NalaGenetics

RxReady Report

The RxReady is a genetic test that gives your physician additional information about how your DNA impacts your body's interaction with drugs. This test is best used with your physician's or other care provider's input. For more information about this test, contact our patient care manager or counselor.

Patient Detail

NALAGENETICS ID	ALWA9710041
PATIENT NAME	Alan Walker
DATE OF BIRTH	02-01-1997
NATIONAL ID / PASSPORT NO.	S9999999Y
GENDER	Male

Provider Detail

PROVIDER NAME	Nalagenetics
PROVIDER ID	Training
ORDER	#4249-239678

Sample Detail

CLINIC NAME & ADDRESS	Nalagenetics Pte Ltd 1093 Lower Delta Road, #04-05/06/07/08, Singapore 169204	TESTING LAB NAME & ADDRESS	Nalagenetics Diagnostics Laboratory (SG) 1093 Lower Delta Road
TYPE OF SAMPLE	Buccal Swab	COLLECTED DATE	02/04/2023 (11:05 PM)
TEST METHOD	Quantitative PCR	RECEIVED DATE	10/04/2023 (11:20 PM)

Table of Contents

This report was validated and generated automatically. No signature is required. Recommendations given in this report are made using a lab developed test which should notsupersede clinical judgement or medical expertise.

II. Legend

A. Summary of Follow Up Actions

Our knowledge base ranks and summarizes clinical recommendations published by expert consortia, regulatory bodies, and other trusted sources for drugs based on genetic information, along with clinical information of the patient. These symbols are a summary of the recommendation text next to it.

Change Prescription
There is a high chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism.

Increase Monitoring
Although patient has a varied genetic profile, the intended medication can still be prescribed as recommended, but with more frequent monitoring for quick action to be taken in the event of unwanted reactions.

Decrease Starting Dose
Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Increase Starting Dose
Patient has altered metabolism rate or reduced activation rate for drug indicated. Increased starting dose has shown to help patient into target therapeutic range faster and/or reduce the risk of drug clinical inefficacy.

Follow standard dosing
There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

B. Recommendation Caveats

These caveats are taken from pharmacogenomics guidelines, which will usually specify the required conditions and situations wherethe guideline is relevant. The various caveats are grouped below:

Indication
This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Initiation
This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Turnaround Time
The benefit of waiting for a genetic test result may be less than starting the medication without a genetic test result.

Predictive Value
Low positive predictive value. Testing positive for this phenotype does not mean that the patient will develop the adverse effect.

C. Level of Scientific Evidence

Our knowledge base ranks and summarizes the strength of clinical recommendations published by expert consortia, regulatory bodies, and other trusted sources for drugs based on DNA information, along with other clinical information of the patient. These texts are a summary of the level of scientific evidence available for the respective clinical recommendation as presented below.

STRONG RECOMMENDATION
You can follow the recommendation confidently because its effect has been categorized to improve clinical outcome by at least one ofthe following medical societies or regulatory bodies. Each guideline has different kinds of strength of evidence. We reclassified the following categories from each guideline into Strong Recommendation:
CPIC/CPNDS - Strong Recomndation OR DPWG - Level 3 or 4 level of evidence OR PRO - strong, essential or advisable test OR FDA/Other regulatory bodies - Testing required

MODERATE RECOMMENDATION
You can consider the recommendation as it has been categorized to have some potential clinical benefit by at least one of the following medical societies or regulatory bodies. We reclassified the following categories from each guideline into Moderate Recommendation:
CPIC/CPNDS - Moderate or optional recommendation OR DPWG - Level 2 level of evidence OR PRO - conditional or possibly helpful test OR FDA/Other regulatory bodies - Testing recommended or actionable PGx

INFORMATION AVAILABLE
The information provided serves as an additional point of consideration for the patient's therapy. The recommendation with insufficient data is also included as this category. We reclassified the following categories from each guideline into Information Available:
DPWG - Level 0 or 1 level of evidence OR FDA/Other regulatory bodies - Informative PGx

PGx Medical Societies

CPIC (Clinical Pharmacogenetics Implementation Consortium)

An international consortium of professionals interested in applying pharmacogenetics for patient care. Established in 2009, it consists of PGRN members, PharmGKB staff, and various experts. The guidelines are indexed in PubMed as clinical guidelines, endorsed by ASHP and ASCPT , and referenced in ClinGen and PharmGKB.

DPWG (Dutch Pharmacogenetics Working Group)

A multidisciplinary group of physicians, pharmacists, and other healthcare professionals. It was established in 2005 by the Royal Dutch Pharmacists Association (KNMP) with the objective of developing pharmacogenomic-based therapeutic (dose) recommendations. The guidelines are endorsed by the EACPT and the EAHP.

CPNDS (Canadian Pharmacogenomics Network for Drug Safety)

A pan-Canadian active surveillance network consisting of trained surveillance clinicians in 10 pediatric teaching hospitals across Canada, serving >75% of Canada's children. Established in 2005, the network's goal is to improve the safe use of medication by identifying genomic biomarkers of drug risk for serious ADRs.

PRO (Professional Societies)

A source that includes the French National Network of Pharmacogenetics (RNPGx), the Cystic Fibrosis Foundation and the American College of Rheumatology for approriate drug presented.

Regulatory Bodies

FDA (Food and Drug Administration)

An agency within the US Department of Health and Human Services. It is responsible for protecting the public health by ensuring the safety, efficacy, and security of human and veterinary drugs, biological products, and medical devices.

EMA (European Medicines Agency)

A decentralised agency of the European Union (EU) responsible for the scientific evaluation, supervision and safety monitoring of medicines in the EU. EMA is a networking organisation whose activities involve thousands of experts from across Europe. These experts carry out the work of EMA's scientific committees.

PMDA (Pharmaceuticals and Medical Devices Agency)

A Japan agency that was established and came into service on April 1, 2004, under the Law for the Pharmaceuticals and Medical Devices Agency, as a part of the Japan Association for the Advancement of Medical Equipment (JAAME).

Swissmedic

The Swiss authority responsible for the authorisation and supervision of therapeutic products. The activities of Swissmedic are based on the Law on Therapeutic Products.

HCSC (Health Canada Santé Canada)

A federal department responsible for helping Canadians maintain and improve their health, while respecting individual choices and circumstances.

Each guideline and label annotation has its own strength of evidence for every drug-gene pair interaction.

D. Localizations of Evidence

- The drugs presented in this report are all drugs that are available in your country.
- Our PGx recommendations are always supported by research findings from studies done in your ethnic population (e.g. if you are Chinese, we provide supporting scientific evidence from studies in the Chinese population).
- RxReady tests for genetic polymorphisms that are relevant in the Asian population.

E. Disclaimers

Recommendations given in this report are made using a lab-developed test which should not supersede clinical judgement or medical expertise.

The DNA test results are not intended to be used by you as a substitute for professional medical advice. You should always seek the advice of a healthcare provider or physician for any diagnostic purpose with any questions you may have regarding the diagnosis, cure, treatment, mitigation or prevention of any disease or other medical conditions or impairment or the status of your health. The laboratory may not be able to process your sample and the laboratory process may result in errors. The laboratory may not be able to process your DNA sample if it does not contain sufficient amount of DNA. Furthermore, if the DNA sample that you have provided is contaminated and/or corrupted, the accuracy of the DNA test result may be impacted. Even with stringent acceptance criteria for sample processing that meets our high standards, a small, unknown fraction of the data generated during the laboratory process may be un-interpretable or incorrect and may therefore not be able to generate corresponding report. The test detects five genes and twenty-one variants using real-time qPCR genotyping. The recommendations in this report are obtained from various medical societies and regulatory bodies. The following genetic variants will be detected in the assay: CYP2D6 rs1065852, rs5030655, rs3892097, rs35742686, rs16947, rs28371725, rs1135840, rs769258, rs5030865, rs5030656, rs59421388, rs267608319, exon 9 conversion (*36), deletion (*5) and duplication; CYP2C9 rs1799853, rs1057910; CYP2C19 rs4244285, rs4986893, rs12248560 ; SLCO1B1 rs4149056; HLA-B*58:01. The copy number assays in this test do not differentiate between partial and whole gene deletions and/or duplications. Copy number variants that are more than three cannot be detected with this test, and may have to be detected with a different platform. Tandem-hybrid arrangements in CYP2D6 are not distinguished. Any complex rearrangements or mosaicisms are also not detected in this test. A normal (wild type) genotype signifies the absence of the targeted alleles and does not indicate the absence of other mutations not covered by the assay. The possibility cannot be ruled out that the indicated genotypes may be present and are below the limits of detection for this assay. The DNA test may not capture scientific findings which are not yet validated or not provided. Like all diagnostic tests, pharmacogenomic tests are one of multiple pieces of information that clinicians should consider when making their therapeutic choice for each patient.

III. Executive Report

PATIENT NAME	NATIONAL ID / PASSPORT NO.	ORDERING PROVIDER
Alan Walker	S9999999Y	Nalagenetics
GENDER	**DATE OF BIRTH**	**ORDER ID**
Male	02-01-1997	4249-239678

A. Genomic Information

Gene	Genotype	Phenotype
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer
HLA-B	HLA-B*58:01 negative	No increased risk of Allopurinol-induced SCAR caused by HLA-B*58:01
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function

B. Current Medications

Information not available.

C. Pharmacogenomics Summary

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
CARDIOVASCULAR SYSTEM	ANGIOTENSIN II RECEPTOR BLOCKERS					• Losartan || CYP2C9
	ANTIANGINA					• Ranolazine
	ANTIARRHYTHMICS CLASS I					• Disopyramide • Flecainide • Propafenone • Quinidine
	ANTIARRHYTHMICS CLASS I/III					• Vernakalant
	ANTIARRHYTHMICS CLASS III					• Amiodarone • Dronedarone || CYP2D6
	ANTICOAGULANTS			• Warfarin		• Acenocoumarol || CYP2C9 • Phenprocoumon || CYP2C9
	ANTIHEMORRHAGICS					• Avatrombopag
	ANTIPLATELETS	• Clopidogrel				• Aspirin || CYP2C9 • Prasugrel || CYP2C19 • Prasugrel || CYP2C9 • Ticagrelor
	BETA BLOCKING AGENTS					• Atenolol • Bisoprolol • Carvedilol • Metoprolol • Nebivolol • Propranolol • Sotalol • Timolol
	CENTRAL AGONISTS					• Clonidine
	FIBRATES					• Fenofibrate

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
CARDIOVASCULAR SYSTEM	NON-SELECTIVE NSAIDS					• Aspirin || CYP2C9
	STATINS	• Fluvastatin • Fluvastatin || CYP2C9				• Atorvastatin • Fluvastatin || SLCO1B1 • Lovastatin • Pitavastatin • Pravastatin • Rosuvastatin || SLCO1B1 • Simvastatin

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
DERMATOLOGY	OTHERS					• Abrocitinib || CYP2C9 • Abrocitinib || CYP2C19

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
ENDOCRINOLOGY	BLOOD GLUCOSE LOWERING DRUGS, EXCL. INSULINS					• Nateglinide
	SULFONYLUREAS					• Glibenclamide || CYP2C9 • Gliclazide || CYP2C9 • Glimepiride || CYP2C9 • Tolbutamide || CYP2C9

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
GASTROINTESTINAL SYSTEM	ANTIEMETICS AND ANTINAUSEANTS				• Dronabinol	• Ondansetron • Palonosetron • Tropisetron
	OTHERS					• Eliglustat
	PROPULSIVES					• Metoclopramide || CYP2D6
	PROTON PUMP INHIBITORS				• Lansoprazole	• Dexlansoprazole • Esomeprazole • Omeprazole • Pantoprazole • Rabeprazole

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
GYNECOLOGY	ALPHA BLOCKERS					• Tamsulosin
	ANTIMUSCARINICS					• Darifenacin • Fesoterodine • Tolterodine
	BETA AGONIST					• Mirabegron
	HYPOTHALAMIC HORMONES					• Elagolix
	OTHERS					• Drospirenone And Ethinylestradiol • Flibanserin || CYP2C19 • Flibanserin || CYP2C9 • Flibanserin || CYP2D6
	SEX HORMONES AND MODULATORS OF THE GENITAL SYSTEM					• Ospemifene || CYP2C9

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
IMMUNOLOGY	IMMUNOSUPPRESSANTS			• Siponimod		

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
INFECTIOUS DISEASE	ANTIFUNGALS					• Terbinafine • Voriconazole || CYP2C19 • Voriconazole || CYP2C9
	ANTIMALARIALS					• Quinine || CYP2D6
	ANTIRETROVIRALS				• Atazanavir	• Nelfinavir • Ritonavir
	ANTIVIRALS					• Letermovir

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
MUSCULOSKELETAL SYSTEM	ANTIGOUT PREPARATIONS					• Allopurinol • Lesinurad
	MUSCLE RELAXANTS					• Tolperisone

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
NEUROLOGY	ANTI-DEMENTIA DRUGS					• Donepezil • Galantamine
	ANTIEPILEPTICS	• Fosphenytoin		• Clobazam • Phenytoin || CYP2C9		• Brivaracetam || CYP2C19 • Brivaracetam || CYP2C9 • Diazepam • Lacosamide • Phenytoin || CYP2C19
	ANXIOLYTICS					• Diazepam
	OTHERS					• Cevimeline • Deutetrabenazine • Eletriptan • Tetrabenazine • Valbenazine

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
ONCOLOGY	ANTIMETABOLITES					• Methotrexate
	ESTROGEN RECEPTOR ANTAGONISTS					• Tamoxifen
	IMMUNOSUPPRESSANTS					• Upadacitinib
	OTHER ANTINEOPLASTIC AGENTS					• Rucaparib
	PROTEIN KINASE INHIBITORS					• Axitinib • Erdafitinib • Gefitinib • Ibrutinib

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
OPHTHALMOLOGY	BETA BLOCKING AGENTS					• Timolol

