PHARMACOGENETIC TESTING

REPORT

Ayass bioscience
Bridging Science and Precision Patient Care LLC™

Patient Name: XXXX, XXXX
Birth Date: Jun XX, 19XX
Accession: XXXXXXXX

Ayass Bioscience

8501 Wade Blvd, Bldg 9, Frisco, TX 75034
Phone: 972-668-6005 **Fax:** 972-668-6720 **Web:** www.AyassBioscience.com
Laboratory Director: Dr. Ihsan Housini, MD **Laboratory Certification:** CLIA # 45D2034891

Report ID: XXXXXXXX
Report Date: 2024-09-XX
Sample ID: XXXXXXXX
Order Date: 2024-09-XX
Requested by: Mohamad A Ayass

Patient Name: XXXX, XXXX
Birth Date: Jun XX, 19XX
Gender: Male

Annotated Test Results

ABCB1 G/G	Normal Activity
APOE E3/E3	Normal APOE Function
COMT A/G	Intermediate COMT Activity
CYP1A2 *1A/*1F	Ultrarapid Metabolizer
CYP2B6 *1/*1	Normal Metabolizer
CYP2C19 *1/*2	Intermediate Metabolizer
CYP2C9 *1/*2	Intermediate Metabolizer
CYP2D6 *1/*4	Intermediate Metabolizer
CYP2D6 Normal (2N) Active Copy Number	Likely Normal Metabolizer
CYP3A4 *1/*1	Normal Metabolizer
CYP3A5 *3/*3	Poor Metabolizer
DRD2 WT/Taq1A	Possible Reduced Dopamine Receptor Density
F2 WT/WT	Normal Thrombosis Risk
F5 WT/R506Q	Hypercoagulability (prone to clotting)
MTHFR (rs1801131) C/C	Lower MTHFR Activity
MTHFR (rs1801133) C/C	Normal MTHFR Activity
OPRM1 A/G	Decreased Mu Opiod Receptor Expression
SLCO1B1 *1/*1 (rs4149056 TT)	Normal Function
VKORC1 -1639G>A G/A	Intermediate Expression

Consult Notes

Notes:
Made By:

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Sophic™ Integrated Knowledge Environment Software and Services

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Drug has a published guideline in one of the major reference sources (CPIC, DPWG, FDA, or PharmGKB curation of FDA Labels) related to a variant found in the patient test results	Drug has supported or likely level evidence from sources in the Sophic Knowledgebase for interaction with one or more variants found in the patient test results. While there is not a specific guideline for treatment, it may be useful information	Drug has unsupported, unlikely, or unknown evidence only from sources in the Sophic Knowledgebase for interaction with one or more variants found in the patient test results. While there is not a specific guideline for treatment, it may be useful information	Drug has no known interactions with the patient test results in the sources contained in the Sophic Knowledgebase.

Drugs Covered in this Report

ampicillin, rivaroxaban

rivaroxaban

Drug Classes:
- other antithrombotic agents

Source: PharmGKB

Variant: F5

Annotation of FDA Label for rivaroxaban and F5 (On FDA Biomarker List)

https://www.pharmgkb.org/labelAnnotation/PA166182726

ampicillin

Drug Classes:
- penicillins with extended spectrum
- extended spectrum penicillin
- antibiotics

Drug Class: alimentary tract and metabolism

SubClass	Supported or Likely	Additional Info
stomatological preparations	None	None
drugs for acid related disorders	None	None
drugs for functional gastrointestinal disorders	None	None
antiemetics and antinauseants	None	granisetron [CYP3A5]
bile and liver therapy	None	None
laxatives, drugs for constipation	None	naloxone [OPRM1]
antidiarrheals, intestinal antiinflammatory/antiinfective	None	None
antiobesity preparations, excl. diet products	None	None
digestives, incl. enzymes	None	None
drugs used in diabetes	glyburide [CYP2C9] glimepiride [CYP2C9] gliclazide [CYP2C9] tolbutamide [CYP2C9]	None
vitamins	None	None
mineral supplements	None	None
tonics	None	None
anabolic agents for systemic use	None	None
appetite stimulants	None	None
other alimentary tract and metabolism products	None	None

Drug Class: blood and blood forming organs

SubClass	Supported or Likely	Additional Info
antithrombotic agents	warfarin [CYP2C9] acenocoumarol [CYP2C9] phenprocoumon [CYP2C9] warfarin [VKORC1] acenocoumarol [VKORC1] phenprocoumon [VKORC1]	warfarin [CYP2C19] cilostazol [CYP3A5] acenocoumarol [VKORC1] phenprocoumon [VKORC1]
antihemorrhagics	None	None
antianemic preparations	None	None
blood substitutes and perfusion solutions	None	None
other hematological agents	None	None

Drug Class: cardiovascular system

SubClass	Supported or Likely	Additional Info
cardiac therapy	None	None
antihypertensives	None	None
diuretics	None	None
peripheral vasodilators	None	ergot alkaloids [COMT] ergot alkaloids [OPRM1]
vasoprotectives	None	None
beta blocking agents	None	None
calcium channel blockers	None	nimodipine [CYP3A5]

agents acting on the renin-angiotensin system	None	None
lipid modifying agents	None	atorvastatin [CYP3A5]

Drug Class: genito urinary system and sex hormones

SubClass	Supported or Likely	Additional Info
gynecological antiinfectives and antiseptics	None	None
other gynecologicals	None	ergot alkaloids [COMT] ergot alkaloids [OPRM1]
sex hormones and modulators of the genital system	estradiol [F5]	progesterone [CYP2C19] hormonal contraceptives for systemic use [F5]
urologicals	None	None

Drug Class: antiinfectives for systemic use

SubClass	Supported or Likely	Additional Info
antibacterials for systemic use	None	None
antimycotics for systemic use	None	None
antimycobacterials, antimycobacterial	None	None
antivirals for systemic use	None	maraviroc [CYP3A5]
immune sera and immunoglobulins	None	None
vaccines	None	None

Drug Class: antineoplastic and immunomodulating agents

SubClass	Supported or Likely	Additional Info
antineoplastic agents	belzutifan [CYP2C19]	paclitaxel [CYP3A5] carboplatin [CYP3A5]
endocrine therapy	None	tamoxifen [CYP2C19]
immunostimulants, immune enhancement agent	None	None
immunosuppressants	siponimod [CYP2C9] tacrolimus [CYP3A5]	None

Drug Class: musculo-skeletal system

SubClass	Supported or Likely	Additional Info
muscle relaxants	None	carisoprodol [CYP2C19] tolperisone [CYP2D6]
antiinflammatory and antirheumatic products	None	None
topical products for joint and muscular pain	None	tolperisone [CYP2D6]
antigout preparations	None	None
drugs for treatment of bone diseases	None	None
other drugs for disorders of the musculo-skeletal system	None	None

Drug Class: nervous system

SubClass	Supported or Likely	Additional Info

local anesthetics, anesthetic agent	sufentanil [COMT] remifentanil [COMT]	fentanyl [COMT] fentanyl [CYP3A5] sufentanil [CYP3A5] opioid anesthetics [OPRM1] other general anesthetics [OPRM1] fentanyl [OPRM1] sufentanil [OPRM1] alfentanil [OPRM1] cocaine [OPRM1]
analgesics	opioids [COMT] oxycodone [COMT] morphine [COMT] tramadol [COMT] opioids [OPRM1]	opioids [ANKK1] ergot alkaloids [COMT] analgesics [COMT] opioids [COMT] buprenorphine [COMT] sumatriptan [COMT] fentanyl [COMT] oxycodone [COMT] tramadol [COMT] fentanyl [CYP3A5] oxycodone [CYP3A5] ergot alkaloids [OPRM1] analgesics [OPRM1] opioids [OPRM1] buprenorphine [OPRM1] sumatriptan [OPRM1] fentanyl [OPRM1] oxycodone [OPRM1] morphine [OPRM1] tramadol [OPRM1]
antiepileptics	phenytoin [CYP2C9] fosphenytoin [CYP2C9]	benzodiazepine derivatives [OPRM1]
anti-parkinson drugs	None	entacapone [COMT]
psycholeptics	None	antipsychotics [ANKK1] olanzapine [ANKK1] risperidone [ANKK1] prochlorperazine [ANKK1] aripiprazole [ANKK1] antipsychotics [COMT] risperidone [COMT] clozapine [COMT] haloperidol [COMT] clozapine [CYP1A2] diazepam [CYP2C19] olanzapine [CYP2C9] midazolam [CYP3A5] benzodiazepine derivatives [OPRM1] antipsychotics [OPRM1]
psychoanaleptics	None	bupropion [ANKK1] methylphenidate [COMT] venlafaxine [COMT] paroxetine [COMT] modafinil [COMT] fluvoxamine [COMT] caffeine [CYP1A2] bupropion [CYP2C19] donepezil [CYP2D6] maprotiline [CYP2D6] opipramol [CYP2D6] antidepressants [OPRM1] tianeptine [OPRM1]
other nervous system drugs	nicotine [COMT] methadone [COMT]	nicotine [ANKK1] disulfiram [ANKK1] nicotine [COMT] buprenorphine [COMT] drugs used in nicotine dependence [OPRM1] nicotine [OPRM1] buprenorphine [OPRM1] naltrexone [OPRM1] methadone [OPRM1]

Drug Class: antiparasitic products, insecticides and repellents

SubClass	Supported or Likely	Additional Info
antiprotozoals	None	None
anthelmintics, anthelmintic agent	None	None
ectoparasiticides, incl. scabicides, insecticides and repellents	None	disulfiram [ANKK1]

Drug Class: respiratory system

SubClass	Supported or Likely	Additional Info
antihistamines for systemic use	None	None
nasal preparations	None	sympathomimetics [OPRM1]
throat preparations	None	cocaine [OPRM1]
drugs for obstructive airway diseases	None	None
cough and cold preparations	None	hydrocodone [OPRM1] codeine [OPRM1]
other respiratory system products	None	None

Drug Class: sensory organs

SubClass	Supported or Likely	Additional Info
ophthalmologicals	None	cocaine [OPRM1]
otologicals	None	cocaine [OPRM1]
ophthalmological and otological preparations	None	None

Drug Class: various

SubClass	Supported or Likely	Additional Info
diagnostic agents	tolbutamide [CYP2C9]	None
allergens	None	None
all other therapeutic products	None	ethanol [ANKK1] ethanol [OPRM1] naloxone [OPRM1]
general nutrients	None	None
all other non-therapeutic products	None	None
contrast media	None	None
diagnostic radiopharmaceuticals, diagnostic radioisotope	None	None
therapeutic radiopharmaceuticals	None	None
surgical dressings	None	None

