T>A;c.14918C>T;c.14968A>G;c.15059G>C;c.15060G>C