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
PAIN MANAGEMENT	ANALGESICS					• Paracetamol, Caffeine, And Dihydrocodeine • Paracetamol, Combinations Excl. Psycholeptics • Rimegepant
	ANTIPLATELETS					• Aspirin || CYP2C9
	COX-2 SELECTIVE NSAIDS			• Celecoxib		• Lumiracoxib
	MUSCLE RELAXANTS					• Carisoprodol
	NON-SELECTIVE NSAIDS	• Meloxicam • Piroxicam • Tenoxicam		• Flurbiprofen • Ibuprofen • Lornoxicam		• Aceclofenac • Aspirin || CYP2C9 • Diclofenac || CYP2C9 • Dipyrone • Indomethacin • Nabumetone • Naproxen
	OPIOIDS					• Oliceridine • Oxycodone • Tramadol || CYP2D6

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
PSYCHIATRY	1ST GEN ANTIPSYCHOTICS					• Flupenthixol • Haloperidol • Perphenazine • Pimozide • Thioridazine • Zuclopenthixol
	2ND GEN ANTIPSYCHOTICS					• Aripiprazole • Aripiprazole Lauroxil • Brexpiprazole • Cariprazine • Clozapine || CYP2D6 • Iloperidone • Olanzapine || CYP2D6 • Paliperidone • Quetiapine || CYP2D6 • Risperidone • Sertindole
	ANTIDEPRESSANTS MONOAMINE OXIDASE A INHIBITORS					• Moclobemide
	ANTIEPILEPTICS					• Diazepam
	ANXIOLYTICS					• Diazepam
	ATYPICAL ANTIDEPRESSANTS					• Bupropion • Mirtazapine || CYP2C19 • Mirtazapine || CYP2D6
	DRUGS USED IN ADDICTIVE DISORDERS					• Lofexidine

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
PSYCHIATRY	DRUGS USED IN OPIOID DEPENDENCE					• Methadone || CYP2D6
	OTHER ANTIDEPRESSANTS				• Vortioxetine	
	PSYCHOSTIMULANTS			• Atomoxetine		• Amfetamine • Methylphenidate • Modafinil • Pitolisant
	SELECTIVE SEROTONIN AND NOREPINEPHRINE REUPTAKE INHIBITORS					• Venlafaxine
	SELECTIVE SEROTONIN REUPTAKE INHIBITORS			• Escitalopram || CYP2C19	• Fluoxetine	• Citalopram || CYP2C19 • Citalopram || CYP2D6 • Escitalopram || CYP2D6 • Fluvoxamine || CYP2C19 • Fluvoxamine || CYP2D6 • Paroxetine • Sertraline || CYP2C19 • Sertraline || CYP2D6
	SEROTONIN REUPTAKE INHIBITORS					• Nefazodone
	SEROTONIN/NOREPINEPHRINE REUPTAKE INHIBITORS					• Desvenlafaxine • Duloxetine

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
PSYCHIATRY	TRICYCLIC ANTIDEPRESSANTS			• Amitriptyline || CYP2C19 • Clomipramine || CYP2C19 • Doxepin || CYP2C19 • Imipramine || CYP2C19 • Imipramine || CYP2D6 • Trimipramine • Trimipramine || CYP2C19 • Trimipramine || CYP2D6		• Amitriptyline || CYP2D6 • Amitriptyline • Amoxapine • Clomipramine • Clomipramine || CYP2D6 • Desipramine • Doxepin • Doxepin || CYP2D6 • Imipramine • Nortriptyline • Protriptyline

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
RESPIRATORY SYSTEM	ANTICHOLINERGICS					• Tiotropium • Umeclidinium
	ANTIHISTAMINES					• Meclizine
	COUGH SUPPRESSANTS					• Dextromethorphan • Dextromethorphan And Quinidine
	LONG-ACTING BETA AGONISTS					• Arformoterol • Formoterol || CYP2C19 • Formoterol || CYP2D6
	OPIOID COUGH SUPPRESSANTS					• Codeine • Hydrocodone

Category	Drug Class	Change Prescription	Increase Starting Dose	Decrease Starting Dose	Monitor	Follow Standard Dosing
UROLOGY	ALPHA BLOCKERS					• Tamsulosin
	ANTIMUSCARINICS					• Darifenacin • Fesoterodine • Tolterodine
	BETA AGONIST					• Mirabegron
	SELECTIVE SEROTONIN REUPTAKE INHIBITORS					• Dapoxetine

IV. Individual Drug Report

Abrocitinib || CYP2C19

Abrocitinib

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation available for this drug-gene pair.

Body weight, gender, CYP2C19 genotype, race and age did not have a clinically meaningful effect on abrocitinib exposure.

Recommendations based on specific guidelines

EMA **No actionable recommendation available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **HCSC**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Abrocitinib || CYP2C9

Abrocitinib

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation available for this drug-gene pair.

Body weight, gender, CYP2C9 genotype, race and age did not have a clinically meaningful effect on abrocitinib exposure.

Recommendations based on specific guidelines

EMA	**No actionable recommendation available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **HCSC**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Aceclofenac

ACB, Airtal, Aceclofenac

START INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

The pharmacokinetics of this drug is not significantly impacted by CYP2C9 genetic variants in vivo and/or there is insufficient evidence to provide a recommendation to guide clinical practice at this time.

Recommendations based on specific guidelines

CPIC — **No actionable recommendation is available for this drug-gene pair.**

Caveat

Rare CYP2C9 variants may not be included in the genotype test used, and patients with rare variants may be assigned an NM phenotype based on a default CYP2C9*1/*1 test result. Thus, an assigned CYP2C9*1 allele could potentially harbor a decreased or no function variant. Therefore, it is important that genetic test reports include information on which variant alleles were genotyped or which single-nucleotide polymorphisms were interrogated. As with any diagnostic test, CYP2C9 genotype is just one factor that clinicians should consider when prescribing NSAIDs to an individual patient. Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or GI adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and GI adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with antiplatelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Acenocoumarol || CYP2C9

Acenocoumarol

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

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 (i.e. with frequent INR monitoring).

Recommendations based on specific guidelines

DPWG	**No actionable recommendation is available for this drug-gene pair.**
SWISSMEDIC	No actionable recommendation is available for this drug-gene pair.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Allopurinol

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
HLA-B	HLA-B*58:01 negative	No increased risk of Allopurinol-induced SCAR caused by HLA-B*58:01

Recommendation

Use allopurinol per standard dosing guidelines.
Low or reduced risk of allopurinol SCAR.

Recommendations based on specific guidelines

CPIC	**Use allopurinol per standard dosing guidelines.**
PMDA	No actionable recommendation is available for this drug-gene pair.

More information about this drug-phenotype can also be found at **HCSC**.

Caveat

The positive predictive value for HLA-B*58:01 is ~1.5% and the negative predictive value is 100% (based on the data from the Han-Chinese and Thai populations). Therefore, a significant number of patients carrying the allele will not develop SCAR when they receive allopurinol treatment. New genetic factors may be identified in the future to differentiate the HLA-B*58:01 carriers who are or are not likely to develop SCAR. The most severe SCAR (toxic epidermal necrolysis) carries a 30% mortality rate. However, further study is warranted on the development of SCAR in European populations. HLA-B*58:01 predicts only allopurinol-induced SCAR, not other adverse events (such as mild skin rash) that a patient might experience during allopurinol treatment. The marker also does not predict the efficacy of treatment with allopurinol. Regardless of the genotyping results, physicians should monitor patients closely.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

26632391 25327504

Follow standard dosing
There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Predictive Value
Low positive predictive value. Testing positive for this phenotype does not mean that the patient will develop the adverse effect.

Amfetamine

Amphetamine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Although the enzymes involved in amphetamine metabolism have not been clearly defined, CYP2D6 is known to be involved with formation of 4-hydroxy-amphetamine. Since CYP2D6 is genetically polymorphic, population variations in amphetamine metabolism are a possibility.

Recommendations based on specific guidelines

FDA	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Amiodarone

Amiodarone, Cordarone, Kendaron, Tiaryt, Rexidron, Lamda, Aratac

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Amitriptyline

Amitriptyline, Apo-Amitryptiline, Trilin, Tripta

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.

CYP2D6 NM: Normal metabolism of TCAs. CYP2C19 IM: Reduced metabolism of tertiary amines.

Recommendations based on specific guidelines

CPIC **Initiate therapy with recommended starting dose.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

12172336 27288795 28296334 12012142

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Amitriptyline || CYP2C19

Amitriptyline, Apo-Amitryptiline, Trilin, Tripta

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose.

Reduced metabolism of tertiary amines compared to normal metabolizers.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose.**
DPWG	No actionable recommendation is available for this drug-gene pair.

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose

Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Amitriptyline || CYP2D6

Amitriptyline, Apo-Amitryptiline, Trilin, Tripta

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.

Normal metabolism of TCAs.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose.|| Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Amoxapine

Amoxapine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Arformoterol

Arformoterol

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Aripiprazole

Aripiprazole, Abilify, Aripi, Ariski, Arinia, Avram, Zipren, Zonia

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Aripiprazole lauroxil

Aripiprazole Lauroxil

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Aspirin || CYP2C9

Aspirin, Bayer Aspirin, Aptor, Ascardia, Aspilets, Astika, Bodrexin, Cardio Aspirin, Cartylo, Contrexyn, Farmasal, Gramasal, Inzana, Miniaspi, Naspro, Nospirinal, Thrombo Aspilets

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

The pharmacokinetics of this drug is not significantly impacted by CYP2C9 genetic variants in vivo and/or there is insufficient evidence to provide a recommendation to guide clinical practice at this time.

Recommendations based on specific guidelines

CPIC — **No actionable recommendation is available for this drug-gene pair.**

Caveat

Rare CYP2C9 variants may not be included in the genotype test used, and patients with rare variants may be assigned an NM phenotype based on a default CYP2C9*1/*1 test result. Thus, an assigned CYP2C9*1 allele could potentially harbor a decreased or no function variant. Therefore, it is important that genetic test reports include information on which variant alleles were genotyped or which single-nucleotide polymorphisms were interrogated. As with any diagnostic test, CYP2C9 genotype is just one factor that clinicians should consider when prescribing NSAIDs to an individual patient. Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or GI adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and GI adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with antiplatelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Atazanavir

Atazanavir, Reyataz

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Patients with at least one functional CYP2C19 allele, close clinical monitoring for a loss of both voriconazole (clinical signs) and atazanavir (virologic response) efficacy is recommended.

In the majority of patients with at least one functional CYP2C19 allele, a reduction in both voriconazole and atazanavir exposures are expected.

Recommendations based on specific guidelines

EMA	**Patients with at least one functional CYP2C19 allele, close clinical monitoring for a loss of both voriconazole (clinical signs) and atazanavir (virologic response) efficacy is recommended.|| If genotyping is not feasible, full monitoring of safety and efficacy should be performed. Co-administration of voriconazole and atazanavir with ritonavir is not recommended unless an assessment of the benefit/risk to the patient justifies the use of voriconazole.**

More information about this drug-phenotype can also be found at **HCSC**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Increase Monitoring

Although patient has a varied genetic profile, the intended medication can still be prescribed as recommended, but with more frequent monitoring for quick action to be taken in the event of unwanted reactions.

Atenolol

Atenolol, Betablok, Farnormin, Internolol, Lotensi, Urosin, Alonet, Normaten, Prenolol, Hypernol, Tenormin, Tenol, Vascoten, Velorin, Pretenol, Apo-Atenol, Tenolol, Nif-Ten, Tensig, Lotenal, Atenosan, Catenol, Aiti, Noten

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Atomoxetine

Atomoxetine, Strattera

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate with 40 mg/day and increase to 80 mg/day after 3 days.

Normal metabolizers have a lower likelihood of response as compared to poor metabolizers. This is associated with increase discontinuation due to lack of efficacy.

Recommendations based on specific guidelines

CPIC	**Initiate with 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 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 to approach 400 ng/ml. Therapeutic range of 200 to 1000 ng/ml has been proposed. Modest improvement in response (reduction in ADHD-RS) is observed at peak concentrations >400 ng/ml. Dosages >100 mg/day may be needed to achieve target concentrations.**

Caveat

Available exposure-response data from clinical trials are derived from concentrations drawn 60–90 minutes after dosing; although this measure may not be the best predictor of response, the relationship between other exposure measures, such as trough concentration at steady state, steady-state AUC, unbound atomoxetine concentrations, or total active compounds (unbound atomoxetine + unbound 4-OH aglycone), has not been evaluated.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

21543662 17610534

Decrease Starting Dose

Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Predictive Value

Low positive predictive value. Testing positive for this phenotype does not mean that the patient will develop the adverse effect.

Atorvastatin

Atorvastatin, Atavor, Beatorva, Atorsan, Torvatec, Atswift, Atorvachol, Atorvon, Tulip, Atoris, Torvalip, Eturion, Lipitor, Actalipid, Removchol, Fastor, Stavinor, Genlipid, Atofit, Litorcom, Simtor, Tavora, Stator, Apo-Atorvastatin

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function

Recommendation

Prescribe desired starting dose and adjust doses based on disease-specific guidelines.

Typical myopathy risk and statin exposure.

Recommendations based on specific guidelines

CPIC	**Prescribe desired starting dose and adjust doses based on disease-specific guidelines.**

Caveat

Genetic variation is just one factor when prescribing statins. Rare variants may not be included in the genotype test. Patients with rare variants that reduce SLCO1B1 function may be incorrectly assigned a normal phenotype. Many patients' statin therapy is never restarted after Statin-related musculoskeletal symptoms. As a result, LDL cholesterol values are higher as is their risk for cardiovascular disease. The evidenced-based recommendations for genotype-guided statin therapy are focused on reducing the risk of SAMS.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Avatrombopag

Avatrombopag

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Results in higher systemic concentrations.

Recommendations based on specific guidelines

FDA	**No actionable recommendation is available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **EMA**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Axitinib

Axitinib, Inlyta

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Population pharmacokinetic analyses in patients with advanced cancer (including advanced RCC) and healthy volunteers indicate that there are no clinically relevant effects of age, gender, body weight, race, renal function, UGT1A1 genotype, or CYP2C19 genotype.