Drug Class: dermatalogical agents

SubClass	Supported or Likely	Additional Info
antifungals for dermatological use	None	None
emollients and protectives	None	None
preparations for treatment of wounds and ulcers	None	None
antipruritics, incl. antihistamines, anesthetics, etc.	None	None

antipsoriatics	None	None
antibiotics and chemotherapeutics for dermatological use	None	None
corticosteroids, dermatological preparations	None	None
antiseptics and disinfectants	None	ethanol [ANKK1] ethanol [OPRM1]
medicated dressings	None	None
anti-acne preparations	None	None
other dermatological preparations, other dermatologicals	tacrolimus [CYP3A5]	caffeine [CYP1A2]

Drug Class: systemic hormonal preparations, excl. sex hormones and insulins

SubClass	Supported or Likely	Additional Info
pituitary and hypothalamic hormones and analogues	None	None
corticosteroids for systemic use	None	None
thyroid therapy	None	None
pancreatic hormones	None	None
calcium homeostasis	None	None

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olanzapine

Drug Classes:
diazepines, oxazepines and thiazepines
diazepines, oxazepines, thiazepines and oxepines
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0001560.PDF

Additional Evidence

Variant: DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
Variant: CYP2C9 *1/*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: CYP2C9*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: MTHFR E429A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link

belzutifan

Drug Classes:
other antineoplastic agents
Source: PharmGKB
Variant: CYP2C19 *1/*2, CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for belzutifan and CYP2C19, UGT2B17 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166268882

carvedilol

Drug Classes:
alpha and beta blocking agents
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for carvedilol and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104813
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
NO action is required for this gene-drug interaction. The plasma concentration of carvedilol can be elevated. This does not, however, result in an increase in side effects.
https://www.g-standaard.nl/risicoanalyse/B0002345.PDF

Additional Evidence

Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Dosage Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Dosage Evidence Link

estradiol

Drug Classes:
natural and semisynthetic estrogens, plain
Source: DPWG
Variant: F5 WT/R506Q
The heterozygously present genetic polymorphism â■■factor V Leidenâ■■ causes an increased tendency to coagulation, resulting in an increased risk of venous thromboembolism. Contraceptives containing oestrogens can increase this risk even further. Recommendation: If the patient has a FAMILY HISTORY WITH A LOT OF THROMBOSIS, or has had a PREVIOUS THROMBOSIS: 1. Advise the prescriber to avoid the use of contraceptives that contain oestrogens and prescribe a non-hormone contraceptive - such as a copper IUD - as an alternative. One could also opt for a progestogen-only contraceptive method, such as the depot injection, an IUD with levonorgestrel or an implant with etonogestrel. OTHER CASES: 1. Advise the patient to avoid additional risk factors for thrombosis (obesity, smoking, etc.).
https://www.g-standaard.nl/risicoanalyse/B0001567.PDF

clopidogrel

Drug Classes:
platelet aggregation inhibitors excl. heparin
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for clopidogrel and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104777
Source: CPIC
Variant: CYP2C19 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2C19 intermediate metabolizer. Avoid standard dose clopidogrel (75 mg) if possible due to the risk of therapeutic failure in patients that had a recent acute coronary syndrome and/or a percutaneous coronary intervention, or a neurovascular indication for clopidogrel. Consider use of an alternative antiplatelet agent at standard dose if no contraindication. Prasugrel is contraindicated in patients with a history of transient ischemic attack or stroke. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/guideline-for-clopidogrel-and-cyp2c19/
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
The risk of serious cardiovascular and cerebrovascular events is increased in patients undergoing balloon angioplasty or stent placement (percutaneous coronary intervention) and in patients with a stroke or TIA, as the genetic variation reduces the activation of clopidogrel. NO negative clinical consequences have been observed in other patients. PERCUTANEOUS CORONARY INTERVENTION, STROKE or TIA: choose an alternative or double the dose to 150 mg/day (600 mg loading dose) Prasugrel, ticagrelor and acetylsalicylic acid/dipyridamole are not metabolised by CYP2C19 (or to a lesser extent). OTHER INDICATIONS: NO action required
https://www.g-standaard.nl/risicoanalyse/B0002549.PDF
Source: FDA
Variant: CYP2C19 Intermediate Metabolizer
Results in lower systemic active metabolite concentrations, lower antiplatelet response, and may result in higher cardiovascular risk. Consider use of another platelet P2Y12 inhibitor.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

Additional Evidence

Variant: CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Metabolism Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy, Toxicity Evidence Link

celecoxib

Drug Classes:
other antineoplastic agents
coxibs
Source: PharmGKB
Variant: CYP2C9
Guideline: Actionable PGx
Annotation of FDA Label for celecoxib and CYP2C9 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104843
Source: CPIC
Variant: CYP2C9 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2C9 Intermediate Metabolizer with an activity score of 1 and is expected to have higher plasma concentrations of celecoxib which may increase the risk of toxicities. Initiate therapy with lowest recommended starting dose. Titrate dose to clinical effect or maximum recommended dose with caution.
https://cpicpgx.org/guidelines/cpic-guideline-for-nsaids-based-on-cyp2c9-genotype/

carisoprodol

Drug Classes:
carbamic acid esters
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for carisoprodol and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104832

Additional Evidence
Variant: CYP2C19 *1/*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link

glimepiride

Drug Classes:
sulfonamides, urea derivatives
sulfonylureas
Source: DPWG
Variant: CYP2C9 *1/*2
NO action is required for this gene-drug interaction. NO significant kinetic or clinical consequences have been found for the genetic variation.
https://www.g-standaard.nl/risicoanalyse/B0001891.PDF
Source: DPWG
Variant: CYP2C9 Intermediate Metabolizer
NO action is required for this gene-drug interaction. The genetic variation increases the effectiveness of glimepiride.
https://www.g-standaard.nl/risicoanalyse/B0001896.PDF

Additional Evidence
Variant: CYP2C9 *1/*2, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
Variant: CYP2C9 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link

voriconazole

Drug Classes:
triazole derivatives
triazole and tetrazole derivatives
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for voriconazole and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104818
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
The gene variation can reduce the conversion of voriconazole and consequently increase the plasma concentration. This could result in improved efficacy or an increase in the risk of side effects. Recommendation: Monitor the plasma concentration
https://www.g-standaard.nl/risicoanalyse/B0001683.PDF
Source: FDA
Variant: CYP2C19 Intermediate Metabolizer
Results in higher systemic concentrations and may result in higher adverse reaction risk.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

Additional Evidence

Variant: CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Supported, **Type:** Metabolism Evidence Link

citalopram

Drug Classes:
selective serotonin reuptake inhibitors
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for citalopram and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104852
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for citalopram and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166224101
Source: CPIC
Variant: CYP2C19 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2C19 intermediate metabolizer and is at risk for higher plasma concentrations and increased probability of side effects with standard dosing. Initiate therapy with recommended starting dose, but consider a slower titration schedule and lower maintenance dose. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-ssri-and-snri-antidepressants/
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
The risk of QT prolongation and torsades de pointes is theoretically increased because the gene variation leads to an increased citalopram plasma concentration. If you follow the dose recommendation below, the increased plasma concentration and the theoretically increased risk of QT prolongation will be offset. Do not exceed the following daily doses: 1. adults up to 65 years: 30 mg as tablets or 22 mg as drops 2. adults 65 years or older: 15 mg as tablets or 10 mg as drops
https://www.g-standaard.nl/risicoanalyse/B0004195.PDF

Additional Evidence

Variant: CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Efficacy Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy, Toxicity Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy, Toxicity Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity Evidence Link

risperidone

Drug Classes:
other antipsychotics
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for risperidone and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104793
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
NO action is needed for this gene-drug interaction. There is little evidence to support an increase in side effects caused by the genetic variation. The genetic variation may lead to a decrease in the required maintenance dose. However, as the effect on the dose is smaller than that of the normal biological variation, action is not useful.
https://www.g-standaard.nl/risicoanalyse/B0001536.PDF

Additional Evidence
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Metabolism Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Likely, **Type:** Other Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Likely, **Type:** Other Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link
Variant: DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: COMT A/G, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Efficacy Evidence Link
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
Variant: COMT V158M, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Efficacy Evidence Link

desvenlafaxine

Drug Classes:
other antidepressants
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for desvenlafaxine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166177483

tetrabenazine

Drug Classes:
other nervous system drugs
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for tetrabenazine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104829

clobazam

Drug Classes:
benzodiazepine derivatives
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for clobazam and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104884
Source: FDA
Variant: CYP2C19 Intermediate Metabolizer
Results in higher systemic active metabolite concentrations. Poor metabolism results in higher adverse reaction risk. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

Additional Evidence
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy, Metabolism Evidence Link

diazepam

Drug Classes:
benzodiazepine derivatives
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for diazepam and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104784

Additional Evidence
Variant: CYP2C19 *1/*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link

lansoprazole

Drug Classes:
proton pump inhibitors
Source: PharmGKB
Variant: CYP2C19
Annotation of FDA Label for lansoprazole and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104898
Source: CPIC
Variant: CYP2C19 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2C19 intermediate metabolizer. Initiate standard starting daily dose. If this proton pump inhibitor has been given for chronic therapy (>12 weeks) and after efficacy has been achieved, consider 50% reduction in daily dose to minimize the incidence of adverse events and monitor for continued efficacy. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-proton-pump-inhibitors-and-cyp2c19/
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
NO action is needed for this gene-drug interaction. The higher plasma concentration of lansoprazole results in an increase in the therapeutic effectiveness, without an increase in the incidence of side effects.
https://www.g-standaard.nl/risicoanalyse/B0001831.PDF

Additional Evidence
Variant: CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

abrocitinib

Drug Classes:
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for abrocitinib and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166272961

piroxicam

Drug Classes:
- oxicams
- antiinflammatory preparations, non-steroids for topical use
- antiinflammatory agents, non-steroids

Source: PharmGKB
Variant: CYP2C9
Guideline: Actionable PGx

Annotation of FDA Label for piroxicam and CYP2C9 (On FDA Biomarker List)

https://www.pharmgkb.org/labelAnnotation/PA166105222

Source: CPIC
Variant: CYP2C9 Intermediate Metabolizer

Based on the genotype result, this patient is predicted to be a CYP2C9 Intermediate Metabolizer with an activity score of 1 and is expected to have higher plasma concentrations of piroxicam which may increase the risk of toxicities. Choose an alternative therapy not metabolized by CYP2C9 or not significantly impacted by CYP2C9 genetic variants in vivo or choose an NSAID metabolized by CYP2C9 but with a shorter half-life (such as celecoxib, flurbiprofen, lornoxicam, or ibuprofen). Please consult a clinical pharmacistb for more information.

https://cpicpgx.org/guidelines/cpic-guideline-for-nsaids-based-on-cyp2c9-genotype/

Source: FDA
Variant: CYP2C9 Intermediate Metabolizer

Results in higher systemic concentrations. Consider reducing dosage in poor metabolizers.

https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

phenytoin

Drug Classes:
hydantoin derivatives
Source: PharmGKB
Variant: CYP2C9 *1/*2, CYP2C19, CYP2C9
Guideline: Actionable PGx
Annotation of FDA Label for phenytoin and CYP2C19, CYP2C9, HLA-B (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104860

Source: DPWG
Variant: CYP2C9 *1/*2
Genetic variation reduces conversion of phenytoin to inactive metabolites. This increases the risk of side effects. Recommendation: 1. The loading dose does not need to be adjusted. 2. For the other doses, use 75% of the standard dose and assess the dose based on effect and serum concentration after 7-10 days. 3. Advise the patient to get in touch if side effects (such as ataxia, nystagmus, slurred speech, sedation or rash) occur.
https://www.g-standaard.nl/risicoanalyse/B0001678.PDF

Source: CPIC
Variant: CYP2C9 Intermediate Metabolizer
HLA-B*15:02 genotype may be important for phenytoin adverse events. An HLA-B*15:02 genotype does not appear to have been ordered for this patient. Use of an alternative antiepileptic may be recommended. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/guideline-for-phenytoin-and-cyp2c9-and-hla-b/

Source: CPIC
Variant: CYP2C9 Intermediate Metabolizer
CYP2C9 and HLA-B*15:02 genotype can affect a patient's response to phenytoin. Based on the genotype result, this patient is predicted to be a CYP2C9 Intermediate Metabolizer and is at increased risk for developing phenytoin-induced toxicities. For first dose, use typical initial or loading dose. For subsequent doses, use approximately 25% less than typical maintenance dose. Subsequent doses should be adjusted according to therapeutic drug monitoring, response and side effects. An HLA-B*15:02 genotype does not appear to have been ordered for this patient. Use of an alternative antiepileptic may be recommended. Please consult a clinical pharmacist for more information
https://cpicpgx.org/guidelines/guideline-for-phenytoin-and-cyp2c9-and-hla-b/

Source: DPWG
Variant: CYP2C9 Intermediate Metabolizer
Genetic variation reduces conversion of phenytoin to inactive metabolites. This increases the risk of side effects. Recommendation: 1. The loading dose does not need to be adjusted. 2. For the other doses, use 75% of the standard dose and assess the dose based on effect and serum concentration after 7-10 days. 3. Advise the patient to get in touch if side effects (such as ataxia, nystagmus, slurred speech, sedation or rash) occur.
https://www.g-standaard.nl/risicoanalyse/B0001676.PDF

Source: FDA
Variant: CYP2C9 Intermediate Metabolizer
May result in higher systemic concentrations and higher adverse reaction risk (central nervous system toxicity). Refer to FDA labeling for specific dosing recommendations. Carriers of CYP2C9*3 alleles may be at increased risk of severe cutaneous adverse reactions. Consider avoiding phenytoin as an alternative to carbamazepine in patients who are CYP2C9*3 carriers. Genotyping is not a substitute for clinical vigilance and patient management.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

Additional Evidence
Variant: CYP2C9*2, **Source:** PharmGKB, **Significance:** Supported, **Type:** Toxicity, Metabolism Evidence Link
Variant: CYP2C9 *1/*2, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link
Variant: CYP2C9 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link

upadacitinib

Drug Classes:
selective immunosuppressants
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for upadacitinib and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166190761

siponimod

Drug Classes:
selective immunosuppressants
Source: PharmGKB
Variant: CYP2C9 *1/*2, CYP2C9
Annotation of FDA Label for siponimod and CYP2C9 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166182738
Source: FDA
Variant: CYP2C9 Intermediate Metabolizer
Results in higher systemic concentrations. Adjust dosage based on genotype. Do not use in patients with CYP2C9 *3/*3 genotype. Refer to FDA labeling for specific dosing recommendations.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

flurbiprofen

Drug Classes:
propionic acid derivatives
antiinflammatory preparations, non-steroids for topical use
antiinflammatory agents, non-steroids
Source: PharmGKB
Variant: CYP2C9
Guideline: Actionable PGx
Annotation of FDA Label for flurbiprofen and CYP2C9 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104922
Source: CPIC
Variant: CYP2C9 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2C9 Intermediate Metabolizer with an activity score of 1 and is expected to have higher plasma concentrations of flurbiprofen which may increase the risk of toxicities. Initiate therapy with lowest recommended starting dose. Titrate dose to clinical effect or maximum recommended dose with caution.
https://cpicpgx.org/guidelines/cpic-guideline-for-nsaids-based-on-cyp2c9-genotype/

Additional Evidence
Variant: CYP2C9*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link

atenolol

Drug Classes:
beta blocking agents, selective
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0002454.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link

fluoxetine

Drug Classes:
selective serotonin reuptake inhibitors
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for fluoxetine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104835
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
NO action is needed for this gene-drug interaction. The ratio of fluoxetine/norfluoxetine increases as a result of the reduced activity of CYP2D6. However, this does not affect the sum of the plasma concentrations of the active substances (fluoxetine and norfluoxetine). There isNO effect on adverse events or response.
https://www.g-standaard.nl/risicoanalyse/B0005997.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link

quetiapine

Drug Classes:
diazepines, oxazepines and thiazepines
diazepines, oxazepines, thiazepines and oxepines
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0002394.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link

metoclopramide

Drug Classes:
propulsives
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for metoclopramide and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166178750

clozapine

Drug Classes:
diazepines, oxazepines and thiazepines
diazepines, oxazepines, thiazepines and oxepines
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for clozapine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104815
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0001530.PDF

Additional Evidence

Variant: COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: CYP1A2 *1A/*1F, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link
Variant: COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: CYP1A2*1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: CYP1A2*1F, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: MTHFR E429A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link

atomoxetine

Drug Classes:
centrally acting sympathomimetics
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for atomoxetine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104827
Source: CPIC
Variant: CYP2D6 Intermediate Metabolizer
Although this patient is predicted to be a CYP2D6 normal metabolizer, this patient may not achieve adequate serum concentrations for the intended effect at standard dosing. 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 100mg/day may be needed to achieve target concentrations. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-atomoxetine-based-on-cyp2d6-genotype/
Source: CPIC
Variant: CYP2D6 Intermediate Metabolizer
This patient is predicted to be a CYP2D6 intermediate metabolizer and may be at an increased risk of a atomoxetine-related adverse events. Initiate with a dose of 40 mg/day and if no clinical response and in the absence of adverse events after 2 weeks increase dose to 80 mg/day. If response is inadequate after 2 weeks consider obtaining a plasma concentration 2-4 h after dosing. If concentration is <200 ng/ml, consider a proportional dose increase to achieve a concentration to approach 400 ng/ml. If unacceptable side effects are present at any time, consider a reduction in dose. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-atomoxetine-based-on-cyp2d6-genotype/
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The genetic variation increases the plasma concentration of atomoxetine and can thereby reduce the dose requirement. Recommendation: 1. in the event of side effects occurring and/or a response later than 9 weeks: reduce the dose and check whether the effect is conserved The plasma concentration of atomoxetine is a factor of 2-3 times higher for IM than for EM at the same dose.
https://www.g-standaard.nl/risicoanalyse/B0001599.PDF
Source: CPIC
Variant: CYP2D6 Normal metabolizer
Although this patient is predicted to be a CYP2D6 normal metabolizer, this patient may not achieve adequate serum concentrations for the intended effect at standard dosing. 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 100mg/day may be needed to achieve target concentrations. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-atomoxetine-based-on-cyp2d6-genotype/

Additional Evidence

Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Metabolism Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity Evidence Link

fluvastatin

Drug Classes:
hmg coa reductase inhibitors
Source: CPIC
Variant: CYP2C9 Intermediate Metabolizer
This patient is predicted to be a CYP2C9 intermediate metabolizer and may be at an increased risk of fluvastatin-induced myopathy. Prescribe â■¤40mg per day as a starting dose and adjust doses of fluvastatin based on disease-specific guidelines. If a dose >40mg is needed for desired efficacy, consider an alternative statin or combination therapy. Because SLCO1B1 phenotype could not be assigned based on genotyping performed, it is not known if SLCO1B1 results would further influence the recommended dose or drug. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-statins/

ibuprofen

Drug Classes:
other cardiac preparations
antiinflammatory products for vaginal administration
propionic acid derivatives
antiinflammatory preparations, non-steroids for topical use
Source: CPIC
Variant: CYP2C9 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2C9 Intermediate Metabolizer with an activity score of 1 and is expected to have higher plasma concentrations of ibuprofen which may increase the risk of toxicities. Initiate therapy with lowest recommended starting dose. Titrate dose to clinical effect or maximum recommended dose with caution.
https://cpicpgx.org/guidelines/cpic-guideline-for-nsaids-based-on-cyp2c9-genotype/

omeprazole

Drug Classes:
proton pump inhibitors
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for omeprazole and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104921
Source: CPIC
Variant: CYP2C19 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2C19 intermediate metabolizer. Initiate standard starting daily dose. If this proton pump inhibitor has been given for chronic therapy (>12 weeks) and after efficacy has been achieved, consider 50% reduction in daily dose to minimize the incidence of adverse events and monitor for continued efficacy. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-proton-pump-inhibitors-and-cyp2c19/
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
NO action is required for this gene-drug interaction. The higher plasma concentration of omeprazole results in an increase in the therapeutic effectiveness, without an increase in the side effects.
https://www.g-standaard.nl/risicoanalyse/B0001839.PDF

Additional Evidence
Variant: CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy Evidence Link

esomeprazole

Drug Classes:
proton pump inhibitors
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for esomeprazole and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104816
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for omeprazole and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104921
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
NO action is needed for this gene-drug interaction. Although the genetic variation leads to a higher plasma concentration of esomeprazole, there is insufficient evidence to support an effect on the therapeutic effectiveness and side effects.
https://www.g-standaard.nl/risicoanalyse/B0001824.PDF

Additional Evidence
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link

haloperidol

Drug Classes:
butyrophenone derivatives
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
NO action is required for this gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0001551.PDF