Recommendations based on specific guidelines

EMA — **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Bisoprolol

Bisoprolol, Bisopro, Bisohexal, Concor, Bisocor, Selbix, Hapsen, Bisovell, Maintate, B-Beta, Beta-One, Biofin, Konblobet, Carbisol

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Brexpiprazole

Brexpiprazole, Rexulti

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

It is recommended that individuals receiving strong CYP2D6 or CYP3A4 inhibitors receive a half the maintenance dose.

Brexpiprazole is metabolized primarily by CYP3A4 and CYP2D6. Based on estimates from population pharmacokinetic analyses, extensive CYP2D6 metabolizers receiving both CYP3A4 and CYP2D6 inhibitors, or slow CYP2D6 metabolizers receiving strong CYP3A4 inhibitors, are expected to have a 4-5-fold increase in brexpiprazole concentrations.

Recommendations based on specific guidelines

SWISSMEDIC	**It is recommended that individuals receiving strong CYP2D6 or CYP3A4 inhibitors receive a half the maintenance dose.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Brivaracetam || CYP2C19

Brivaracetam

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation available for this drug-gene pair.

Results in higher systemic concentrations and higher adverse reaction risk.

Recommendations based on specific guidelines

FDA	**No actionable recommendation available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **EMA**, **HCSC**, and **SWISSMEDIC**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Brivaracetam || CYP2C9

Brivaracetam

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

In vitro, the hydroxylation of brivaracetam is mediated mainly by CYP2C19. Another metabolite (the hydroxy acid metabolite) is produced predominantly by hydroxylation of the propyl side chain of the carboxylic acid metabolite (mainly by CYP2C9).

Recommendations based on specific guidelines

SWISSMEDIC No actionable recommendation is available for this drug-gene pair.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Bupropion

Bupropion, Wellbutrin, Zyban

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation available for this drug-gene pair.

Co-administration of bupropion with drugs that are metabolized by CYP2D6 can increase the exposures of drugs that are substrates of CYP2D6.

Recommendations based on specific guidelines

FDA	No actionable recommendation available for this drug-gene pair.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Cariprazine

Cariprazine, Symvenu

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Carisoprodol

Carisoprodol

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Carvedilol

Vacodil, Carvepen, Carvedilol Sandoz, Dilatrend, Blorec, Carvilol, Bloved, V-Bloc, Carvedilol

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Celecoxib

Celecoxib, Celecoxib Sandoz, Celebrex, Celcox, Remabrex, Novexib, Celdol, Actrel

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

Initiate therapy with lowest recommended starting dose.

Moderately reduced metabolism; higher plasma concentrations may increase probability of toxicities.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with lowest recommended starting dose.|| Titrate dose upward to clinical effect or maximum recommended dose with caution. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. Carefully monitor adverse events such as blood pressure and kidney function during course of therapy.**
PMDA	No actionable recommendation is available for this drug-gene pair.

Caveat

Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or gastrointestinal adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and gastrointestinal adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with anti-platelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

27864660 26360837 18419640

Decrease Starting Dose

Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Cevimeline

Cevimeline

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Citalopram || CYP2C19

Citalopram

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Initiate therapy with recommended starting dose.

Reduced metabolism when compared to extensive metabolizers.

Recommendations based on specific guidelines

✓	**CPIC**	**Initiate therapy with recommended starting dose.**
	DPWG	Reduce dose based on age.|| Adults up to 65 years: 30 mg as tablets or 22 mg as drops. Adults 65 years or older: 15 mg as tablets or 10 mg as drops.
	SWISSMEDIC	For those known to have reduced metabolism via CYP2C19, a starting dose of 10 mg daily is recommended in the first 2 weeks.|| Depending on the individual response of the patient, the dose may be increase to a maximum of 20 mg per day.

Caveat

Patients on a stable and effective dose of an SSRI most likely will not benefit from additional dose modifications based on CYP2D6 or CYP2C19 genotype results. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Citalopram || CYP2D6

Citalopram

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

In vivo studies have shown that polymorphisms (branchine/debrisoquin oxidation (CYP2D6) and mephenytoin hydroxylation (CYP2C19)) contribute to the variability of pharmacokinetics in the metabolism of citalopram. The clinical significance is currently unclear.

Recommendations based on specific guidelines

SWISSMEDIC **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Clobazam

Clobazam, Anxibloc, Asabium, Clofritis, Frisium, Proclozam

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Dosage adjustment is recommended based on the drug labeling for specific dosing recommendations.
Results in higher systemic active metabolite concentrations.

Recommendations based on specific guidelines

FDA	**Dosage adjustment is recommended based on the drug labeling for specific dosing recommendations.|| FDA label on Clobazam for CYP2C19 PM : the starting dose should be 5 mg/day and dose titration should proceed slowly according to weight, but to half of the usual dose, as tolerated. If necessary and based upon clinical response, an additional titration to the maximum dose (20 mg/day or 40 mg/day, depending on the weight group) may be started on day 21.**

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

23666564 19552653 18466100

Decrease Starting Dose
Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Clomipramine

Clomipramine, Depranil, Anafranil, Apo-Clomipramine

START MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.

CYP2D6 NM: Normal metabolism of TCAs. CYP2C19 IM: Reduced metabolism of tertiary amines.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose.|| Patients may receive an initial low dose of TCAs, which is then increased over several days to the recommended steady-state dose.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

11763000

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Clomipramine || CYP2C19

Clomipramine, Depranil, Anafranil, Apo-Clomipramine

START MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose.

Reduced metabolism of tertiary amines compared to normal metabolizers.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose.**
DPWG	No actionable recommendation is available for this drug-gene pair.

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose
Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Initiation
This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Clomipramine || CYP2D6

Clomipramine, Depranil, Anafranil, Apo-Clomipramine

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.

Normal metabolism of TCAs.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose.|| Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Clonidine

Clonidine, Catapres

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Clopidogrel

Clopidogrel, Clopivid, Clotromboz, G Plus - Clopidogrel, Clopigrel, Thinoclo, Clopidogrel Stada, Platless, Clopido, Plavesco, Gridokline, Ceruvin, Placta, Deplatt, Clopidogrel Sandoz, Apo-Clopidogrel, Plavix, Therodel, Medigrel, Pidovix, Pladogrel, Artepid, Caplor, Cpg, Trombikaf

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Avoid standard dose clopidogrel (75 mg) if possible.

Reduced clopidogrel active metabolite formation; increase on-treatment platelet reactivity; increase risk for adverse cardiac and cerebrovascular events.

Recommendations based on specific guidelines

CPIC	**Avoid standard dose clopidogrel (75 mg) if possible.|| Use prasugrel or ticagrelor at standard dose if no contraindication.**
DPWG	PCI, 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 metabolized by CYP2C19 (or to a lesser extent). OTHER INDICATIONS: no action required.
PRO	Alternative antiaggregant that isn't a CYP2C19 substrate (prasugrel, ticagrelor, acetylsalicylic acid, etc) is preferable.|| In patients carrying at least one deleterious CYP2C19*2 or CYP2C19*3 allele who have a high risk of thromboembolic recurrence. Based on current knowledge, it is not recommended to increase the clopidogrel dose in patients carrying the CYP2C19*2 or *3 allele.
FDA	Consider use of another platelet P2Y12 inhibitor.

More information about this drug-phenotype can also be found at **EMA** and **PMDA**.

Caveat

It is advantageous to have the CYP2C19 results before initiating antiplatelet therapy because the largest number of potentially preventable recurrent events occur early in treatment. For example, CYP2C19*2 has recently been associated with definite early stent thrombosis in a case–control study. These recommendations apply predominantly to ACS patients undergoing PCI. Current data do not support the use of CYP2C19 genotype data to guide treatment in other scenarios. In addition, there are no data available on the possible role of CYP2C19 in clopidogrel response in pediatric patient populations; however, there is no reason to suspect that CYP2C19 variant alleles would affect clopidogrel metabolism differently in children as compared with adults.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

25800075 22955794 26727381 28597175 27756942 23431496

Change Prescription
There is a high chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism.

Turnaround Time
The benefit of waiting for a genetic test result may be less than starting the medication without a genetic test result.

Clozapine || CYP2D6

Clozapine, Clozaril, Clorilex, Sizoril, Lozap, Nucloz, Nuzip, Cycozam, Clozer, Clozapine Sandoz, Clopine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Codeine

Codeine, Sp-Codin Linctus, Linctus Tussis Rubra, L.T.R. Cough Linctus, Codikaf

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

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

Expected morphine formation.

Recommendations based on specific guidelines

	CPIC	**Use codeine label recommended age- or weight-specific dosing.**
	CPNDS	In individuals with IM (intermediate metabolizer) or EM (extensive metabolizer) CYP2D6 genotypes, codeine can be used as per standard of care.|| Existing evidence suggests that caution is still warranted in CYP2D6 EMs receiving codeine if they are receiving maximal therapeutic doses of codeine and have additional risk factors for toxicity.

Caveat

Like all diagnostic tests, CYP2D6 genotype is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. Furthermore, there are several other factors that cause potential uncertainty in the genotyping results and phenotype predictions. These are discussed in detail in the Supplementary Data online.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Dapoxetine

Dapoxetine, Priligy

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Darifenacin

Darifenacin

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

The metabolism of darifenacin in CYP2D6 poor metabolizers is principally mediated by CYP3A4.

Recommendations based on specific guidelines

EMA	**No actionable recommendation is available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **HCSC**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Desipramine

Desipramine

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.

Normal metabolism of TCAs.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose.|| Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Desvenlafaxine

Pristiq, Desvenlafaxine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

The pharmacokinetics of desvenlafaxine was similar in subjects with CYP2D6 poor and extensive metabolizer phenotype.

The pharmacokinetics of desvenlafaxine was similar in subjects with CYP2D6 poor and extensive metabolizer phenotype.

Recommendations based on specific guidelines

FDA	**The pharmacokinetics of desvenlafaxine was similar in subjects with CYP2D6 poor and extensive metabolizer phenotype.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Deutetrabenazine

Deutetrabenazine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Dexlansoprazole

Dexilant, Dexlansoprazole

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Initiate standard starting daily dose.

Increased plasma concentration of PPI compared with CYP2C19 NMs; increase chance of efficacy and potentially toxicity.

Recommendations based on specific guidelines

CPIC	**Initiate standard starting daily dose.|| For chronic therapy (> 12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy.**
FDA	No actionable recommendation is available for this drug-gene pair.

More information about this drug-phenotype can also be found at **HCSC**.

Caveat

There are some important limitations to CYP2C19 genetic tests. Targeted genotyping tests focus on interrogating previously described star (*) alleles and therefore are not designed to detect novel variants. Furthermore, rare allelic CYP2C19 variants may not be included in the genotype test used, and patients with these rare variants may be assigned an NM phenotype (CYP2C19*1/*1) by default. As such, an assigned *1 allele could potentially harbor an undetected CYP2C19 genetic variant that results in altered metabolism and drug exposure. In addition, rare alleles with gene deletions at the CYP2C19 locus have recently been reported (*36 and *37); however, most clinical laboratories do not currently test for CYP2C19 copy number variants or deletions. Therefore, it is important that clinical providers appreciate the limitations of targeted genotyping tests and understand which CYP2C19 variant alleles were genotyped when interpreting results. As with any diagnostic test, CYP2C19 genotype is just one factor that clinicians should consider when prescribing PPIs.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Dextromethorphan

Dextromethorphan, Sunthorphan, Axcel Dextromethorphan, Nospan, Tussils, Metophan, Tussidex Forte Linctus, Beathorphan, Pusiran, Dexcophan, Dextromethorphan Linctus

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Dextromethorphan and Quinidine

Dextromethorphan and Quinidine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Diazepam

Diazepam, Diazepam Lipuro, Stesolid, Dbl Diazepam, Diapo, Apo-Diazepam, Valisanbe, Valium, Valdimex, Anxicalm, Dzp, Nozepav, Trazep

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Diclofenac || CYP2C9

Diclofenac, Flamar, Zorvolex, Anuva

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

The pharmacokinetics of this drug is not significantly impacted by CYP2C9 genetic variants in vivo and/or there is insufficient evidence to provide a recommendation to guide clinical practice at this time.

Recommendations based on specific guidelines

CPIC — **No actionable recommendation is available for this drug-gene pair.**

Caveat

Rare CYP2C9 variants may not be included in the genotype test used, and patients with rare variants may be assigned an NM phenotype based on a default CYP2C9*1/*1 test result. Thus, an assigned CYP2C9*1 allele could potentially harbor a decreased or no function variant. Therefore, it is important that genetic test reports include information on which variant alleles were genotyped or which single-nucleotide polymorphisms were interrogated. As with any diagnostic test, CYP2C9 genotype is just one factor that clinicians should consider when prescribing NSAIDs to an individual patient. Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or GI adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and GI adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with antiplatelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Dipyrone

Dipyrone

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

The pharmacokinetics of this drug is not significantly impacted by CYP2C9 genetic variants in vivo and/or there is insufficient evidence to provide a recommendation to guide clinical practice at this time.

Recommendations based on specific guidelines

CPIC — **No actionable recommendation is available for this drug-gene pair.**

Caveat

Rare CYP2C9 variants may not be included in the genotype test used, and patients with rare variants may be assigned an NM phenotype based on a default CYP2C9*1/*1 test result. Thus, an assigned CYP2C9*1 allele could potentially harbor a decreased or no function variant. Therefore, it is important that genetic test reports include information on which variant alleles were genotyped or which single-nucleotide polymorphisms were interrogated. As with any diagnostic test, CYP2C9 genotype is just one factor that clinicians should consider when prescribing NSAIDs to an individual patient. Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or GI adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and GI adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with antiplatelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Disopyramide

Disopyramide

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Donepezil

Donepezil, Aripezil, Torpezil, Donacept, Aricept, Dopezil, Donepezil Mevon, Fepezil, Alzim, Fordesia, Hetero Donepezil Hydrochloride, Doncept, Aricept Evess

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Doxepin

Doxepin, Apo-Doxepin, Sagalon

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.

CYP2D6 NM: Normal metabolism of TCAs. CYP2C19 IM: Reduced metabolism of tertiary amines compared to normal metabolizers.

Recommendations based on specific guidelines

CPIC **Initiate therapy with recommended starting dose.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Doxepin || CYP2C19

Doxepin, Apo-Doxepin, Sagalon

START MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.