Additional Evidence
Variant: COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link
Variant: COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link

lacosamide

Drug Classes:
other antiepileptics
Source: PharmGKB
Variant: CYP2C19
Annotation of FDA Label for lacosamide and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166160049

ondansetron

Drug Classes:
serotonin (5ht3) antagonists
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for ondansetron and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166105211

Additional Evidence
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy Evidence Link

tacrolimus

Drug Classes:
calcineurin inhibitors
Source: PharmGKB
Variant: CYP3A5
Annotation of FDA Label for tacrolimus and CYP3A, CYP3A5 ()
https://www.pharmgkb.org/labelAnnotation/PA166234801
Source: DPWG
Variant: CYP3A5 homozygote expressor
Genetic variation results in an increased conversion of tacrolimus to inactive metabolites and as a result a higher dose is required. Adjustment of the initial dose results in an increased chance of reaching a tacrolimus concentration within the target range before the start of therapeutic drug monitoring on day three. However, there isNO direct evidence that this results in improved clinical results. Recommendation: Indications OTHER than liver transplantation: 1. Start with 2.5 times the standard initial dose that would yield the desired result in non-expressors Adjustment of the dose should then be based on therapeutic drug monitoring. NOTE: The initial dose that yields the desired result in non-expressors can be lower than the standard initial dose. In the example provided below, this dose was 75 % of the standard initial dose. A 2.5 time dose increase corresponds in this case to a 2 time dose increase of the standard initial dose. For example: After three days, Thervet et al. found a median trough concentration for tacrolimus of 14.0 ng/mL at an initial dose of 0.15 mg/kg twice daily for four kidney transplant patients, who were homozygous expressors. This was 5.6 ng/mL (n = 6) for an initial dose of 0.1 mg/kg twice daily. Their target value was 10 - 15 ng/mL. This is lower than the target value that is used in the Netherlands in the first two - four weeks after kidney transplantation (15 - 20 ng/mL). For the reference group of non-expressors, a median trough concentration of 16.6 ng/mL and 12.0 ng/mL was achieved at a dosage of 0.1 mg/kg twice daily and 0.075 mg/kg twice daily respectively. In this hospital, the first dose is administered before the CYP3A5 genotype is known. The second dose is reduced according to the genotype. LIVER transplantation: In addition to the patientâ■■s genotype, the metabolism of tacrolimus is also determined by the genotype of the transplanted liver. LIVER is also of the genotype HOMOZYGOUS EXPRESSOR: 1. Start with 2.5 times the standard initial dose Adjustment of the dose should then be based on therapeutic drug monitoring. LIVER has a DIFFERENT genotype: There is insufficient evidence in the literature to support a dose recommendation.
https://www.g-standaard.nl/risicoanalyse/B0002357.PDF

Additional Evidence
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

umeclidinium bromide

Drug Classes:
anticholinergics
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for umeclidinium and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166177521

ticagrelor

Drug Classes:
platelet aggregation inhibitors excl. heparin
Source: PharmGKB
Variant: CYP2C19
Annotation of FDA Label for ticagrelor and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104851
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0003516.PDF

Additional Evidence
Variant: CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link

duloxetine

Drug Classes:
other antidepressants
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for duloxetine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166105010
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0001673.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link

doxepin

Drug Classes:
non-selective monoamine reuptake inhibitors
other antipruritics
Source: PharmGKB
Variant: CYP2D6, CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for doxepin and CYP2C19, CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104820
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The risk of side effects may be increased, because the gene variation leads to increased plasma concentrations of doxepin and the active metabolite nordoxepin. use 80% of the standard dose and monitor the effect and side effects or the plasma concentrations of doxepin and nordoxepin in order to set the maintenance dose The therapeutic range is 100-250 ng/mL for the sum of doxepin and nordoxepin plasma concentrations. Values higher than 400 ng/mL are considered toxic.
https://www.g-standaard.nl/risicoanalyse/B0002015.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy Evidence Link

gefitinib

Drug Classes:
protein kinase inhibitors
epidermal growth factor receptor inhibitor
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for gefitinib and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166170929
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
NO action is needed for this gene-drug interaction. Side effects can occur more frequently, as the gene variation increases the gefitinib plasma concentration. However, the side effects are reversible and manageable, to an extent that adjustment of the therapy in advance is not necessary.
https://www.g-standaard.nl/risicoanalyse/B0004871.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity, Metabolism Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity, Metabolism Evidence Link

formoterol

Drug Classes:
selective beta-2-adrenoreceptor agonists
Source: PharmGKB
Variant: CYP2D6, CYP2C19
Annotation of FDA Label for formoterol and CYP2C19, CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166177509
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for arformoterol and CYP2D6, UGT1A1 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166127662

perphenazine

Drug Classes:
phenothiazines with aliphatic side-chain
phenothiazines with piperazine structure
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for perphenazine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104893

clonidine

Drug Classes:
imidazoline receptor agonists
other antimigraine preparations
sympathomimetics in glaucoma therapy
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0002531.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link

mirtazapine

Drug Classes:
other antidepressants
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
NO action is required for this gene-drug interaction. The higher plasma concentration of mirtazapine does not result in an increase in the side effects.
https://www.g-standaard.nl/risicoanalyse/B0002002.PDF
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0003507.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
Variant: CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy, Toxicity Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy, Toxicity Evidence Link

paliperidone

Drug Classes:
other antipsychotics
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for paliperidone and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166184539

prasugrel

Drug Classes:
platelet aggregation inhibitors excl. heparin
Source: PharmGKB
Variant: CYP2C19, CYP2C9, CYP3A5
Annotation of FDA Label for prasugrel and CYP2B6, CYP2C19, CYP2C9, CYP3A5 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104917
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0002546.PDF

Additional Evidence
Variant: CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link

methylphenidate

Drug Classes:
centrally acting sympathomimetics
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0002528.PDF

Additional Evidence
Variant: COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link
Variant: COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

escitalopram

Drug Classes:
selective serotonin reuptake inhibitors
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for escitalopram and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166105012
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for escitalopram and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166224121
Source: CPIC
Variant: CYP2C19 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2C19 intermediate metabolizer and is at risk for higher plasma concentrations and increased probability of side effects with standard dosing. Initiate therapy with recommended starting dose, but consider a slower titration schedule and lower maintenance dose. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-ssri-and-snri-antidepressants/
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
The risk of QT prolongation and torsades de pointes is theoretically increased because the gene variation leads to an increased escitalopram plasma concentration. If you follow the dose recommendation below, the increased plasma concentration and the theoretically increased risk of QT prolongation will be offset. Do not exceed the following doses (75% of the standard maximum dose): adults < 65 years 15 mg/day, =65 years 7.5 mg/day
https://www.g-standaard.nl/risicoanalyse/B0001821.PDF

Additional Evidence
Variant: CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy, Toxicity Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy, Toxicity Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity Evidence Link

mirabegron

Drug Classes:
urinary antispasmodics
drugs for urinary frequency and incontinence
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for mirabegron and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166177514

dronabinol

Drug Classes:
other antiemetics
Source: PharmGKB
Variant: CYP2C9
Guideline: Actionable PGx
Annotation of FDA Label for dronabinol and CYP2C9 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166163422
Source: FDA
Variant: CYP2C9 Intermediate Metabolizer
May result in higher systemic concentrations and higher adverse reaction risk. Monitor for adverse reactions.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

venlafaxine

Drug Classes:
other antidepressants
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for venlafaxine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104847
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The genetic polymorphism leads to decreased metabolic capacity of CYP2D6. This can cause an increase in the plasma concentration of venlafaxine and a decrease in the plasma concentration of the active metabolite O-desmethylvenlafaxine. Recommendation: It is not possible to offer adequately substantiated advice for dose reduction based on the literature. 1. Choose an alternative Antidepressants that are not metabolised by CYP2D6 - or to a lesser extent - include, for example, citalopram and sertraline. 2. If an alternative is not an option and side effects occur: 1. reduce the dose 2. check the plasma concentrations of venlafaxine and O-desmethylvenlafaxine It is not known whether it is possible to reduce the dose to such an extent that the side effects disappear, while the effectiveness is maintained. In general, it is assumed that the effectiveness is determined by the sum of the plasma concentrations of venlafaxine and O-desmethylvenlafaxine. However, the side effects do not appear to be related to this sum.
https://www.g-standaard.nl/risicoanalyse/B0001539.PDF

Additional Evidence

- **Variant:** COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link
- **Variant:** CYP2C19*2, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Efficacy Evidence Link
- **Variant:** COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy, Toxicity Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Metabolism Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy, Toxicity Evidence Link

paroxetine

Drug Classes:
selective serotonin reuptake inhibitors
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for paroxetine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104864
Source: CPIC
Variant: CYP2D6 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2D6 intermediate metabolizer and is at risk for higer plasma concentrations and increased probability of side effects with standard dosing. Consider a lower starting dose and slower titration schedule. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-ssri-and-snri-antidepressants/
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
NO action is needed for this gene-drug interaction. The plasma concentration of paroxetine can increase as a result of the reduced activity of CYP2D6. However, studies did not find any clinical effects.
https://www.g-standaard.nl/risicoanalyse/B0001563.PDF

Additional Evidence

- **Variant:** COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity, Metabolism Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity, Metabolism Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

nateglinide

Drug Classes:
other blood glucose lowering drugs, excl. insulins
Source: PharmGKB
Variant: CYP2C9
Guideline: Actionable PGx
Annotation of FDA Label for nateglinide and CYP2C9 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166269121

amoxapine

Drug Classes:
non-selective monoamine reuptake inhibitors
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for amoxapine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166182729

meloxicam

Drug Classes:
oxicams
Source: PharmGKB
Variant: CYP2C9
Guideline: Actionable PGx
Annotation of FDA Label for meloxicam and CYP2C9 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166182753
Source: CPIC
Variant: CYP2C9 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2C9 Intermediate Metabolizer with an activity score of 1 and is expected to have higher plasma concentrations of meloxicam which may increase the risk of toxicities. Initiate therapy with 50% of the lowest recommended starting dose. Titrate dose to clinical effect or 50% of the maximum recommended dose with caution. In accordance with the meloxicam prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. Dose titration should not occur until after steady state is reached (at least 7 days). Carefully monitor adverse events such as blood pressure and kidney function during course of therapy. Alternatively, consider alternative therapy. Choose an alternative therapy not metabolized by CYP2C9 or not significantly impacted by CYP2C9 genetic variants in vivo or choose an NSAID metabolized by CYP2C9 but with a shorter half-life (such as celecoxib, celecoxib, fluriprofen, lornoxicam, and ibuprofen). Please consult a clinical pharmacistb for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-nsaids-based-on-cyp2c9-genotype/

sertraline

Drug Classes:
selective serotonin reuptake inhibitors
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0003513.PDF
Source: CPIC
Variant: CYP2C19 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2C19 intermediate metabolizer and may be at risk for higer plasma concentrations with standard dosing. Initiate therapy with recommended starting dose. Consider a slower titration schedule and lower maintenance dose. Because a CYP2B6 genotype does not appear to have been ordered for this patient, it is not known if CYP2B6 results would further influence the recommended dose or drug. Please consult a clinical pharmacist for more information.Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-ssri-and-snri-antidepressants/
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
NO action is needed for this gene-drug interaction. The gene variation has a minor effect on the sertraline plasma concentration.NO effect on side effects was found.
https://www.g-standaard.nl/risicoanalyse/B0002008.PDF

Additional Evidence

- **Variant:** CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link
- **Variant:** CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** CYP2C19*2, **Source:** PharmGKB, **Significance:** Supported, **Type:** Metabolism Evidence Link

aripiprazole

Drug Classes:
other antipsychotics
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for aripiprazole and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104839
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
NO action is needed for this gene-drug interaction. The genetic variation increases the plasma concentration of the sum of aripiprazole and the active metabolite dehydroaripiprazole to a limited degree. There is insufficient evidence that this increases the risk of side effects.
https://www.g-standaard.nl/risicoanalyse/B0001541.PDF

Additional Evidence

- **Variant:** DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link

meclizine

Drug Classes:
piperazine derivatives
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for meclizine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166180000
Source: FDA
Variant: CYP2D6 Intermediate Metabolizer
May affect systemic concentrations. Monitor for adverse reactions and clinical effect.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

metoprolol

Drug Classes:
beta blocking agents, selective
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for metoprolol and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104836
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The gene variation reduces the conversion of metoprolol to inactive metabolites. However, the clinical consequences are limited mainly to the occurrence of asymptomatic bradycardia. Recommendation: If a GRADUAL REDUCTION in HEART RATE is desired, or in the event of SYMPTOMATIC BRADYCARDIA: 1. increase the dose in smaller steps and/or prescribeNO more than 50% of the standard dose OTHER CASES: 1.NO action required
https://www.g-standaard.nl/risicoanalyse/B0001554.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Metabolism Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Likely, **Type:** Metabolism Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Other Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Likely, **Type:** Metabolism Evidence Link

modafinil

Drug Classes:
centrally acting sympathomimetics
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for modafinil and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104868

Additional Evidence
Variant: COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

tolterodine
Drug Classes:
urinary antispasmodics
drugs for urinary frequency and incontinence
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for tolterodine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104806

Additional Evidence
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Likely, **Type:** Other Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Metabolism Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Likely, **Type:** Other Evidence Link

oxycodone
Drug Classes:
natural opium alkaloids
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
NO action is required for this gene-drug interaction. The reduced conversion of oxycodone to the more active metabolite oxymorphone does not result in reduced analgesia for patients.
https://www.g-standaard.nl/risicoanalyse/B0001587.PDF

Additional Evidence
Variant: COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: COMT A/G, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage, Efficacy Evidence Link
Variant: CYP3A5 *3/*3, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Efficacy Evidence Link
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy, Toxicity Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy, Toxicity Evidence Link
Variant: COMT V158M, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage, Efficacy Evidence Link
Variant: OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

galantamine
Drug Classes:
anticholinesterases
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for galantamine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104869

Additional Evidence
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link

nebivolol
Drug Classes:
beta blocking agents, selective
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for nebivolol and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166105028

darifenacin
Drug Classes:
urinary antispasmodics
drugs for urinary frequency and incontinence
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for darifenacin and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166122971

palonosetron
Drug Classes:
serotonin (5ht3) antagonists
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for palonosetron and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166160052

betaine
Drug Classes:
amino acids and derivatives
Source: PharmGKB
Variant: MTHFR
Annotation of FDA Label for betaine and CBS, MMADHC, MTHFR (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166293301

amphetamine
Drug Classes:
centrally acting sympathomimetics
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for amphetamine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166182730

propafenone
Drug Classes:
antiarrhythmics, class ic
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for propafenone and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104837

Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
Genetic variation increases the sum of the plasma concentrations of propafenone and the active metabolite 5-hydroxypropafenone. This may increase the risk of side effects. Recommendation: It is not possible to offer adequately substantiated recommendations for dose adjustment based on the literature. 1. Either guide the dose by therapeutic drug monitoring, perform an ECG and be alert to side effects 2. Or choose an alternative Antiarrhythmic drugs that are hardly if at all metabolised by CYP2D6 include, for example, sotalol, disopyramide, quinidine and amiodarone.
https://www.g-standaard.nl/risicoanalyse/B0001596.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage Evidence Link

dexlansoprazole

Drug Classes:
proton pump inhibitors
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for dexlansoprazole and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104863
Source: CPIC
Variant: CYP2C19 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2C19 intermediate metabolizer. Initiate standard starting daily dose. If this proton pump inhibitor has been given for chronic therapy (>12 weeks) and after efficacy has been achieved, consider 50% reduction in daily dose to minimize the incidence of adverse events and monitor for continued efficacy. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-proton-pump-inhibitors-and-cyp2c19/

pantoprazole

Drug Classes:
proton pump inhibitors
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for pantoprazole and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104901
Source: CPIC
Variant: CYP2C19 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2C19 intermediate metabolizer. Initiate standard starting daily dose. If this proton pump inhibitor has been given for chronic therapy (>12 weeks) and after efficacy has been achieved, consider 50% reduction in daily dose to minimize the incidence of adverse events and monitor for continued efficacy. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-proton-pump-inhibitors-and-cyp2c19/
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
NO action is required for this gene-drug interaction. The higher plasma concentration of pantoprazole results in an increase in the therapeutic effectiveness, without an increase in the side effects.
https://www.g-standaard.nl/risicoanalyse/B0001847.PDF
Source: FDA
Variant: CYP2C19 Intermediate Metabolizer
Results in higher systemic concentrations. Consider dosage reduction in children who are poor metabolizers. No dosage adjustment is needed for adult patients who are intermediate or poor metabolizers.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

Additional Evidence

Variant: CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

iloperidone

Drug Classes:
other antipsychotics
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for iloperidone and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104887

warfarin

Drug Classes:
vitamin k antagonists
Source: PharmGKB
Variant: CYP2C9 *1/*2, CYP2C9, VKORC1
Guideline: Actionable PGx
Annotation of FDA Label for warfarin and CYP2C9, PROC, PROS1, VKORC1 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104776
Source: DPWG
Variant: CYP2C9 *1/*2
NO action is required for this gene-drug interaction. Genetic variation may lead to a decrease in the required maintenance dose. However, there is insufficient evidence that this causes problems when therapy is initiated as usual.
https://www.g-standaard.nl/risicoanalyse/B0006228.PDF
Source: DPWG
Variant: VKORC1 -1639G>A G/A
NO action is required for this gene-drug interaction. The genetic variation results in a reduction in the required dose and an increase in the risk of excessively severe inhibition of blood clotting during the first month of the treatment. However, the effect is small and GA is also the most common genotype, meaning that the standard treatment will primarily be based on patients with this genotype.
https://www.g-standaard.nl/risicoanalyse/B0006235.PDF
Source: FDA
Variant: VKORC1 -1639G>A G/A
Alters dosage requirements. Select initial dosage, taking into account clinical and genetic factors. Monitor and adjust dosages based on INR.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations
Source: DPWG
Variant: CYP2C9 Intermediate Metabolizer
This gene variation reduces the conversion of warfarin to inactive metabolites. This can increase the risk of bleeding. Recommendation: 1. use 65% of the standard initial dose The genotype-specific initial dose and maintenance dose can be calculated using an algorithm. Algorithms for Caucasian patients usually contain only the *2 and *3 allele. If the activity of the reduced-activity alleles is comparable to the activity of *2 or *3, then the algorithm can be completed as if *1/*2 or *1/*3 is present. See https://www.knmp.nl/producten-en-diensten/gebruiksrecht-gstandaard/medicatiebewaking-g-standaard/background-information-pharmacogenetics for Excel files containing calculation modules for oral and equivalent intravenous doses. From day 6 on the standard algorithm without genotype information can be used to calculate the dose. Modified dose algorithms have been developed for patients of African or (East) Asian heritage.
https://www.g-standaard.nl/risicoanalyse/B0006233.PDF
Source: FDA
Variant: CYP2C9 Intermediate Metabolizer
Alters systemic concentrations and dosage requirements. Select initial dosage, taking into account clinical and genetic factors. Monitor and adjust dosages based on INR.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

Additional Evidence

- **Variant:** CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** CYP2C9*2, **Source:** PharmGKB, **Significance:** Supported, **Type:** Dosage Evidence Link
- **Variant:** CYP2C9*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Toxicity Evidence Link
- **Variant:** CYP2C9*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** CYP2C9*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** CYP2C9*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** CYP2C9*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Toxicity Evidence Link
- **Variant:** CYP2C19 *1/*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** CYP2C9 *1/*2, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
- **Variant:** CYP2C9 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Metabolism Evidence Link
- **Variant:** VKORC1 -1639G>A G/A, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy Evidence Link
- **Variant:** VKORC1 -1639G>A G/A, **Source:** PharmGKB, **Significance:** Likely, **Type:** Toxicity Evidence Link
- **Variant:** VKORC1 -1639G>A G/A, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy Evidence Link
- **Variant:** VKORC1 -1639G>A G/A, **Source:** PharmGKB, **Significance:** Likely, **Type:** Toxicity Evidence Link
- **Variant:** VKORC1 -1639G>A G/A, **Source:** PharmGKB, **Significance:** Supported, **Type:** Dosage Evidence Link

pimozide

Drug Classes:
diphenylbutylpiperidine derivatives
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for pimozide and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104870
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The risk of QT-prolongation â■■ and thereby also the risk of torsade de points â■■ is theoretically increased, because the genetic variation results in an increase in the plasma concentration of pimozide. The risk of an excessively high plasma concentration can be negated by following the dose recommendations provided below. Recommendation: useNO more than the following doses (80% of the standard maximum dose): adults 16 mg/day children 0.08 mg/kg per day to a maximum of 3 mg/day
https://www.g-standaard.nl/risicoanalyse/B0002448.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Efficacy Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Other Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Other Evidence Link

rivaroxaban

Drug Classes:
other antithrombotic agents
Source: PharmGKB
Variant: F5
Annotation of FDA Label for rivaroxaban and F5 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166182726

brivaracetam

Drug Classes:
other antiepileptics
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for brivaracetam and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166153492
Source: FDA
Variant: CYP2C19 Intermediate Metabolizer
Results in higher systemic concentrations and higher adverse reaction risk. Consider dosage reductions in poor metabolizers.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