Reduced metabolism of tertiary amines compared to normal metabolizers.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.**
DPWG	No actionable recommendation is available for this drug-gene pair.

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose
Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Initiation
This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Doxepin || CYP2D6

Doxepin, Apo-Doxepin, Sagalon

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.

Normal metabolism of TCAs.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose.|| Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Dronabinol

Dronabinol

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

Monitor for adverse reactions.

May result in higher systemic concentrations and higher adverse reaction risk.

Recommendations based on specific guidelines

FDA	**Monitor for adverse reactions.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Increase Monitoring

Although patient has a varied genetic profile, the intended medication can still be prescribed as recommended, but with more frequent monitoring for quick action to be taken in the event of unwanted reactions.

Dronedarone || CYP2D6

Dronedarone, Multaq

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Dronedarone 800 mg daily increase metoprolol exposure by 1.6-fold and propranolol exposure by 1.3-fold (i.e. much below the 6-fold differences observed between poor and extensive CYP2D6 metabolizers).

Recommendations based on specific guidelines

EMA — **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Drospirenone and Ethinylestradiol

Synfonia, Yasmin, Yaz, Gveza, Jastinda, Liza, Drospera

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

In the study with 24 women with homozygous (wild type) and heterozygous CYP2C19 genotype, the daily oral administration of 3 mg for 14 days did not affect the oral clearance of omeprazole (40 mg, single oral dose) and the CYP2C19 product 5-hydroxy omeprazole. These results demonstrate that drospirenone did not inhibit CYP2C19 in vivo.

Recommendations based on specific guidelines

FDA	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Duloxetine

Cymbalta, Dulxota, Duloxetine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Elagolix

Elagolix

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Eletriptan

Eletriptan, Relpax

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Clinical studies indicate that there is no clinically relevant effect of CYP2D6 polymorphism on the PK of eletriptan.

In vitro studies show that eletriptan is mainly metabolized by the hepatic cytochrome P-450 enzyme CYP3A4. In vitro studies also suggest low involvement of CYP2D6, although clinical studies indicate that there is no clinically relevant effect of CYP2D6 polymorphism on the pharmacokinetics of eletriptan.

Recommendations based on specific guidelines

SWISSMEDIC **Clinical studies indicate that there is no clinically relevant effect of CYP2D6 polymorphism on the PK of eletriptan.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Eliglustat

Eliglustat

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

A specific dosage cannot be recommended for CYP2D6 indeterminate metabolizers.CYP2D6 EMs or IMs: 84 mg orally 2x daily.

Alters systemic concentrations, effectiveness, and adverse reaction risk (QT prolongation). Indicated for normal, intermediate, and poor metabolizer patients.

Recommendations based on specific guidelines

FDA	**A specific dosage cannot be recommended for CYP2D6 indeterminate metabolizers.CYP2D6 EMs or IMs: 84 mg orally 2x daily.**

More information about this drug-phenotype can also be found at **EMA**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Erdafitinib

Erdafitinib, Balversa

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Erdafitinib exposure was similar in subjects with CYP2C9*1/*2 and *1/*3 genotypes relative to subjects with CYP2C9*1/*1 genotype (wild type). Simulation suggested no clinically meaningful differences in erdafitinib exposure in subjects with CYP2C9*2/*2 and *2/*3 genotypes.

Recommendations based on specific guidelines

FDA	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Escitalopram || CYP2C19

Escitalopram, Lepax, Lexapro, Cipralex, Depram, Elxion, Escipra, Escitalopram Oxalate

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Do not exceed the following doses (75% of the standard maximum dose): adults < 65 years 15 mg/day, =65 years 7.5 mg/day.

The risk of QT prolongation and torsades de pointes is theoretically increase because the gene variation leads to an increase escitalopram plasma concentration. If you follow the dose recommendation below, the increase plasma concentration and the theoretically increase risk of QT prolongation will be offset.

Recommendations based on specific guidelines

DPWG	**Do not exceed the following doses (75% of the standard maximum dose): adults < 65 years 15 mg/day, =65 years 7.5 mg/day.**

Caveat

Patients on a stable and effective dose of an SSRI most likely will not benefit from additional dose modifications based on CYP2D6 or CYP2C19 genotype results. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose
Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Initiation
This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Escitalopram || CYP2D6

Escitalopram, Lepax, Lexapro, Cipralex, Depram, Elxion, Escipra, Escitalopram Oxalate

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Esomeprazole

Esomeprazole, Sompraz, Emazole, Epivetier, Jubium, Emanera, Esoz, Esomeprazole Sandoz, Nexium, Nexium Mups, Simprazol, Esoferr, Ezol, Exocid, Depump, Nexigas, Arcolase, Ezocon, Axiago, Esmozin, E-Some, Emp, Esola, Esomax, Esozid, Ezomeb, Lanxium, Proxium, S - Omevell

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

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.

Recommendations based on specific guidelines

DPWG	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Fenofibrate

Fenofibrate, Lipanthyl, Fenosup Lidose, Fenogal Lidose, Apo-Feno-Micro, Trolip, Fenoflex, Fibesco, Profibrat, Evothyl, Yosenob, Fibramed, Hicholfen, Fenopi, Lexemin, Fenolip, Hyperchol, Trichol

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Fesoterodine

Fesoterodine

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

The interaction with CYP2D6 inhibitors was not tested clinically. Mean Cmax and AUC of the active metabolite are 1.7 and 2-fold higher, respectively, in CYP2D6 poor metabolizers as compared to extensive metabolizers. Co-administration of a potent CYP2D6 inhibitor may result in increased exposure and adverse events.

Recommendations based on specific guidelines

EMA	**No actionable recommendation is available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **HCSC**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Flecainide

Flecainide, Tambocor

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

16944116 18754843 20435235

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Flibanserin || CYP2C19

Flibanserin

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Flibanserin || CYP2C9

Flibanserin

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Flibanserin || CYP2D6

Flibanserin

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation available for this drug-gene pair.

In 12 poor metabolizers of CYP2D6, steady state Cmax and AUC of flibanserin 50 mg twice daily was decreased by 4% and increased by 18%, respectively, compared to exposures among 19 extensive metabolizers, intermediate metabolizers and ultrarapid metabolizers of CYP2D6.

Recommendations based on specific guidelines

FDA — **No actionable recommendation available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Fluoxetine

Fluoxetine, Fluoxetine-Teva, Fluoxone Divule, Proctin, Pms-Fluoxetine, Apo-Fluoxetine, Magrilan, Prozac, Prestin, Sactine, Antiprestine, Foransi, Kalxetin, Zac, Nopres, Deprezac, Doxetin, Elizac, Noxetine

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Consumption of fluoxetine or with other drugs (fluoxetine/olanzapine) metabolized by CYP2D6 should be done with caution.

Fluoxetine inhibits the activity of CYP2D6 and may make individuals with normal CYP2D6 metabolic activity resemble a poor metabolizer.

Recommendations based on specific guidelines

FDA	**Consumption of fluoxetine or with other drugs (fluoxetine/olanzapine) metabolized by CYP2D6 should be done with caution.**

More information about this drug-phenotype can also be found at **SWISSMEDIC**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Increase Monitoring

Although patient has a varied genetic profile, the intended medication can still be prescribed as recommended, but with more frequent monitoring for quick action to be taken in the event of unwanted reactions.

Flupenthixol

Flupenthixol, Fluanxol

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Flurbiprofen

Flurbiprofen, Strepfen, Froben

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

Initiate therapy with lowest recommended starting dose. Titrate dose upward to clinical effect or maximum recommended dose with caution. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. Carefully monitor adverse events such as blood pressure and kidney function during course of therapy.

Moderately reduced metabolism; higher plasma concentrations may increase probability of toxicities.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with lowest recommended starting dose. Titrate dose upward to clinical effect or maximum recommended dose with caution. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. Carefully monitor adverse events such as blood pressure and kidney function during course of therapy.**

Caveat

Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or gastrointestinal adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and gastrointestinal adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with anti-platelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

25712887 27298492

Decrease Starting Dose

Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Fluvastatin

Fluvastatin, Lescol

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

If dose >40mg needed for desired efficacy, consider an alternative statin or combination therapy.

CYP2C9 Intermediate metabolizer: Increased fluvastatin exposure. SLCO1B1 Normal function: Typical myopathy risk and statin exposure.

Recommendations based on specific guidelines

CPIC	**If dose >40mg needed for desired efficacy, consider an alternative statin or combination therapy.|| Alternatively, prescribe <=40mg per day as a starting dose and adjust doses of fluvastatin based on disease-specific guidelines.**

Caveat

Genetic variation is just one factor when prescribing statins. Rare variants may not be included in the genotype test. Patients with rare variants that reduce SLCO1B1 function may be incorrectly assigned a normal phenotype. Many patients' statin therapy is never restarted after Statin-related musculoskeletal symptoms. As a result, LDL cholesterol values are higher as is their risk for cardiovascular disease. The evidenced-based recommendations for genotype-guided statin therapy are focused on reducing the risk of SAMS.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Change Prescription

There is a high chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Fluvastatin || CYP2C9

Fluvastatin, Lescol

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

If dose >40mg needed for desired efficacy, consider an alternative statin or combination therapy.

Increased fluvastatin exposure as compared to normal metabolizer which may translate to increase myopathy risk.

Recommendations based on specific guidelines

CPIC	**If dose >40mg needed for desired efficacy, consider an alternative statin or combination therapy.|| Alternatively, prescribe <=40mg per day as a starting dose and adjust doses of fluvastatin based on disease-specific guidelines.**

Caveat

Genetic variation is just one factor when prescribing statins. Rare variants may not be included in the genotype test. Patients with rare variants that reduce SLCO1B1 function may be incorrectly assigned a normal phenotype. Many patients' statin therapy is never restarted after Statin-related musculoskeletal symptoms. As a result, LDL cholesterol values are higher as is their risk for cardiovascular disease. The evidenced-based recommendations for genotype-guided statin therapy are focused on reducing the risk of SAMS.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Change Prescription

There is a high chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Fluvastatin || SLCO1B1

Fluvastatin, Lescol

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function

Recommendation

Prescribe desired starting dose and adjust doses based on disease-specific guidelines.

Typical myopathy risk and statin exposure.

Recommendations based on specific guidelines

CPIC	**Prescribe desired starting dose and adjust doses based on disease-specific guidelines.**

Caveat

Genetic variation is just one factor when prescribing statins. Rare variants may not be included in the genotype test. Patients with rare variants that reduce SLCO1B1 function may be incorrectly assigned a normal phenotype. Many patients' statin therapy is never restarted after Statin-related musculoskeletal symptoms. As a result, LDL cholesterol values are higher as is their risk for cardiovascular disease. The evidenced-based recommendations for genotype-guided statin therapy are focused on reducing the risk of SAMS.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Fluvoxamine || CYP2C19

Fluvoxamine, Luvox, Apo-Fluvoxamine, Faverin

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

This is not a gene-drug interaction.

Recommendations based on specific guidelines

DPWG	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Fluvoxamine || CYP2D6

Fluvoxamine, Luvox, Apo-Fluvoxamine, Faverin

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.

Normal metabolism.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose.**

Caveat

Patients on a stable and effective dose of an SSRI most likely will not benefit from additional dose modifications based on CYP2D6 or CYP2C19 genotype results. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Formoterol || CYP2C19

Formoterol, Atimos, Foradil, Duaklir Genuair

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Some patients may be deficient in CYP2D6 or 2C19 or both. Whether a deficiency in one or both of these isozymes results in elevated systemic exposure to formoterol or systemic adverse effects has not been adequately explored.

Recommendations based on specific guidelines

FDA	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Formoterol || CYP2D6

Formoterol, Atimos, Foradil, Duaklir Genuair

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Fosphenytoin

Fosphenytoin

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

Consider avoiding fosphenytoin as an alternative to carbamazepine in patients who are CYP2C9*3 carriers.

May result in higher systemic concentrations and higher adverse reaction risk (central nervous system toxicity).

Recommendations based on specific guidelines

FDA	**Consider avoiding fosphenytoin as an alternative to carbamazepine in patients who are CYP2C9*3 carriers.|| Alternatively, consider starting at the lower end of the dosage range and monitor serum concentrations. Refer to FDA labeling for specific dosing recommendations. Genotyping is not a substitute for clinical vigilance and patient management.**

More information about this drug-phenotype can also be found at **HCSC**.

Caveat

The application of genotype-based dosing is most appropriate when initiating phenytoin maintenance therapy. Obtaining genetic information after months of drug therapy is less informative, given that the drug dose may have already been adjusted based on therapeutic drug monitoring. As with all diagnostic tests, genetic tests are only one of several pieces of clinical information that should be considered before initiating and maintaining drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Change Prescription

There is a high chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Galantamine

Galantamine, Reminyl

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

CYP2D6 is involved in the metabolism of galantamine but there were limited differences between CYP2D6 extensive and poor metabolizers.

Recommendations based on specific guidelines

HCSC **No actionable recommendation is available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **SWISSMEDIC**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Gefitinib

Gefitinib, Iressa, Genessa, Gefinib, Iretinib, Gefitero, Gefiza, Ingefitinib, Actagef

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Glibenclamide || CYP2C9

Glibenclamide, Glyboral, T.O.Nil, Sp-Diatab, Clamide, Benil, Apo-Glyburide, Glimide, Daonil, Harmida, Latibet, Fimediab, Renabetic, Hisacha, Trodeb, Dibelet, Prodiabet

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

For CYP2C9 *2/*2, *1/*3, *1/*2, and IM: The only relevant clinical consequence that was found is an increase effectiveness of glibenclamide without an increase in frequency and severity of hypoglycemia for a group of 1 *1/*2 and 15 *1/*3.

Recommendations based on specific guidelines

DPWG — **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Gliclazide || CYP2C9

Gliclazide, Gliavis, Gliclada, Apo-Gliclazide, Diamicron, Diapro, Glizide, Diverin, Melicron, Mexan, Dianorm, Sp-Glimed, Sun-Glizide, Glimicron, Glyclazide, Medoclazide, Glucodex, Glikamel, Glicab, Xepabet, Fonylin, Linodiab, Glucored, Glidex, Glyade, Glukolos, Gored, Pedab

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

For CYP2C9 *1/*3, IM: The genetic variation increases the effectiveness of gliclazide without significantly increasing the risk of hypoglycemia.

Recommendations based on specific guidelines

DPWG — **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Glimepiride || CYP2C9

Glimepiride, Anpiride, Velacom, Gliaride, Dialosa, Diapride, Amaryl, Glimepix, Glimetic, Glimefion, Glucoryl, Versibet, Diaversa, Metrix, Amaglu, Gluvas, Norizec, Friladar, Glamarol, Glucokaf, Amidiab, Simryl, Relide

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

For CYP2C9 *1/*2: No significant kinetic or clinical consequences have been found for the genetic variation.

Recommendations based on specific guidelines

DPWG	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Haloperidol

Haloperidol, Myung In Haloperidol, Manace, Haloxen, Motivan, Seradol, Lodomer, Govotil, Upsikis, Dores, Apo-Haloperidol

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Hydrocodone

Hydrocodone

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Use hydrocodone label recommended age- or weight-specific dosing.

Normal hydromorphone formation.

Recommendations based on specific guidelines

CPIC	**Use hydrocodone label recommended age- or weight-specific dosing.**

Caveat

Like all diagnostic tests, CYP2D6 genotype is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. Furthermore, there are several other factors that cause potential uncertainty in the genotyping results and phenotype predictions.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Ibrutinib

Ibrutinib, Imbruvica

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No precautions are required in patients with different CYP2D6 genotypes.

In vitro studies have shown that CYP2D6 is less than 2 % involved in the oxidative metabolism of ibrutinib. In the human mass balance study, subjects genotyped as poor CYP2D6 metabolizers also showed a pharmacokinetic profile comparable to that of extensive metabolizers.

Recommendations based on specific guidelines

SWISSMEDIC **No precautions are required in patients with different CYP2D6 genotypes.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Ibuprofen

Ibuprofen, Spedifen, Nurofen, Panafen, Advil, Bifen, Zofen, Brufen, Perofen, Apo-Ibuprofen, Ibufen, Proris, Prosinal, Hufagripp, Fenatic, Arbupon, Mofen, Etafen, Medcofen, Ibuleve, Junifen, Anafen, Arfen, Arthrifen, Axofen, Bodrexin Ibp, Bufect, Bunofa, Caldolor, Coldy's Jr, Dofen Forte, Dolofen F, Dratadin, Etafen Forte, Farsifen, Febryn, Fenida, Fenpro, Fenris, Ibrosic, Ifen, Insic, Intrafen, Iprox, Irgafen, Lexaprofen, Liflamal, Mediprofen, Moris, Neo Linucid, Novaxifen, Oraprofen, Ostarin, Peinlos, Profen, Prointi, Proris Forte, Prosinal Forte, Provinas, Repass, Rhelafen, Ribunal, Salfenal, Simris, Termofen, Tiafen, Trobuges, Xepafen, Zentarin

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

Initiate therapy with lowest recommended starting dose. Titrate dose upward to clinical effect or maximum recommended dose with caution. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. Carefully monitor adverse events such as blood pressure and kidney function during course of therapy.

Moderately reduced metabolism; higher plasma concentrations may increase probability of toxicities.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with lowest recommended starting dose. Titrate dose upward to clinical effect or maximum recommended dose with caution. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. Carefully monitor adverse events such as blood pressure and kidney function during course of therapy.**

Caveat

Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or gastrointestinal adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and gastrointestinal adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with anti-platelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose
Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Indication
This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Iloperidone

Iloperidone

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Imipramine

Imipramine, Apo-Imipramine

START MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.

CYP2D6 NM: Normal metabolism of TCAs. CYP2C19 IM: Reduced metabolism of tertiary amines.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose.|| Patients may receive an initial low dose of TCAs, which is then increased over several days to the recommended steady-state dose.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Imipramine || CYP2C19

Imipramine, Apo-Imipramine

START MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a TCA, which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.

Reduced metabolism of tertiary amines compared to normal metabolizers.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a TCA, which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.**
DPWG	No action is required for this gene-drug interaction.

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose
Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Initiation
This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Imipramine || CYP2D6

Imipramine, Apo-Imipramine

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a tricyclic antidepressant (TCA), which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.

Normal metabolism of TCAs.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a tricyclic antidepressant (TCA), which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose

Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Indomethacin

Indomethacin

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No recommendation is available for this drug-gene pair.

The pharmacokinetics of this drug is not significantly impacted by CYP2C9 genetic variants in vivo and/or there is insufficient evidence to provide a recommendation to guide clinical practice at this time.

Recommendations based on specific guidelines

CPIC — **No recommendation is available for this drug-gene pair.**

Caveat

Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or gastrointestinal adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and gastrointestinal adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with anti-platelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Lacosamide

Lacosamide, Vimpat

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Lansoprazole

Lansoprazole, Lasoprol, Prevacid, Prazotec, Lapraz, Prosogan, Digest, Nufaprazol, Lasgan, Loprezol, Caprazol, Dobrizol, Erphalanz, Inazol, Inhipraz, Lagas, Lancid, Lanpracid, Lanzogra, Laz, Lexid, Prosogan Fd, Zolesco

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Initiate standard starting daily dose. Monitor for continued efficacy.

Increased plasma concentration of PPI compared with CYP2C19 NMs; increase chance of efficacy and potentially toxicity.

Recommendations based on specific guidelines

CPIC	**Initiate standard starting daily dose. Monitor for continued efficacy.|| For chronic therapy (> 12 weeks) and efficacy achieved, consider 50% reduction in daily dose.**
DPWG	No actionable recommendation is available for this drug-gene pair.

Caveat

There are some important limitations to CYP2C19 genetic tests. Targeted genotyping tests focus on interrogating previously described star (*) alleles and therefore are not designed to detect novel variants. Furthermore, rare allelic CYP2C19 variants may not be included in the genotype test used, and patients with these rare variants may be assigned an NM phenotype (CYP2C19*1/*1) by default. As such, an assigned *1 allele could potentially harbor an undetected CYP2C19 genetic variant that results in altered metabolism and drug exposure. In addition, rare alleles with gene deletions at the CYP2C19 locus have recently been reported (*36 and *37); however, most clinical laboratories do not currently test for CYP2C19 copy number variants or deletions. Therefore, it is important that clinical providers appreciate the limitations of targeted genotyping tests and understand which CYP2C19 variant alleles were genotyped when interpreting results. As with any diagnostic test, CYP2C19 genotype is just one factor that clinicians should consider when prescribing PPIs.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

16402242 21769476 26832653 20559522

Increase Monitoring

Although patient has a varied genetic profile, the intended medication can still be prescribed as recommended, but with more frequent monitoring for quick action to be taken in the event of unwanted reactions.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Lesinurad

Lesinurad

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

At the 400 mg dose, when compared with CYP2C9 NM, increase lesinurad exposures were observed in CYP2C9 IM, approximately 22% increase in AUC) and in CYP2C9 PM, approximately 111% increase in AUC) accompanied with higher lesinurad renal excretion.

Recommendations based on specific guidelines

EMA **No actionable recommendation is available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **SWISSMEDIC**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Letermovir

Letermovir

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function

Recommendation

No actionable recommendation is available for this drug-gene pair.

The effect of genetic variants in the OATP1B1 gene SLCO1B1 (rs4149056, rs2306283, rs4149032) and UGT1A1 (rs4148323 and promoter TA repeat variants) on the pharmacokinetics of Letermovir was evaluated in 299 study participants. There were no clinically relevant effects of these variants on Letermovir exposure.

Recommendations based on specific guidelines

SWISSMEDIC **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Lofexidine

Lofexidine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Lornoxicam

Lornoxicam

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

Initiate therapy with lowest recommended starting dose.

Moderately reduced metabolism; higher plasma concentrations may increase probability of toxicities.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with lowest recommended starting dose.|| Titrate dose upward to clinical effect or maximum recommended dose with caution. In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals. Carefully monitor adverse events such as blood pressure and kidney function during course of therapy.**

Caveat

Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or gastrointestinal adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and gastrointestinal adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with anti-platelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose

Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Losartan || CYP2C9

Cozaar, Losartan, A-Losartan, Angizaar, Hyperten, Lortan, Losagen, Losartan Bluepharma, Losartan Hexal, Losartas, Lozarsin, Myotan, Rosart, Sartocad, Trosan, Acetensa, Angioten, Insaar, Lifezar, Losargard, Losartan Potassium, Santesar

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Approximately 14% of a perorally administered dose of losartan is converted to an active metabolite. In vitro studies show that cytochrome P450 2C9 and 3A4 are involved in the conversion of losartan into its metabolites.

Recommendations based on specific guidelines

SWISSMEDIC **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Lovastatin

Lovastatin, Lovatin, Apo-Lovastatin, Ellanco, Elstatin, Lochol, Loctin, Lofacol, Medostatin, Rovacor, Cholvastin, Justin, Lotyn, Minipid

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function

Recommendation

Prescribe desired starting dose and adjust doses based on disease-specific guidelines.

Typical myopathy risk and statin exposure.

Recommendations based on specific guidelines

CPIC	**Prescribe desired starting dose and adjust doses based on disease-specific guidelines.**

Caveat

As with any diagnostic test, genetic variation is just one factor that clinicians should consider when prescribing statins. Furthermore, rare variants may not be included in the genotype test used, and patients with rare variants that reduce SLCO1B1 function may be incorrectly assigned a normal phenotype based on a default to wild-type (*1) test result. In summary, statins are a powerful class of medications for lowering LDL cholesterol and cardiovascular risk with an established track record of safety and efficacy. However, statin- related musculoskeletal symptoms are the most frequently cited reason for discontinuing statin therapy. Although clinicians are well-tuned to trial stopping and later reinitiating statin therapy in those who develop SAMS, in many patients statin therapy is never restarted. As a result, LDL cholesterol values are higher as is their risk for cardiovascular disease. We applied a rigorous approach evaluating the collective evidence around SLCO1B1, ABCG2, and CYP2C9 on systemic drug exposure and risk of SAMS. Our evidenced-based recommendations for genotype-guided statin therapy are focused on reducing the risk of SAMS. Based on this foundation, future research can evaluate the extent to which implementation of these guidelines impacts prescribing, SAMS risk, statin adherence, LDL cholesterol levels, and risk for cardiovascular events in patients prescribed statin therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Lumiracoxib

Lumiracoxib

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No recommendation is available for this drug-gene pair.

The pharmacokinetics of this drug is not significantly impacted by CYP2C9 genetic variants in vivo and/or there is insufficient evidence to provide a recommendation to guide clinical practice at this time.

Recommendations based on specific guidelines

CPIC — **No recommendation is available for this drug-gene pair.**

Caveat

Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or gastrointestinal adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and gastrointestinal adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with anti-platelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Meclizine

Meclizine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Meloxicam

Artrilox, Nufaxicam, Nulox, Remelox, Arrox, Melox, Mobic, Arimed, Atrocox, Cameloc, Coxilab, Denilox, Flamoxi, Flasicox, Fri-Art, Futamel, Genxicam, Hexcam, Hufaxicam, Koniflam, Liloxicam, Loxicox, Loxil, Loximei, Mecox, Meflam, Melet, Melfion, Melicam, Melocid, Melogra, Melovix, Meloxicam, Meloxin, Mevilox, Mexpharm, Mobiflex, Movi-Cox, Movix, Moxam, Moxic, Nucoxi, Ostelox, Oxcam, Relox, Velcox, X-Cam

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

Consider alternative therapy.

Moderately reduced metabolism; higher plasma concentrations may increase probability of toxicities.

Recommendations based on specific guidelines

CPIC	**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. Alternatively, initiate therapy with 50% of the lowest recommended starting dose. Titrate dose upward 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. Upward 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.**
HCSC	No actionable recommendation is available for this drug-gene pair.

Caveat

Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or gastrointestinal adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and gastrointestinal adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with anti-platelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Change Prescription

There is a high chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Methadone || CYP2D6

Methadone

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Use methadone label recommended age- or weight-specific dosing.

Expected metabolism.

Recommendations based on specific guidelines

CPIC	**Use methadone label recommended age- or weight-specific dosing.**

Caveat

Like all diagnostic tests, CYP2D6 genotype is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. Furthermore, there are several other factors that cause potential uncertainty in the genotyping results and phenotype predictions. These are discussed in detail in the Supplementary Data online.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Methotrexate

Abitrexate, Dbl Methotrexate, Ebetrexat, Emthexate, Methotrexate, Trexan, Ferxate, Kemotrexate, Methotrexate "Ebewe", Metoject, Rheu-Trex, Sanotrexate

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function

Recommendation

No actionable recommendation is available for this drug-gene pair.

Several polymorphisms of the SLCO1B1 gene, notably rs4149081 and rs11045879 have been strongly associated for the first time with methotrexate clearance and gastrointestinal toxicity.

Recommendations based on specific guidelines

PRO — **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Methylphenidate

Concerta, Methylphenidate, Medikinet Mr, Ritalin, Rubifen, Prohiper

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Metoclopramide || CYP2D6

Apo-Metoclop, Emeliv, Emeran, Ethiferan, Gavistal, Hufaclop, Maril, Metoclopramide, Nausile, Navoren, Nilatika, Omevomid, Primpen, Primperan, Pulin, Sotatic, Syntomide, Tivomit, Vosea, Xylastin, Damaben, Norvom, Tomit, Vertivom, Vopram

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Metoprolol

Apo-Metoprolol, Denex, Fapresor, Lopresor, Loprolol, Metoprolol, Betaloc Zok

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

CYP2D6 extensive metabolizers exhibit several-fold lower plasma concentrations of metoprolol than poor metabolizers with normal CYP2D6 activity.

Recommendations based on specific guidelines

HCSC **No actionable recommendation is available for this drug-gene pair.**

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

16476126 18979093 25823457 19094446

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Mirabegron

Betmiga, Mirabegron

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Mirtazapine || CYP2C19

Apo-Mirtazapine, Mirtazapine, Mirtazapine Sandoz, Remeron Soltab, Mirzap

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

This is NOT a gene-drug interaction.