Additional Evidence
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Metabolism Evidence Link

betaine hydrochloride

Drug Classes:
acid preparations
Source: PharmGKB
Variant: MTHFR
Annotation of FDA Label for betaine and CBS, MMADHC, MTHFR (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166293301

vortioxetine

Drug Classes:
other antidepressants
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for vortioxetine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166122607

Additional Evidence
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link

eliglustat

Drug Classes:
various alimentary tract and metabolism products
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for eliglustat and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166123487

Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This gene variation reduces the conversion of eliglustat to inactive metabolites. However, in the absence of CYP2D6 and CYP3A inhibitors, this does not result in a clinically significant increased risk of side effects. Recommendation: Co-medication with BOTH a MODERATE to STRONG CYP2D6 INHIBITOR AND a MODERATE to STRONG CYP3A INHIBITOR: Eliglustat is contra-indicated. 1. choose an alternative if possible Strong CYP2D6 inhibitor: for example paroxetine, fluoxetine, quinidine, bupropione. Moderate CYP2D6 inhibitor: for example duloxetine, terbinafine, moclobemide, mirabegron, cinacalcet, dronedarone. Strong CYP3A inhibitor: for example ketoconazole, clarithromycin, itraconazole, cobicistat, indinavir, lopinavir, ritonavir, saquinavir, telaprevir, tipranavir, posaconazole, voriconazole, telithromycin, conivaptan, boceprevir. Moderate CYP3A inhibitor: for example erythromycin, ciprofloxacin, fluconazole, diltiazem, verapamil, aprepitant, atazanavir, darunavir, fosamprenavir, imatinib, cimetidine. Co-medication with a STRONG CYP2D6 INHIBITOR (e.g. paroxetine, fluoxetine, quinidine, bupropione): 1. use a dose of 84 mg eliglustat 1x daily Co-medication with a MODERATE CYP2D6 INHIBITOR (for example duloxetine, terbinafine, moclobemide, mirabegron, cinacalcet, dronedarone): 1. consider a dose of 84 mg eliglustat 1x daily 2. be alert to side effects Co-medication with a STRONG CYP3A INHIBITOR (for example ketoconazole, clarithromycin, itraconazole, cobicistat, indinavir, lopinavir, ritonavir, saquinavir, telaprevir, tipranavir, posaconazole, voriconazole, telithromycin, conivaptan, boceprevir): choose an alternative if possible if an alternative is not an option: consider a dose of 84 mg eliglustat 1x daily be alert to side effects Co-medication with a MODERATE CYP3A INHIBITOR (for example erythromycin, ciprofloxacin, fluconazole, diltiazem, verapamil, aprepitant, atazanavir, darunavir, fosamprenavir, imatinib, cimetidine): 1. choose an alternative 2. if an alternative is not an option: 1. consider a dose of 84 mg eliglustat 1x daily 2. be alert to side effects Co-medication with a STRONG CYP3A INDUCER (for example rifampicin, carbamazepine, phenobarbital, phenytoin, rifabutine, hypericum): Eliglustat is not recommended. The plasma concentration may decrease so sharply that a therapeutic effect cannot be achieved. 1. choose an alternative if possible NO co-medication with a moderate or strong CYP2D6 or CYP3A inhibitor or strong CYP3A inducer: 1. use the standard dose of 84 mg 2x daily
https://www.g-standaard.nl/risicoanalyse/B0006138.PDF

Source: FDA
Variant: CYP2D6 Intermediate Metabolizer
Alters systemic concentrations, effectiveness, and adverse reaction risk (QT prolongation). Indicated for normal, intermediate, and poor metabolizer patients. Ultrarapid metabolizers may not achieve adequate concentrations to achieve a therapeutic effect. The recommended dosages are based on CYP2D6 metabolizer status. Coadministration with strong CYP3A inhibitors is contraindicated in intermediate and poor CYP2D6 metabolizers. Refer to FDA labeling for specific dosing recommendations.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link

flibanserin

Drug Classes:
other gynecologicals
Source: PharmGKB
Variant: CYP2D6, CYP2C9, CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for flibanserin and CYP2C19, CYP2C9, CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166153432

brexpiprazole
Drug Classes:
other antipsychotics
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for brexpiprazole and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166160054

lusutrombopag
Drug Classes:
other systemic hemostatics
Source: PharmGKB
Variant: F5
Guideline: Actionable PGx
Annotation of FDA Label for lusutrombopag and F2, F5, PROC, PROS1, SERPINC1 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166182749

ospemifene
Drug Classes:
selective estrogen receptor modulators
Source: PharmGKB
Variant: CYP2C9
Annotation of FDA Label for ospemifene and CYP2B6, CYP2C9 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166185190

erdafitinib
Drug Classes:
fibroblast growth factor receptor (fgfr) tyrosine kinase inhibitors
Source: PharmGKB
Variant: CYP2C9
Guideline: Actionable PGx
Annotation of FDA Label for erdafitinib and CYP2C9 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166182722

quinine
Drug Classes:
methanolquinolines
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for quinine and CYP2D6, G6PD (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166105232

cariprazine
Drug Classes:
other antipsychotics
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for cariprazine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166177479

terbinafine

Drug Classes:
other antifungals for topical use
antifungals for systemic use
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for terbinafine and CYP2D6 (Formerly on FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104822

hydrocodone

Drug Classes:
opium alkaloids and derivatives
Source: CPIC
Variant: CYP2D6 Intermediate Metabolizer
This patient is predicted to be a CYP2D6 intermediate metabolizer possibly resulting in decreased analgesia to hydrocodone, codeine and tramadol. Initiate therapy at the recommended age and weight specific dosing. If no adequate analgesic response, consider selecting an alternative agent. If opioid use is warranted, avoid codeine and tramadol. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/guideline-for-codeine-and-cyp2d6/

Additional Evidence
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link

bupropion

Drug Classes:
other antidepressants
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for bupropion and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166223861

Additional Evidence
Variant: DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: CYP2C19 *1/*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link

cevimeline

Drug Classes:
other parasympathomimetics
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for cevimeline and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104787

rabeprazole
Drug Classes:
proton pump inhibitors
Source: PharmGKB
Variant: CYP2C19
Guideline: Actionable PGx
Annotation of FDA Label for rabeprazole and CYP2C19 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104848
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
NO action is required for this gene-drug interaction. The higher plasma concentration of rabeprazole does not result in an increase in side effects.
https://www.g-standaard.nl/risicoanalyse/B0001856.PDF

Additional Evidence
Variant: CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Metabolism Evidence Link

deutetrabenazine
Drug Classes:
other nervous system drugs
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for deutetrabenazine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166169882

desipramine
Drug Classes:
non-selective monoamine reuptake inhibitors
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for desipramine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104862

Additional Evidence
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Likely, **Type:** Other Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Likely, **Type:** Other Evidence Link

rucaparib
Drug Classes:
poly (adp-ribose) polymerase (parp) inhibitors
Source: PharmGKB
Variant: CYP2D6, CYP1A2
Guideline: Actionable PGx
Annotation of FDA Label for rucaparib and CYP1A2, CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166170935

valbenazine
Drug Classes:
other nervous system drugs
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for valbenazine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166170052

oliceridine
Drug Classes:
other opioids
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for oliceridine and CYP2D6 ()
https://www.pharmgkb.org/labelAnnotation/PA166225161

amiodarone
Drug Classes:
antiarrhythmics, class iii
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0002543.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link

amitriptyline
Drug Classes:
non-selective monoamine reuptake inhibitors
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for amitriptyline and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104856
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The genetic polymorphism leads to decreased metabolic capacity of CYP2D6, which may cause an increase in the plasma concentrations of amitriptyline and its active metabolite nortriptyline and decreased plasma concentrations of the active metabolites E-10-OHamitriptyline and E-10-OH-nortriptyline. Recommendation: 1. Choose an alternative if possible Antidepressants that are not metabolised via CYP2D6 - or to a lesser extent - include, for example, citalopram and sertraline. 2. If an alternative is not an option: use 60% of the standard dose and monitor the plasma concentrations of amitriptyline and nortriptyline As side effects are related to nortriptyline plasma concentrations and the efficacy to amitriptyline plus nortriptyline plasma concentrations, which are influenced to a lesser extent by CYP2D6, it is not known whether it is possible to reduce the dose to such an extent that the side effects disappear, but the efficacy is maintained.
https://www.g-standaard.nl/risicoanalyse/B0001920.PDF
Source: CPIC
Variant: CYP2C19 Intermediate Metabolizer
This patient is predicted to be a CYP2C19 intermediate metabolizer. There is no reason to selectively adjust the dose of this medication based on the CYP2C19 result.
https://cpicpgx.org/guidelines/guideline-for-tricyclic-antidepressants-and-cyp2d6-and-cyp2c19/

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Metabolism Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity Evidence Link
Variant: CYP2C19*2, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity Evidence Link

bisoprolol
Drug Classes:
beta blocking agents, selective
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0002457.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link

clomipramine

Drug Classes:
non-selective monoamine reuptake inhibitors
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for clomipramine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104875
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The risk of side effects may be increased, because the gene variation leads to increased plasma concentrations of clomipramine and the active metabolite desmethylclomipramine. use 70% of the standard dose and monitor the effect and side effects or the plasma concentrations of clomipramine and desmethylclomipramine For depression, the therapeutic range is 200-400 ng/mL for the sum of the plasma concentrations of clomipramine and desmethylclomipramine. 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/mLFor obsessive compulsive disorder, the therapeutic plasma concentration of clomipramine is higher than 200 ng/mL, in combination with a plasma concentration of desmethylclomipramine that is as low as possible. A sum of the plasma concentrations of clomipramine and desmethylclomipramine higher than 600 ng/mL is considered toxic.
https://www.g-standaard.nl/risicoanalyse/B0001481.PDF