Recommendations based on specific guidelines

DPWG	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Mirtazapine || CYP2D6

Apo-Mirtazapine, Mirtazapine, Mirtazapine Sandoz, Remeron Soltab, Mirzap

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Moclobemide

Moclobemide Hexal, Moclobemide

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Although the moclobemide plasma concentration may increase as a result of the decreased CYP2C19 activity, this does not lead to an increase incidence of side effects, in as far as is known.

Recommendations based on specific guidelines

DPWG	No actionable recommendation is available for this drug-gene pair.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Modafinil

Modafinil

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Nabumetone

Goflex

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No recommendation is available for this drug-gene pair.

The pharmacokinetics of this drug is not significantly impacted by CYP2C9 genetic variants in vivo and/or there is insufficient evidence to provide a recommendation to guide clinical practice at this time.

Recommendations based on specific guidelines

CPIC — **No recommendation is available for this drug-gene pair.**

Caveat

Rare CYP2C9 variants may not be included in the genotype test used, and patients with rare variants may be assigned an NM phenotype based on a default CYP2C9*1/*1 test result. Thus, an assigned CYP2C9*1 allele could potentially harbor a decreased or no function variant. Therefore, it is important that genetic test reports include information on which variant alleles were genotyped or which single-nucleotide polymorphisms were interrogated. As with any diagnostic test, CYP2C9 genotype is just one factor that clinicians should consider when prescribing NSAIDs to an individual patient. Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or GI adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and GI adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with antiplatelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Naproxen

Alif, Xenifar

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

The pharmacokinetics of this drug is not significantly impacted by CYP2C9 genetic variants in vivo and/or there is insufficient evidence to provide a recommendation to guide clinical practice at this time.

Recommendations based on specific guidelines

CPIC — **No actionable recommendation is available for this drug-gene pair.**

Caveat

Rare CYP2C9 variants may not be included in the genotype test used, and patients with rare variants may be assigned an NM phenotype based on a default CYP2C9*1/*1 test result. Thus, an assigned CYP2C9*1 allele could potentially harbor a decreased or no function variant. Therefore, it is important that genetic test reports include information on which variant alleles were genotyped or which single-nucleotide polymorphisms were interrogated. As with any diagnostic test, CYP2C9 genotype is just one factor that clinicians should consider when prescribing NSAIDs to an individual patient. Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or GI adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and GI adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with antiplatelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Nateglinide

Starlix Tablet, Nateglinide

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation available for this drug-gene pair.

In vitro drug metabolism studies indicate that nateglinide is predominantly metabolized by the cytochrome P450 isozyme CYP2C9 (70%) and to a lesser extent CYP3A4 (30%). Nateglinide is a potential inhibitor of the CYP2C9 isoenzyme in vivo as indicated by its ability to inhibit the in vitro metabolism of tolbutamide.

Recommendations based on specific guidelines

FDA **No actionable recommendation available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **EMA**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Nebivolol

Nebilet, Nebivolol, Nevodio, Linoven

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Nefazodone

Nefazodone

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Nelfinavir

Nelfinavir

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Nelfinavir is metabolized by CYP3A and CYP2C19. Coadministration of nelfinavir and drugs that induce CYP3A or CYP2C19, such as rifampin, may decrease nelfinavir plasma concentrations and reduce its therapeutic effect. Coadministration of nelfinavir and drugs that inhibit CYP3A or CYP2C19 may increase nelfinavir plasma concentrations.

Recommendations based on specific guidelines

FDA — **No actionable recommendation is available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **EMA**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Nortriptyline

Apo-Nortriptyline, Nortriptyline

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.

Normal metabolism of TCAs.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose.|| Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

10770451 28296334

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Olanzapine || CYP2D6

Apo-Olanzapine, Jubrexa, Olankline, Olanzapine, Olanzapine Mevon, Olanzapine Stada, Olanzavitae, Olzan, Olzanid, Onzapin, Prolanza, Sopavel, Tolanz, Zyprexa Zydis, Olancor Fc, Olaz, Remital, Zypin, Zyprexa, Zyprexa Im

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Oliceridine

Oliceridine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Omeprazole

Inhipump, Losec, Losec Mups, Norsec, Ocid, Olit, Omenole, Omepradex, Omeprazole, Omeprazole Kabi, Omeprazole Sandoz, Omesec, Omezol Lyo-, Omezole, Omicap, Omz, Penrazol, Probitor Gastro-Resistant, Proceptin, Promesec, Pumpitor, Ramezol, Romesec, Solcer, Zenpro, Zimor, Etagastrin, Gastrazol, Gastrofer, Lanacer, Lokev, Meisec, Ofizol, Omberzol, Omed, Omevell, Omeyus, Protop, Ulpraz Zolacap, Redusec, Rindopump, Rocer, Zollocid

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Initiate standard starting daily dose.

Increased plasma concentration of PPI compared with CYP2C19 NMs; increase chance of efficacy and potentially toxicity.

Recommendations based on specific guidelines

CPIC	**Initiate standard starting daily dose.|| For chronic therapy (> 12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy.**
DPWG	No actionable recommendation is available for this drug-gene pair.
FDA	No actionable recommendation is available for this drug-gene pair.

Caveat

There are some important limitations to CYP2C19 genetic tests. Targeted genotyping tests focus on interrogating previously described star (*) alleles and therefore are not designed to detect novel variants. Furthermore, rare allelic CYP2C19 variants may not be included in the genotype test used, and patients with these rare variants may be assigned an NM phenotype (CYP2C19*1/*1) by default. As such, an assigned *1 allele could potentially harbor an undetected CYP2C19 genetic variant that results in altered metabolism and drug exposure. In addition, rare alleles with gene deletions at the CYP2C19 locus have recently been reported (*36 and *37); however, most clinical laboratories do not currently test for CYP2C19 copy number variants or deletions. Therefore, it is important that clinical providers appreciate the limitations of targeted genotyping tests and understand which CYP2C19 variant alleles were genotyped when interpreting results. As with any diagnostic test, CYP2C19 genotype is just one factor that clinicians should consider when prescribing PPIs.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

10626755 29033601 16719541 24390778 20804307 22070512

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Ondansetron

Cendatron, Ceteron, Dansefion, Dantroxal, Entron, Frazon, Fudanton, Gencetron, Glotron, Imorfoz, Insetron, Invomit, Kliran, Lametic, Mefoz, Narfoz, Natzo, Nausimex, Odanostin, Odnatron, ODR, Ondacap, Ondamet, Ondane, Ondansetron, Ondansetron Hexal, Ondansetron Kabi, Ondansetron Sandoz, Ondansetron-Aft, Ondarin, Ondaster, Ondavell, Ondesco, Onetic, Onron, Rivomet, Setronax, Sydnatron, Trisetron, Tronadex, Trovensis, Vomceran, Vometraz, Vometron, Vomigo, Vondatum, Zofran, Ondero, Maxtron, Ondavar, Vastercon, Zetral, Zetron

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.

Normal metabolism.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose.**
FDA	No actionable recommendation is available for this drug-gene pair.

Caveat

Rare CYP2D6 variants may not be included in the genotype test used and patients with rare variants may be assigned a “wildtype” (CYP2D6*1) genotype by default. Thus, an assigned “wildtype” allele could potentially harbor a no or decreased function variant. Furthermore, it is important that the genetic testing platform include testing for gene copy number to identify CYP2D6 UMs. Caution should be used regarding molecular diagnostics of CYP2D6 gene copy-number variation because commercially available genotyping results may differ between diagnostic laboratories depending on assay design. Like all diagnostic tests, CYP2D6 genotype is one of multiple pieces of information that clinicians should consider when making their therapeutic choice.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Ospemifene || CYP2C9

Ospemifene, Sensio

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Ospemifene is metabolized primarily by CYP3A4 and CYP2C9. CYP2C19 and other pathways contribute to the metabolism of ospemifene. In order of decreasing potency, ospemifene was suggested to be a weak inhibitor for CYP2B6, CYP2C9, CYP2C19, CYP2C8, CYP2D6 and CYP3A4 in in vitro studies.

Recommendations based on specific guidelines

FDA	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Oxycodone

Oxycodone, Oxycontin, Oxycontin Neo, Oxyneo, Oxynorm, Oxycodone Wockhardt, Targin

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Use oxycodone label recommended age- or weight-specific dosing.

Expected oxymorphone formation.

Recommendations based on specific guidelines

CPIC	**Use oxycodone label recommended age- or weight-specific dosing.**

Caveat

Like all diagnostic tests, CYP2D6 genotype is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. Furthermore, there are several other factors that cause potential uncertainty in the genotyping results and phenotype predictions.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Paliperidone

Invega Trinza, Invega Sustenna, Invega, Paliperidone

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Palonosetron

Aloxi, Palset, Paloset, Paloxi, Palofer, Prosmol, Palonosetron

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

In vitro metabolism studies have suggested that CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in the metabolism of palonosetron. However, clinical pharmacokinetic parameters are not significantly different between poor and extensive metabolizers of CYP2D6 substrates.

Recommendations based on specific guidelines

FDA — **No actionable recommendation is available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **EMA** and **SWISSMEDIC**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Pantoprazole

Alpanzole, Ciprazol, Controloc, Duonazole, Erprazol, Panloc, Pantera, Pantin, Pantomex, Pantoprazole, Pantoprazole Normon, Pantoprazole Sandoz, Pantopump, Panvell, Panzole, Panzolec, Peptazol, Pepzol, Pranza, Prazopump, Pumpisel, Topazol, Vomizole, Pantomet, Pantocapri, Panso, Caprol

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Initiate standard starting daily dose.

Increased plasma concentration of PPI compared with CYP2C19 NMs; increase chance of efficacy and potentially toxicity.

Recommendations based on specific guidelines

CPIC	**Initiate standard starting daily dose.|| For chronic therapy (> 12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy.**
DPWG	No actionable recommendation is available for this drug-gene pair.
FDA	No dosage adjustment is needed for adult patients who are intermediate metabolizers.

Caveat

There are some important limitations to CYP2C19 genetic tests. Targeted genotyping tests focus on interrogating previously described star (*) alleles and therefore are not designed to detect novel variants. Furthermore, rare allelic CYP2C19 variants may not be included in the genotype test used, and patients with these rare variants may be assigned an NM phenotype (CYP2C19*1/*1) by default. As such, an assigned *1 allele could potentially harbor an undetected CYP2C19 genetic variant that results in altered metabolism and drug exposure. In addition, rare alleles with gene deletions at the CYP2C19 locus have recently been reported (*36 and *37); however, most clinical laboratories do not currently test for CYP2C19 copy number variants or deletions. Therefore, it is important that clinical providers appreciate the limitations of targeted genotyping tests and understand which CYP2C19 variant alleles were genotyped when interpreting results. As with any diagnostic test, CYP2C19 genotype is just one factor that clinicians should consider when prescribing PPIs.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Paracetamol, Caffeine, and Dihydrocodeine

Paracetamol, Caffeine, and Dihydrocodeine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Paracetamol, Combinations Excl. Psycholeptics

Paracetamol, Combinations Excl. Psycholeptics

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Paroxetine

Apo-Paroxetine, Seroxat, Paroxetine

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.
Normal metabolism.

Recommendations based on specific guidelines

CPIC **Initiate therapy with recommended starting dose.**

Caveat

Patients on a stable and effective dose of an SSRI most likely will not benefit from additional dose modifications based on CYP2D6 or CYP2C19 genotype results. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

16534507 15349705 20075642

Follow standard dosing
There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation
This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Perphenazine

Apo-Perphenazine, Perphenazine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Phenprocoumon || CYP2C9

Phenprocoumon

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

The genetic variation can result in a reduction in the required maintenance dose. However, there is not enough evidence to confirm that this causes problems with normal initiation of the therapy (i.e. frequent INR monitoring).

Recommendations based on specific guidelines

DPWG	No actionable recommendation is available for this drug-gene pair.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Phenytoin || CYP2C19

Dilantin, Dbl Phenytoin, Ikaphen, Decatona, Kutoin, Curelepz, Phenitin, Phenytoin, Dextoin, Sanbetoin

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Phenytoin is metabolized by the cytochrome P450 enzymes CYP2C9 and CYP2C19.

Recommendations based on specific guidelines

FDA	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Phenytoin || CYP2C9

Dilantin, Dbl Phenytoin, Ikaphen, Decatona, Kutoin, Curelepz, Phenitin, Phenytoin, Dextoin, Sanbetoin

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

The loading dose does not need to be adjusted. For the others, use 75% of the standard dose; use 50% for *2/*2 diplotype and assess the dose based on effect and serum concentration after 7-10 days.

Genetic variation reduces conversion of phenytoin to inactive metabolites. This increases the risk of side effects.

Recommendations based on specific guidelines

DPWG	**The loading dose does not need to be adjusted. For the others, use 75% of the standard dose; use 50% for *2/*2 diplotype and assess the dose based on effect and serum concentration after 7-10 days.|| On patient with *2/*2 diplotype : for the other doses, use 50% of the standard dose and assess the dose based on effect and serum concentration after 7-10 days. Advise the patient to get in touch if side effects (such as ataxia, nystagmus, slurred speech, sedation or rash) occur.**
FDA	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.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose

Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Pimozide

Pimozide

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Piroxicam

Apo-Piroxicam, Aritmatic, Axcel, Benoxicam, Campain, Capxidin, Denicam, Faxiden, Feldco, Feldene, Fleroxi, Genroxi, Grazeo, Infeld, Inpirox, Kifadene, Lanareuma, Lexicam, Licofel, Maxicam, Miradene, Novaxicam, Omeretik, Ovtelis, Pirocam, Pirofel, Piroxicam, Rheficam, Rhumagel, Robilex, Rosic, Rosiden, Roxidene, Roxifen, Samrox, Scandene, Selmatic, Triadene, Tropidene, Wiros, Xicalom, Yasiden, Mesaden, Xicam, Flaxicam

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

Choose an alternative therapy not metabolized by CYP2C9 or not significantly impacted by CYP2C9 genetic variants.

Moderately reduced metabolism; higher plasma concentrations may increase probability of toxicities.

Recommendations based on specific guidelines

CPIC	**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.**
FDA	No actionable recommendation is available for this drug-gene pair.

More information about this drug-phenotype can also be found at **SWISSMEDIC**.

Caveat

Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or gastrointestinal adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and gastrointestinal adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with anti-platelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Change Prescription
There is a high chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism.

Indication
This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Pitavastatin

Vitor, Livalo, Pitavastatin

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function

Recommendation

Prescribe desired starting dose and adjust doses based on disease-specific guidelines.

Typical myopathy risk and statin exposure.

Recommendations based on specific guidelines

CPIC	**Prescribe desired starting dose and adjust doses based on disease-specific guidelines.**

Caveat

Genetic variation is just one factor when prescribing statins. Rare variants may not be included in the genotype test. Patients with rare variants that reduce SLCO1B1 function may be incorrectly assigned a normal phenotype. Many patients' statin therapy is never restarted after Statin-related musculoskeletal symptoms. As a result, LDL cholesterol values are higher as is their risk for cardiovascular disease. The evidenced-based recommendations for genotype-guided statin therapy are focused on reducing the risk of SAMS.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Pitolisant

Pitolisant

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Prasugrel || CYP2C19

Effient, Prasugrel

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

This is NOT a gene-drug interaction.

Recommendations based on specific guidelines

DPWG	**No actionable recommendation is available for this drug-gene pair.**
FDA	No actionable recommendation is available for this drug-gene pair.

More information about this drug-phenotype can also be found at **EMA** and **SWISSMEDIC**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Prasugrel || CYP2C9

Effient, Prasugrel

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

In healthy subjects, patients with stable atherosclerosis, and patients with ACS receiving prasugrel, there was no relevant effect of genetic variation in CYP2B6, CYP2C9, CYP2C19, or CYP3A5 on the pharmacokinetics of prasugrel's active metabolite or its inhibition of platelet aggregation.

Recommendations based on specific guidelines

FDA	**No actionable recommendation is available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **EMA**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Pravastatin

Prafaven, Apo-Pravastatin, Meprastin, Novales, Cholespar, Pravinat, Novosta, Mevachol, Koleskol, Gravastin, Pravastatin

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function

Recommendation

Prescribe desired starting dose and adjust doses based on disease-specific guidelines.

Typical myopathy risk and statin exposure.

Recommendations based on specific guidelines

CPIC	**Prescribe desired starting dose and adjust doses based on disease-specific guidelines.**

Caveat

As with any diagnostic test, genetic variation is just one factor that clinicians should consider when prescribing statins. Furthermore, rare variants may not be included in the genotype test used, and patients with rare variants that reduce SLCO1B1 function may be incorrectly assigned a normal phenotype based on a default to wild-type (*1) test result. In summary, statins are a powerful class of medications for lowering LDL cholesterol and cardiovascular risk with an established track record of safety and efficacy. However, statin- related musculoskeletal symptoms are the most frequently cited reason for discontinuing statin therapy. Although clinicians are well-tuned to trial stopping and later reinitiating statin therapy in those who develop SAMS, in many patients statin therapy is never restarted. As a result, LDL cholesterol values are higher as is their risk for cardiovascular disease. We applied a rigorous approach evaluating the collective evidence around SLCO1B1, ABCG2, and CYP2C9 on systemic drug exposure and risk of SAMS. Our evidenced-based recommendations for genotype-guided statin therapy are focused on reducing the risk of SAMS. Based on this foundation, future research can evaluate the extent to which implementation of these guidelines impacts prescribing, SAMS risk, statin adherence, LDL cholesterol levels, and risk for cardiovascular events in patients prescribed statin therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Propafenone

Rytmonorm, Propafenone

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

In over 90% of patients, propafenone is metabolized rapidly and extensively with an elimination half-life of 2 to 10 hours. These patients metabolize propafenone to two active metabolites: 5-hydroxy-propafenone produced via CYP2D6 and N-depropylpropafenone (norpropafenone), which is produced via CYP3A4 and CYP1A2.

Recommendations based on specific guidelines

SWISSMEDIC **No actionable recommendation is available for this drug-gene pair.**

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

14653957 12421483

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Propranolol

Apo-Propanolol, Emforal, Farmadral, Inpanol, Liblok, Nalol, Propa, Propanol, Propranolol

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

In healthy subjects, no difference was observed between CYP2D6 normal metabolizers (NMs) and poor metabolizers (PMs) with respect to oral clearance or elimination half-life. Partial clearance to 4-hydroxy propranolol was significantly higher and to naphthyloxylactic acid was significantly lower in EMs than PMs.

Recommendations based on specific guidelines

FDA **No actionable recommendation is available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **EMA**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Protriptyline

Protriptyline

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Quetiapine || CYP2D6

Alvoquel, Apo-Quetiapine, Ketipinor, Q-Pin, Quetiapine, Quetiapine Sandoz, Quetvell, Seroquel, Soroquin

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Quinidine

Quinidine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Quinine || CYP2D6

Quinine, Kina

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Desipramine (CYP2D6 substrate): Quinine (750 mg/day for 2 days) decreased the metabolism of desipramine in patients who were extensive CYP2D6 metabolizers, but had no effect in patients who were poor CYP2D6 metabolizers.

Recommendations based on specific guidelines

FDA — **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Rabeprazole

Acilesol, Barole, Bepraz, Pariet, Rabeprazole, Rabeprazole Sandoz

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

The higher plasma concentration of rabeprazole does not result in an increase in side effects.

Recommendations based on specific guidelines

DPWG	**No actionable recommendation is available for this drug-gene pair.**
PMDA	No actionable recommendation is available for this drug-gene pair.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

20457439 25460556

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Ranolazine

Ranexa, Ranolazine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Rimegepant

Rimegepant

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No clinically significant differences in the pharmacokinetics of rimegepant were observed.

CYP2C9 activity is reduced in individuals with genetic variants such as the CYP2C9*2 and CYP2C9*3 alleles.

Recommendations based on specific guidelines

FDA	**No clinically significant differences in the pharmacokinetics of rimegepant were observed.|| Based on age, sex, race/ethnicity, body weight, or CYP2C9 genotype.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Risperidone

Apo-Risperidone, Eperon, Neripros, Noprenia, Nuperdal, Persidal, Respirex, Ridal, Ridkline, Rispator, Rispefar, Risperdal, Risperdal Consta, Risperidex, Risperidone, Risperidone Mevon, Risperidone-Chanelle, Rizodal

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

The concentrations of parent drug and active metabolite differ substantially in extensive and poor metabolizers. However, the concentration of risperidone and 9-hydroxyrisperidone combined did not differ substantially between extensive and poor metabolizers, and elimination half-lives were similar in all subjects.

Recommendations based on specific guidelines

HCSC **No actionable recommendation is available for this drug-gene pair.**

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

26780783 19387994 26872113 16633140 28692863 24828442

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Ritonavir

Norvir, Ritonavir

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Ritonavir has a high affinity for several cytochrome P450 (CYP) isoforms and may inhibit oxidation with the following ranked order: CYP3A4 > CYP2D6.

Recommendations based on specific guidelines

EMA — **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Rosuvastatin || SLCO1B1

Alvostat, Apo-Rosuvastatin, Cholostar, Crestor, Giventor, Nistrol, Rosatin, Rosfion, Rosucard, Rosufer, Rosupid, Rosuvastatin, Rosuvastatin Sandoz, Rosuvastatin Winthrop, Roswin, Rovas, Rovast, Rovastar, Rovaster, Rozact, Simrovas, Suvesco, Tintaros, Vastrol, Vivacor, Celmantin, Eurovastin, Pyfaros, Recansa, Rovator, Ruvastin

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function

Recommendation

Prescribe desired starting dose and adjust doses based on disease-specific guidelines.

Typical myopathy risk and statin exposure.

Recommendations based on specific guidelines

CPIC	**Prescribe desired starting dose and adjust doses based on disease-specific guidelines.**
SWISSMEDIC	Recommended starting dose for Asians is 5 mg and the dose of 40 mg is contraindicated.

Caveat

Genetic variation is just one factor when prescribing statins. Rare variants may not be included in the genotype test. Patients with rare variants that reduce SLCO1B1 function may be incorrectly assigned a normal phenotype. Many patients' statin therapy is never restarted after Statin-related musculoskeletal symptoms. As a result, LDL cholesterol values are higher as is their risk for cardiovascular disease. The evidenced-based recommendations for genotype-guided statin therapy are focused on reducing the risk of SAMS.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Rucaparib

Rucaparib

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Based on population pharmacokinetic analyses, steady-state concentrations following rucaparib 600 mg twice daily did not differ significantly.

In vitro, rucaparib was metabolized primarily by CYP2D6 and to a lesser extent by CYP1A2 and CYP3A4. Based on population pharmacokinetic analyses, steady-state concentrations following rucaparib 600 mg twice daily did not differ significantly across CYP2D6 or CYP1A2 genotype subgroups.

Recommendations based on specific guidelines

FDA	**Based on population pharmacokinetic analyses, steady-state concentrations following rucaparib 600 mg twice daily did not differ significantly.|| Across CYP2D6 or CYP1A2 genotype subgroups.**

More information about this drug-phenotype can also be found at **EMA**.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Sertindole

Sertindole

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Sertraline || CYP2C19

Apo-Sertraline, Deptral, Fatral, Fridep, Iglodep, Inosert, Nudep, Seratine, Serlof, Sernade, Sertraline, Setrof, Zerlin, Zoloft

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Initiate therapy with recommended starting dose.

Reduced metabolism when compared to extensive metabolizers.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose.**
DPWG	No actionable recommendation is available for this drug-gene pair.

Caveat

Patients on a stable and effective dose of an SSRI most likely will not benefit from additional dose modifications based on CYP2D6 or CYP2C19 genotype results. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Sertraline || CYP2D6

Apo-Sertraline, Deptral, Fatral, Fridep, Iglodep, Inosert, Nudep, Seratine, Serlof, Sernade, Sertraline, Setrof, Zerlin, Zoloft

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Simvastatin

Apo-Simvastatin, Cortavas, Covastin, Dha-Simvastatin, Esvat, Ifistatin, Kardak, Kolefion, Mersivas, Priacin, Rechol, Rendapid, Selvat, Selvim, Simcard, Simlo, Simtin, Simvacor, Simvas, Simvasgen, Simvastatin, Simvor, Simzal, Sinova, Statcol, Statkoles, Svt, Tianvas, Valansim, Valemia, Vascor, Vasilip, Zencor, Zochol, Zocor, Cholestat, Colesbat, Lesvatin, Lextatin, Lipivast, Mastatin, Mevastin, Norpid, Preschol, Rocoz, Selvas, Simbado, Simchol, Simvaschol, Simvastal, Simvasto

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
SLCO1B1	rs4149056(TT)	SLCO1B1 Normal function

Recommendation

Prescribe desired starting dose and adjust doses based on disease-specific guidelines.

Typical myopathy risk and statin exposure.

Recommendations based on specific guidelines

✓	**CPIC**	**Prescribe desired starting dose and adjust doses based on disease-specific guidelines.**
	PRO	Continue treatment taking into account the clinical risk. Discontinue if muscle toxicity occurs.
	SWISSMEDIC	The absence of this gene in genotyping does not exclude the possibility of myopathy.|| Including drugs combination Ezetimibe and Simvastatin.

Caveat

Genetic variation is just one factor when prescribing statins. Rare variants may not be included in the genotype test. Patients with rare variants that reduce SLCO1B1 function may be incorrectly assigned a normal phenotype. Many patients' statin therapy is never restarted after Statin-related musculoskeletal symptoms. As a result, LDL cholesterol values are higher as is their risk for cardiovascular disease. The evidenced-based recommendations for genotype-guided statin therapy are focused on reducing the risk of SAMS.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

15548849 28350522 23263738 22668755

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Siponimod

Mayzent, Siponimod

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

Use 50% of the normal maintenance dose.

Theoretically, the risk of adverse effects is increase, as the genetic variation results in higher plasma concentrations of siponimod.

Recommendations based on specific guidelines

DPWG	**Use 50% of the normal maintenance dose.|| Reconsider the choice and the potential benefit of siponimod if the patient is also using a moderate CYP3A4 inducer, such as modafinil. For this genetic variation, a moderate CYP3A4 inducer results in a reduction in the exposure of siponimod by 49%, according to a pharmacokinetic model.**
FDA	Adjust dosage based on genotype according to drug label.|| Patients with the *1/*3 or *2/*3 genotypes should be given a daily maintenance dose of 1mg starting on Day 5 of treatment.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose

Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Sotalol

Sotahexal, Pms-Sotalol, Apo-Sotalol, Sotalol

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Tamoxifen

Novaldex, Tamofen, Tamoxifen

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Avoid moderate and strong CYP2D6 inhibitors. Start therapy with recommended standard of care dosing (TAM 20 mg/day).

Therapeutic endoxifen concentrations.

Recommendations based on specific guidelines

CPIC	**Avoid moderate and strong CYP2D6 inhibitors. Start therapy with recommended standard of care dosing (TAM 20 mg/day).**
CPNDS	If Aromatase Inhibitors (AI) are viable for treatment option then use AI with ovarian suppressor in premenopausal women or tamoxifen (20 mg/day).|| If AI are contraindicated then use Tamoxifen (20 mg/day). In individuals receiving tamoxifen, moderate or strong CYP2D6 inhibitors should be avoided based on the Flockhart P450 Drug Interaction Table for classification of CYP2D6 inhibitors.
PRO	No actionable recommendation is available for this drug-gene pair.

Caveat

For the treatment of ER1 breast cancer, there are well-accepted tumor somatic factors that drive endocrine response, including the tumor expression of ER, PR, and HER2 expression, and other multigene assays that are associated with endocrine sensitivity. Although there are very few data, the implication of reduced CYP2D6 metabolism in patients with low-risk breast cancer (e.g., early-stage breast cancer where the risk of distant recurrence is low) may be substantially different than in patients with later stage disease with a much higher risk of distant recurrence.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

21437611 18407954 28293118 22183189 27924964

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Tamsulosin

Tasulose, Tamsin, Harnal Ocas, Harnal D, Prostam, Tamsulosin, Farlosin Sr

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Tenoxicam

Analcam, Pilopil, Notritis, Tilflam, Tilarco, Tenoxicam, Thenil

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

Choose an alternative therapy not metabolized by CYP2C9 or not significantly impacted by CYP2C9 genetic variants.

Moderately reduced metabolism; higher plasma concentrations may increase probability of toxicities.

Recommendations based on specific guidelines

CPIC	**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.**

Caveat

Age, sex, race and ethnicity, liver dysfunction, comorbidities, concomitant medications, genetic linkage disequilibrium with CYP2C8, and other undiscovered genetic and environmental factors can all impact the likelihood that a patient will experience adverse events with NSAID therapy. For example, regardless of CYP2C9 phenotype, NSAIDs should be avoided in patients with renal dysfunction or heart failure and in those at high risk of cardiovascular or gastrointestinal adverse events. NSAIDs should be used with caution in elderly patients, as hepatic CYP2C9 metabolism decreases with older age and these individuals are at greater risk of renal and gastrointestinal adverse events. Another consideration is the impact of drug-drug interactions. In particular, concomitant use of NSAIDs and agents with anti-platelet or anticoagulant effects should only be with extreme caution, as this can result in an increased risk of bleeding or interfere with platelet inhibition in the case of aspirin. NSAIDs decrease the therapeutic effect of antihypertensive medications and should be used with caution in patients with underlying hypertension.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Change Prescription

There is a high chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Terbinafine

Dermafin, Solveasy Tinea, Lamisil, Meccaderma, Termisil, Haterbin, Lisim, Interbi, Terbinafine, Farmasil

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

In vivo studies have shown that terbinafine is an inhibitor of the CYP450 2D6 isozyme. Thus, terbinafine may convert extensive CYP2D6 metabolizers to poor metabolizer status.

Recommendations based on specific guidelines

FDA	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Tetrabenazine

Tetrabenazine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Thioridazine

Thioridazine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Ticagrelor

Brilinta, Ticagrelor, Briclot, Clotaire

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

This is NOT a gene-drug interaction.

Recommendations based on specific guidelines

DPWG	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Timolol

Duotrav, Isotic Adretor, Nyolol, Opthil, Tiamol, Timabak, Timo-Comod, Timol, Timolol, Timolol-Pos, Tim-Ophtal, Timoptol, Timoptol-Xe, Ximex Opticom, Ophtamol, Optimol

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Potentiated systemic beta-blockade (e.g., decreased heart rate, depression) has been reported during combined treatment with CYP2D6 inhibitors (e.g. quinidine, fluoxetine, paroxetine) and timolol.

Recommendations based on specific guidelines

EMA — **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Tiotropium

Spiriva, Spiolto Respimat, Spiriva Respimat, Tiotropium Bromide, Tiospirex

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

In vitro experiments with human liver microsomes and human hepatocytes suggest that a fraction of the administered dose (74% of an intravenous dose is excreted unchanged in the urine, leaving 25% for metabolism) is metabolized by cytochrome P450-dependent oxidation and subsequent glutathione conjugation to a variety of Phase II metabolites.

Recommendations based on specific guidelines

FDA — **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Tolbutamide || CYP2C9

Tolmide, Tolbutamide, Tobumide

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

There is insufficient evidence to state that the increase tolbutamide plasma concentration has any clinical consequences.

Recommendations based on specific guidelines

DPWG	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Tolperisone

Tolperisone

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Tolterodine

Detrusitol, Tolterodine

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Approximately 7% of Caucasians are poor metabolizers of CYP2D6 substrates. A pharmacokinetic/pharmacodynamic model estimated that QTc interval increases in poor metabolizers treated with tolterodine 2 mg BID are comparable to those observed in extensive metabolizers receiving 4 mg BID.

Recommendations based on specific guidelines

HCSC — **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Tramadol || CYP2D6

Acugesic, Dolgesik, Durotram, Forgesic, Mabron, Orasic, Pengesic, Sefmal, Tracidol, Tradol, Tradonal, Tradyl, Tramadol, Tramadol Stada, Tramal, Tramofal, Zephanal, Tradosik, Thramed, Stronginal, Radol, Dolocap, Centrasic, Tugesal

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Use tramadol label recommended age- or weight-specific dosing.

Expected O-desmethyltramadol (active metabolite) formation.

Recommendations based on specific guidelines

CPIC	**Use tramadol label recommended age- or weight-specific dosing.**
HCSC	No actionable recommendation is available for this drug-gene pair.

Caveat

Like all diagnostic tests, CYP2D6 genotype is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. Furthermore, there are several other factors that cause potential uncertainty in the genotyping results and phenotype predictions. These are discussed in detail in the Supplementary Data online.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Trimipramine

Trimipramine

START MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose. Patients may receive an initial low dose of TCAs, which is then increase over several days to the recommended steady-state dose.

CYP2C19 IM : Reduced metabolism of tertiary amines compared to normal metabolizers. CY2D6 NM : Normal metabolism of TCAs.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose. Patients may receive an initial low dose of TCAs, which is then increase over several days to the recommended steady-state dose.|| Dosing recommendations only apply to higher initial doses of TCAs for treatment of conditions such as depression.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose

Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Initiation

This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Trimipramine || CYP2C19

Trimipramine

START MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.

Reduced metabolism of tertiary amines compared to normal metabolizers.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose
Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Initiation
This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Trimipramine || CYP2D6

Trimipramine

START STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.

Normal metabolism of TCAs.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose. Patients may receive an initial low dose of a tricyclic, which is then increase over several days to the recommended steady-state dose. The starting dose in this guideline refers to the recommended steady-state dose.**

Caveat

The application of genotype-based dosing is most appropriate when initiating therapy with a tricyclic. Obtaining a pharmacogenetic test after months of drug therapy may be less helpful in some instances, as the drug dose may have already been adjusted based on plasma concentrations, response, or side effects. Similar to all diagnostic tests, genetic tests are one of several pieces of clinical information that should be considered before initiating drug therapy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose
Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Initiation
This drug-gene interaction recommendation is useful for initiation of this drug in naive patients. For patients who are already on stable dose or have used this drug before, effective drug monitoring and clinical judgement is more important.

Tropisetron

Setrovel, Tropisetron

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Initiate therapy with recommended starting dose.

Normal metabolism.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended starting dose.|| In accordance with the prescribing information, use the lowest effective dosage for shortest duration consistent with individual patient treatment goals.**

Caveat

Rare CYP2D6 variants may not be included in the genotype test used and patients with rare variants may be assigned a “wildtype” (CYP2D6*1) genotype by default. Thus, an assigned “wildtype” allele could potentially harbor a no or decreased function variant. Furthermore, it is important that the genetic testing platform include testing for gene copy number to identify CYP2D6 UMs. Caution should be used regarding molecular diagnostics of CYP2D6 gene copy-number variation because commercially available genotyping results may differ between diagnostic laboratories depending on assay design. Like all diagnostic tests, CYP2D6 genotype is one of multiple pieces of information that clinicians should consider when making their therapeutic choice.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Indication

This drug-gene interaction recommendation is based on a specific diagnosis ONLY. Exercise prudent clinical judgement when using the drug for other indications.

Umeclidinium

Incruse Ellipta

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

In vitro metabolism of umeclidinium is mediated primarily by CYP2D6. However, no clinically meaningful difference in systemic exposure to umeclidinium (500 mcg) (8 times the approved dose) was observed following repeat daily inhaled dosing to normal (ultrarapid, extensive, and intermediate metabolizers) and CYP2D6 poor metabolizer subjects.

Recommendations based on specific guidelines

FDA — **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Upadacitinib

Rinvoq

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Upadacitinib is metabolized in vitro by CYP3A4 with a minor contribution from CYP2D6. CYP2D6 metabolic phenotype had no effect on upadacitinib pharmacokinetics (based on population pharmacokinetic analyses), indicating that inhibitors of CYP2D6 have no clinically relevant effect on upadacitinib exposures.

Recommendations based on specific guidelines

FDA — **No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Valbenazine

Remleas

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Venlafaxine

Deprevix, Avenfax, Viepax, Efexor, Venlafaxine, Venladex Xr, Venlex Xr

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

In vitro studies indicate that the formation of ODV is catalyzed by CYP2D6; this has been confirmed in a clinical study showing that patients with low CYP2D6 levels (poor metabolizers) had increased levels of venlafaxine and reduced levels of ODV compared to people with normal CYP2D6 levels (extensive metabolizers).

Recommendations based on specific guidelines

FDA — **No actionable recommendation is available for this drug-gene pair.**

More information about this drug-phenotype can also be found at **SWISSMEDIC**.

Source

The curated publications relevant to the drug-gene pair and reported ethnicity are listed below:

10877013 25510856

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Vernakalant

Brinavess

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Therefore, dose adjustment is not necessary due to the CYP2D6 metabolization status.

The main metabolites circulating in human plasma were the glucuronic acid conjugate of 4-O-demethylated vernakalant (in extensive metabolizers) and the glucuronic acid conjugate of vernakalant itself (in weak metabolizers), neither of which is pharmacologically active.

Recommendations based on specific guidelines

SWISSMEDIC **Therefore, dose adjustment is not necessary due to the CYP2D6 metabolization status.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Voriconazole || CYP2C19

Voriconazole Sandoz, Vfend, Vorica, Vorigen, Voriconazole, Voritrop

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C19	*1/*2	CYP2C19 Intermediate metabolizer

Recommendation

Initiate therapy with recommended standard of care dosing.

Higher dose-adjusted trough concentrations of voriconazole compared to normal metabolizers.

Recommendations based on specific guidelines

CPIC	**Initiate therapy with recommended standard of care dosing.|| Further dose adjustments or selection of alternative therapy may be necessary due to other clinical factors, such as drug interactions, hepatic function, renal function, species, site of infection, TDM, and comorbidities.**
DPWG	Monitor the plasma concentration.
FDA	No actionable recommendation is available for this drug-gene pair.

More information about this drug-phenotype can also be found at **EMA** and **PMDA**.

Caveat

CYP2C19 genotyping cannot replace TDM, as other factors (i.e., drug interactions, hepatic function, renal function, species, site of infection, and comorbidities) also influence the use of voriconazole. Rare CYP2C19 variants are typically not included in common genotyping tests and patients are therefore assigned the “wild-type” (CYP2C19*1) allele by default. Thus, in rare cases, an assigned “wild-type” allele may harbor a no, decreased, or increase function variant. An individual’s predicted CYP2C19 metabolizer status may also depend on other factors, including epigenetic phenomena, diet, comorbidities, or comedications.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Predictive Value

Low positive predictive value. Testing positive for this phenotype does not mean that the patient will develop the adverse effect.

Voriconazole || CYP2C9

Voriconazole Sandoz, Vfend, Vorica, Vorigen, Voriconazole, Voritrop

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

No actionable recommendation is available for this drug-gene pair.

Inhibitors or inducers of these isoenzymes may increase or decrease voriconazole plasma concentrations.

Recommendations based on specific guidelines

EMA	**No actionable recommendation is available for this drug-gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.

Vortioxetine

Brintellix, Vortioxetine

MODERATE RECOMMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

No actionable recommendation is available for this drug gene pair.

The plasma concentration of vortioxetine was approximately two times lower in CYP2D6 extensive metabolizers than in poor metabolizers. In the presence of strong CYP3A4/2C9-inhibitors, the exposure could potentially be higher.

Recommendations based on specific guidelines

HCSC — **No actionable recommendation is available for this drug gene pair.**

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Increase Monitoring

Although patient has a varied genetic profile, the intended medication can still be prescribed as recommended, but with more frequent monitoring for quick action to be taken in the event of unwanted reactions.

Warfarin

Apo-Warfarin, Marevan, Notisil, Rheoxen, Simarc, Orfarin, Warfarin

STRONG RECOMENDATION

GENE	GENOTYPE	PHENOTYPE
CYP2C9	*1/*3	CYP2C9 Intermediate metabolizer

Recommendation

Use 65% of the standard initial dose.

This gene variation reduces the conversion of warfarin to inactive metabolites. This can increase the risk of bleeding.

Recommendations based on specific guidelines

DPWG	**Use 65% of the standard initial dose.|| The genotype-specific initial dose and maintenance dose can be calculated using an algorithm, as used in EU-PACT: see Algorithms coumarins. From day 6 on the standard algorithm without genotype information can be used to calculate the dose.**
CPNDS	Testing of all warfarin-naive patients for VKORC1 (-1639G>A), CYP2C9*2, and CYP2C9*3 should be considered before initiation of therapy and within the first 2 weeks of therapy.|| (level B - moderate recommendation). Genetic testing for CYP2C9*5, *6, *8 or *11 and CYP4F2 V433M is currently not recommended (level C - optional recommendation). Management of patients with VKORC1 and CYP2C9 variants Genotyping results should be interpreted using a pharmacogenetic dosing algorithm to estimate the required dose (level A – strong recommendation). After testing for CYP2C9*2, CYP2C9*3, and VKORC1 (-1639G>A), pharmacogenetic dosing algorithms that incorporate both clinical variables and genetic information should be used to predict a stable warfarin dose. Of importance, pharmacogenetic-guided dosing should not replace regular INR monitoring. Rather, test results should be used to help physicians estimate an appropriate warfarin dose, while still using regular INR monitoring to ensure that stable anticoagulation is achieved.
FDA	Select initial dosage, taking into account clinical and genetic factors. Monitor and adjust dosages based on INR.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Decrease Starting Dose

Patient has altered metabolism rate or enhanced activation rate for drug indicated. Decreasing starting dose has shown to help prevent patient from experiencing adverse drug reaction.

Zuclopenthixol

Clopixol, Zuclopenthixol

INFORMATION AVAILABLE

GENE	GENOTYPE	PHENOTYPE
CYP2D6	*2/*36,copy number: >=3.0	CYP2D6 Normal metabolizer

Recommendation

Follow standard dosing guideline

No known increase risk of adverse drug reaction or therapeutic inefficacy.

Source

Publications related to local relevance for this drug-gene pair have not been published yet.

Follow standard dosing

There is a low chance of sub-optimal response or adverse reaction due to patient's genetic polymorphism, no change is necessary.