Additional Evidence

- **Variant:** CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link
- **Variant:** CYP2C19*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Unknown Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity Evidence Link

codeine

Drug Classes:
opium alkaloids and derivatives
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for codeine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104916
Source: CPIC
Variant: CYP2D6 Intermediate Metabolizer
This patient is predicted to be a CYP2D6 intermediate metabolizer possibly resulting in decreased analgesia to codeine and tramadol. Initiate therapy at the recommended age and weight specific dosing. If no adequate analgesic response, consider selecting an alternative agent. If opioid use is warranted, avoid codeine and tramadol. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/guideline-for-codeine-and-cyp2d6/
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The genetic variation reduces the conversion of codeine to morphine. This can result in reduced analgesia. Recommendation: For COUGH: 1.NO action required For PAIN: It is not possible to offer adequately substantiated advice for dose adjustment based on the limited available literature for this phenotype. 1. be alert to a reduced effectiveness 2. in the case of inadequate effectiveness: 1. try a dose increase 2. if this does not work: choose an alternative Do not select tramadol, as this is also metabolised by CYP2D6 Morphine is not metabolised by CYP2D6. Oxycodone is metabolised by CYP2D6 to a limited extent, but this does not result in differences in analgesia in patients. 3. ifNO alternative is selected: advise the patient to report inadequate analgesia
https://www.g-standaard.nl/risicoanalyse/B0001584.PDF

Additional Evidence

- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Metabolism Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Metabolism Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link

disopyramide
Drug Classes:
antiarrhythmics, class ia
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0002537.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link

donepezil
Drug Classes:
anticholinesterases
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for donepezil and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166105113

Additional Evidence
Variant: CYP2D6 *1/*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link

flecainide
Drug Classes:
antiarrhythmics, class ic
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The genetic variation reduces conversion of flecainide to inactive metabolites. This may increase the risk of side effects. Recommendation: Indications other than diagnosis of Brugada syndrome: 1. reduce the dose to 75% of the standard dose and record an ECG and monitor the plasma concentration Provocation test for diagnosis of Brugada syndrome: NO action required. At a dose of 2.0 mg/kg body weight to a maximum of 150 mg, the response is better for patients with alleles that result in reduced activity. All 5 patients with these alleles and 20% of the patients with two fully active alleles exhibited a response within 30 minutes.
https://www.g-standaard.nl/risicoanalyse/B0001593.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Likely, **Type:** Other Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Likely, **Type:** Other Evidence Link

fluphenazine
Drug Classes:
phenothiazines with aliphatic side-chain
phenothiazines with piperazine structure
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction. Despite the fact that the SmPC for fluphenazine lists CYP2D6 as the metabolising enzyme, this cannot be substantiated by the available literature.
https://www.g-standaard.nl/risicoanalyse/B0002451.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link

fluvoxamine

Drug Classes:
selective serotonin reuptake inhibitors
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for fluvoxamine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104854
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
NO action is needed for this gene-drug interaction. The plasma concentration of fluvoxamine can increase as a result of the reduced activity of CYP2D6. However, there is insufficient scientific substantiation of an increase in the risk of side effects.
https://www.g-standaard.nl/risicoanalyse/B0005994.PDF
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
This is NOT a gene-drug interaction
https://www.g-standaard.nl/risicoanalyse/B0003510.PDF

Additional Evidence

- **Variant:** COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
- **Variant:** CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity, Metabolism Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity, Metabolism Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

imipramine

Drug Classes:
non-selective monoamine reuptake inhibitors
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for imipramine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104879
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The risk of side effects may be increased, because the gene variation leads to increased plasma concentrations of imipramine and desipramine. use 70% of the standard dose and monitor the effect and side effects or the plasma concentrations of imipramine and desipramine in order to set the maintenance dose The therapeutic range is 150-300 ng/mL for the sum of the imipramine and desipramine plasma concentrations. Values exceeding 500 ng/mL are considered toxic.
https://www.g-standaard.nl/risicoanalyse/B0001545.PDF
Source: DPWG
Variant: CYP2C19 Intermediate Metabolizer
NO action is required for this gene-drug interaction. The genetic variation increases imipramine plasma concentrations, but not imipramine+desipramine plasma concentrations, which govern effectiveness and side effects.
https://www.g-standaard.nl/risicoanalyse/B0001913.PDF

Additional Evidence

- **Variant:** CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link
- **Variant:** CYP2C19 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage Evidence Link
- **Variant:** CYP2C19*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Other Evidence Link

lofexidine

Drug Classes:
drugs used in opioid dependence
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for lofexidine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166179848

nefazodone

Drug Classes:
other antidepressants
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for nefazodone and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104880

nelfinavir

Drug Classes:
protease inhibitors
Source: PharmGKB
Variant: CYP2C19
Annotation of FDA Label for nelfinavir and CYP2C19, CYP3A (Formerly on FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104808

nortriptyline

Drug Classes:
non-selective monoamine reuptake inhibitors
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for nortriptyline and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104888

Source: CPIC
Variant: CYP2D6 Intermediate Metabolizer
Based on the genotype result, this patient is predicted to be a CYP2D6 intermediate metabolizer and higher than expected plasma concentrations of nortriptyline resulting in an increased the probability of adverse reactions. Consider 25% reduction of recommended starting dosed. Utilize therapeutic drug monitoring to guide dose adjustments. Please consult a clinical pharmacistc for more information.
https://cpicpgx.org/guidelines/guideline-for-tricyclic-antidepressants-and-cyp2d6-and-cyp2c19/

Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The risk of side effects may be increased, because the gene variation leads to an increased plasma concentration of nortriptyline. use 60% of the standard dose and monitor the effect and side effects or the plasma concentration of nortriptyline in order to set the maintenance dose The therapeutic range of nortriptyline is 50-150 ng/mL. Values exceeding 250 ng/mL are considered toxic.
https://www.g-standaard.nl/risicoanalyse/B0001557.PDF

Additional Evidence

Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Toxicity Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity, Metabolism Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Toxicity, Metabolism Evidence Link

propranolol

Drug Classes:
beta blocking agents, non-selective
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for propranolol and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104798

Additional Evidence
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Other Evidence Link

protriptyline

Drug Classes:
non-selective monoamine reuptake inhibitors
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for protriptyline and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104812

quinidine

Drug Classes:
antiarrhythmics, class ia
Source: PharmGKB
Variant: CYP2D6
Annotation of FDA Label for quinidine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104811
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0002534.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link

sotalol

Drug Classes:
beta blocking agents, non-selective
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This is NOT a gene-drug interaction.
https://www.g-standaard.nl/risicoanalyse/B0002540.PDF

Additional Evidence
Variant: CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Unsupported, **Type:** None Evidence Link

tamoxifen

Drug Classes:
anti-estrogens
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for tamoxifen and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166181925
Source: PharmGKB
Variant: F5
Annotation of FDA Label for tamoxifen and F2, F5 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166170936
Source: CPIC
Variant: CYP2D6 Intermediate Metabolizer
This patient is predicted to have lower than normal CYP2D6 activity and may be at an increased risk of a poor tamoxifen response due to low endoxifen (active component of tamoxifen) concentrations. Consider hormonal therapy such as an aromatase inhibitor for postmenopausal women or aromatase inhibitor along with ovarian function suppression in premenopausal women. If aromatase inhibitor use is contraindicated, consideration should be given to use a higher but FDA approved tamoxifen dose (40 mg/day). Avoid CYP2D6 inhibitors. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/cpic-guideline-for-tamoxifen-based-on-cyp2d6-genotype/
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
This gene variation reduces the conversion of tamoxifen to the active metabolite endoxifen. This can result in reduced effectiveness. Recommendation: 1. select an alternative or measure the endoxifen concentration and increase the dose if necessary by a factor of 1.5-2 Aromatase inhibitors are a possible alternative for post-menopausal women. 2. if TAMOXIFEN is selected: avoid co-medication with CYP2D6 inhibitors such as paroxetine and fluoxetine
https://www.g-standaard.nl/risicoanalyse/B0001602.PDF

Additional Evidence

- **Variant:** CYP2C19 *1/*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy, Metabolism Evidence Link
- **Variant:** CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Metabolism Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Metabolism Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Metabolism Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Supported, **Type:** Efficacy, Metabolism Evidence Link
- **Variant:** CYP2C19*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy, Metabolism Evidence Link

tamsulosin

Drug Classes:
alpha-adrenoreceptor antagonists
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for tamsulosin and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166160672

thioridazine

Drug Classes:
phenothiazines with aliphatic side-chain
phenothiazines with piperidine structure
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for thioridazine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104805

tramadol

Drug Classes:
other opioids
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for tramadol and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104799
Source: CPIC
Variant: CYP2D6 Intermediate Metabolizer
This patient is predicted to be a CYP2D6 intermediate metabolizer possibly resulting in decreased analgesia to tramadol and codeine. Initiate therapy at the recommended age and weight specific dosing. If no adequate analgesic response, consider selecting an alternative agent. If opioid use is warranted, avoid tramadole and codeine. Please consult a clinical pharmacist for more information.
https://cpicpgx.org/guidelines/guideline-for-codeine-and-cyp2d6/
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The genetic variation reduces the conversion of tramadol to a metabolite with a higher activity. This can result in reduced analgesia. Recommendation: It is not possible to provide a recommendation for dose adjustment, because the total analgesic effect changes when the ratio between the mother compound and the active metabolite changes. 1. be alert to a reduced effectiveness 2. in the case of inadequate effectiveness: 1. try a dose increase 2. if this does not work: choose an alternative Do not select codeine, as this is also metabolised by CYP2D6. Morphine is not metabolised by CYP2D6. Oxycodone is metabolised by CYP2D6 to a limited extent, but this does not result in differences in analgesia in patients. 3. ifNO alternative is selected: advise the patient to report inadequate analgesia
https://www.g-standaard.nl/risicoanalyse/B0001590.PDF, https://www.g-standaard.nl/risicoanalyse/B0001590.PDF
Source: DPWG
Variant: CYP2D6 Intermediate Metabolizer
The genetic variation reduces the conversion of tramadol to a metabolite with a higher activity. This can result in reduced analgesia. Recommendation: It is not possible to provide a recommendation for dose adjustment, because the total analgesic effect changes when the ratio between the mother compound and the active metabolite changes. 1. be alert to a reduced effectiveness 2. in the case of inadequate effectiveness: 1. try a dose increase 2. if this does not work: choose an alternative Do not select codeine, as this is also metabolised by CYP2D6. Morphine is not metabolised by CYP2D6. Oxycodone is metabolised by CYP2D6 to a limited extent, but this does not result in differences in analgesia in patients. 3. ifNO alternative is selected: advise the patient to report inadequate analgesia
https://www.g-standaard.nl/risicoanalyse/B0001590.PDF, https://www.g-standaard.nl/risicoanalyse/B0001590.PDF

Additional Evidence

- **Variant:** COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** COMT A/G, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage, Efficacy Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** CYP2D6 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** Metabolism Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Supported, **Type:** Dosage, Efficacy, Toxicity, Metabolism Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Supported, **Type:** Dosage, Efficacy, Toxicity, Metabolism Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** COMT V158M, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage, Efficacy Evidence Link
- **Variant:** COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link

trimipramine

Drug Classes:
non-selective monoamine reuptake inhibitors
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for trimipramine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104857

Additional Evidence

- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Supported, **Type:** Other Evidence Link
- **Variant:** CYP2D6*4, **Source:** PharmGKB, **Significance:** Supported, **Type:** Other Evidence Link
- **Variant:** CYP2C19*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Metabolism Evidence Link

viloxazine
Drug Classes:
other antidepressants
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for viloxazine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166251601

fesoterodine
Drug Classes:
urinary antispasmodics
drugs for urinary frequency and incontinence
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for fesoterodine and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166122972

eltrombopag
Drug Classes:
other systemic hemostatics
Source: PharmGKB
Variant: F5
Guideline: Actionable PGx
Annotation of FDA Label for eltrombopag and F5, SERPINC1 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166104912

pitolisant
Drug Classes:
other nervous system drugs
Source: PharmGKB
Variant: CYP2D6
Guideline: Actionable PGx
Annotation of FDA Label for pitolisant and CYP2D6 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166185168

avatrombopag
Drug Classes:
other systemic hemostatics
Source: PharmGKB
Variant: F5
Guideline: Actionable PGx
Annotation of FDA Label for avatrombopag and F2, F5, PROC, PROS1, SERPINC1 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166179855
Source: PharmGKB
Variant: CYP2C9
Annotation of FDA Label for avatrombopag and CYP2C9 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166184917

rimegepant
Drug Classes:
Source: PharmGKB
Variant: CYP2C9
Annotation of FDA Label for rimegepant and CYP2C9 (On FDA Biomarker List)
https://www.pharmgkb.org/labelAnnotation/PA166225042

⚠ *glyburide*

Drug Classes:
- sulfonamides, urea derivatives
- sulfonylureas

Additional Evidence
- **Variant:** CYP2C9 *1/*2, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link
- **Variant:** CYP2C9 Intermediate Metabolizer, **Source:** DPWG, **Significance:** Supported, **Type:** None Evidence Link

⚠ *nicotine*

Drug Classes:
- drugs used in nicotine dependence

Additional Evidence
- **Variant:** DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** COMT A/G, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Dosage, Other Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** COMT V158M, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Dosage, Other Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link

⚠ *aspirin*

Drug Classes:
- other agents for local oral treatment
- platelet aggregation inhibitors excl. heparin
- salicylic acid and derivatives

Additional Evidence
- **Variant:** CYP2C19*2, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy, Toxicity Evidence Link

⚠ *morphine*
Drug Classes:
natural opium alkaloids
Additional Evidence
Variant: COMT A/G, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage, Efficacy Evidence Link
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Metabolism Evidence Link
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: OPRM1 N40D, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Metabolism Evidence Link
Variant: COMT V158M, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage, Efficacy Evidence Link

⚠ *naloxone*
Drug Classes:
antidotes
antidote agent
Additional Evidence
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
Variant: OPRM1 N40D, **Source:** PharmGKB, **Significance:** Likely, **Type:** Efficacy Evidence Link

⚠ *sufentanil*
Drug Classes:
opioid anesthetics
Additional Evidence
Variant: COMT A/G, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage, Efficacy Evidence Link
Variant: CYP3A5 *3/*3, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Dosage Evidence Link
Variant: COMT V158M, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage, Efficacy Evidence Link
Variant: OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link

⚠ *methadone*
Drug Classes:
drugs used in opioid dependence
Additional Evidence
Variant: COMT A/G, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage, Efficacy Evidence Link
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link
Variant: COMT V158M, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage, Efficacy Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Metabolism Evidence Link
Variant: OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link

⚠ *remifentanil*
Drug Classes:
opioid anesthetics
Additional Evidence
Variant: COMT A/G, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage, Efficacy Evidence Link
Variant: COMT V158M, **Source:** PharmGKB, **Significance:** Likely, **Type:** Dosage, Efficacy Evidence Link

? *progesterone*
Drug Classes:
pregnen (4) derivatives
Additional Evidence
Variant: CYP2C19 *1/*2, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link

? *cilostazol*
Drug Classes:
platelet aggregation inhibitors excl. heparin
Additional Evidence
Variant: CYP3A5 *3/*3, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link

? *disulfiram*
Drug Classes:
drugs used in alcohol dependence
sulfur containing products
Additional Evidence
Variant: DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

? *caffeine*
Drug Classes:
other dermatologicals
xanthine derivatives
Additional Evidence
Variant: CYP1A2 *1A/*1F, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: CYP1A2*1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: CYP1A2*1F, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link

? *lovastatin*
Drug Classes:
hmg coa reductase inhibitors
Additional Evidence
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link

? *buprenorphine*
Drug Classes:
oripavine derivatives
drugs used in opioid dependence
Additional Evidence
Variant: COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link

? *dextromethorphan*
Drug Classes:
opium alkaloids and derivatives
Additional Evidence
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Metabolism Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Other Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Other Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Other Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Other Evidence Link
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Other Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Other Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Other Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Other Evidence Link

methotrexate
Drug Classes:
- folic acid analogues
- other immunosuppressants

Additional Evidence
- **Variant:** MTHFR E429A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** MTHFR E429A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** MTHFR E429A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity, Metabolism Evidence Link
- **Variant:** MTHFR E429A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

cisplatin
Drug Classes:
- platinum compounds

Additional Evidence
- **Variant:** MTHFR E429A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

sumatriptan
Drug Classes:
- selective serotonin (5ht1) agonists

Additional Evidence
- **Variant:** COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
- **Variant:** COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link

diclofenac
Drug Classes:
- other dermatologicals
- acetic acid derivatives and related substances
- antiinflammatory preparations, non-steroids for topical use
- antiinflammatory agents, non-steroids

Additional Evidence

entacapone
Drug Classes:
- other dopaminergic agents

Additional Evidence
- **Variant:** COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

fentanyl
Drug Classes:
- opioid anesthetics
- phenylpiperidine derivatives

Additional Evidence
- **Variant:** COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** COMT A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** CYP3A5 *3/*3, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
- **Variant:** CYP3A5 *3/*3, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** COMT V158M, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link

midazolam
Drug Classes:
benzodiazepine derivatives
Additional Evidence
Variant: CYP3A5 *3/*3, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link

indomethacin
Drug Classes:
other cardiac preparations
acetic acid derivatives and related substances
antiinflammatory preparations, non-steroids for topical use
antiinflammatory agents, non-steroids
Additional Evidence

prochlorperazine
Drug Classes:
phenothiazines with aliphatic side-chain
phenothiazines with piperazine structure
Additional Evidence
Variant: DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

paclitaxel
Drug Classes:
taxanes
Additional Evidence
Variant: CYP3A5 *3/*3, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link

carboplatin
Drug Classes:
platinum compounds
Additional Evidence
Variant: CYP3A5 *3/*3, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
Variant: MTHFR E429A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

timolol
Drug Classes:
beta blocking agents, non-selective
beta blocking agents
Additional Evidence
Variant: CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link
Variant: CYP2D6*4, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Other Evidence Link

nimodipine
Drug Classes:
dihydropyridine derivatives
Additional Evidence
Variant: CYP3A5 *3/*3, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link

maraviroc
Drug Classes:
other antivirals
Additional Evidence
Variant: CYP3A5 *3/*3, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy, Metabolism Evidence Link

ethanol
Drug Classes:
- other antiseptics and disinfectants
- antidotes
- antidote agent
- nerve depressants

Additional Evidence
- **Variant:** DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** DRD2 WT/Taq1A, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link

granisetron
Drug Classes:
- serotonin (5ht3) antagonists

Additional Evidence
- **Variant:** CYP3A5 *3/*3, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

atorvastatin
Drug Classes:
- hmg coa reductase inhibitors

Additional Evidence
- **Variant:** CYP3A5 *3/*3, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy, Toxicity Evidence Link

naltrexone
Drug Classes:
- drugs used in alcohol dependence

Additional Evidence
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy, Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy, Toxicity Evidence Link

alfentanil
Drug Classes:
- opioid anesthetics

Additional Evidence
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Dosage Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Metabolism Evidence Link

? cocaine
Drug Classes:
- esters of benzoic acid
- local anesthetics
- anesthetics, local
- analgesics and anesthetics

Additional Evidence
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 A/G, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Toxicity Evidence Link
- **Variant:** OPRM1 N40D, **Source:** PharmGKB, **Significance:** Unsupported, **Type:** Toxicity Evidence Link

? dolasetron
Drug Classes:
- serotonin (5ht3) antagonists

Additional Evidence
- **Variant:** CYP2D6*1, **Source:** PharmGKB, **Significance:** Uncertain, **Type:** Efficacy Evidence Link

✓ atazanavir
Drug Classes:
- protease inhibitors

✓ sirolimus
Drug Classes:
- selective immunosuppressants
- other ophthalmologicals

✓ cyclosporine
Drug Classes:
- calcineurin inhibitors
- other ophthalmologicals

✓ dronedarone
Drug Classes:
- antiarrhythmics, class iii

✓ ritonavir
Drug Classes:
- protease inhibitors

✓ naproxen
Drug Classes:
- antiinflammatory products for vaginal administration
- propionic acid derivatives
- antiinflammatory preparations, non-steroids for topical use

✓ axitinib
Drug Classes:
- vascular endothelial growth factor receptor (vegfr) tyrosine kinase inhibitors

✓ ethinyl estradiol
Drug Classes:
- natural and semisynthetic estrogens, plain
- estrogens

nabumetone
Drug Classes:
other antiinflammatory and antirheumatic agents, non-steroids

simvastatin
Drug Classes:
hmg coa reductase inhibitors

drospirenone
Drug Classes:
progestogens

rosuvastatin
Drug Classes:
hmg coa reductase inhibitors

pitavastatin
Drug Classes:
hmg coa reductase inhibitors

ranolazine
Drug Classes:
other cardiac preparations

ibrutinib
Drug Classes:
bruton's tyrosine kinase (btk) inhibitors

labetalol
Drug Classes:
alpha and beta blocking agents

tafenoquine
Drug Classes:
aminoquinolines

aceclofenac
Drug Classes:
acetic acid derivatives and related substances
antiinflammatory preparations, non-steroids for topical use

eletriptan
Drug Classes:
selective serotonin (5ht1) agonists

hydromorphone
Drug Classes:
natural opium alkaloids

losartan
Drug Classes:
angiotensin ii antagonists
angiotensin ii receptor blockers (arbs), plain

✅ *pravastatin*
Drug Classes:
hmg coa reductase inhibitors

✅ *dolutegravir*
Drug Classes: