

## Pharmacogenetic test summary

Sample ID	<b>Test_2</b>	Laboratory	<b>SYNLAB Eesti OÜ</b>
		Sample collection date	<b>09.09.2024</b>
		Report creation date	<b>07.01.2026</b>

### Overview of the results



You were tested for 29 genes, out of which 5 may affect the efficacy or safety of your medication:  
**CYP2C9, CYP2D6, G6PD, NAT2, VKORC1**



Your genetic factors may affect the efficacy or safety of 69 drugs.

### The latest genetic information is found online

We update our service periodically since pharmacogenetic knowledge is constantly evolving and getting more accurate by new research discoveries.

Log in to your results by scanning this QR code



or by visiting  
[test.geneaccount.com/AfGQQz](https://test.geneaccount.com/AfGQQz)

Your pin code

**9697**

In order to protect your privacy, share this information only after serious consideration and only to trusted persons, e.g. your doctor.



## DRUGS WITH GENETIC VARIATION OF SIGNIFICANT CLINICAL RELEVANCE

C

amifampridine, amifampridine phosphate, dapsone, eliglustat, methylthioninium, nitrofurantoin, pegloticase, primaquine, quinine, rasburicase, siponimod, sulfadiazine, tafenoquine, tetrabenazine



## DRUGS WITH GENETIC VARIATION OF SOME CLINICAL RELEVANCE

articaine, ascorbic acid, atomoxetine, bupivacaine, chloroprocaine, chloroquine, chlorpropamide, dabrafenib, flutamide, glibenclamide, glimepiride, glipizide, hydroxychloroquine, lidocaine, mafenide, mepivacaine, nalidixic acid, prilocaine, probenecid, ropivacaine, sodium nitrite, sulfamethoxazole, sulfasalazine, sulfisoxazole, tetracaine, tolazamide, tolbutamide, warfarin



## DRUGS WITH GENETIC VARIATION OF MINOR CLINICAL RELEVANCE

boceprevir, ciprofloxacin, citalopram, desflurane, dexlansoprazole, digoxin, enflurane, escitalopram, halothane, hydralazine, isoflurane, isoniazid, lansoprazole, levofloxacin, methoxyflurane, moxifloxacin, norfloxacin, omeprazole, pantoprazole, peginterferon alfa-2a, peginterferon alfa-2b, quinidine, ribavirin, sevoflurane, suxamethonium, telaprevir, vincristine

## DRUGS WITH NO CLINICALLY RELEVANT GENETIC VARIATION

acenocoumarol, alcohol, allopurinol, amitriptyline, amoxapine, amphetamine, arformoterol, aripiprazole, aripiprazole lauroxil, atazanavir, atenolol, atorvastatin, avatrombopag, azathioprine, belinostat, binimetinib, bisoprolol, brexpiprazole, brivaracetam, bupropion, cabotegravir, capecitabine, cariprazine, carisoprodol, carvedilol, celecoxib, cevimeline, cisplatin, clobazam, clomipramine, clopidogrel, clozapine, codeine, daclatasvir, darifenacin, desipramine, desvenlafaxine, deutetetabenazine, dexamfetamine, dextromethorphan, diazepam, diclofenac, dolutegravir, donepezil, doxepin, dronabinol, duloxetine, efavirenz, elagolix, eltrombopag, erdafitinib, erlotinib, esomeprazole, estradiol, estriol, ethinylestradiol, fesoterodine, flecainide, flibanserin, flucytosine, fluorouracil, fluoxetine, flupentixol, flurbiprofen, fluvastatin, fluvoxamine, folic acid, fosphenytoin, galantamine, gefitinib, glyceral trinitrate, govitecan, haloperidol, hydrocodone, ibuprofen, iloperidone, imipramine, indacaterol, irbesartan, irinotecan, lacosamide, lesinurad, lisdexamfetamine, lofexidine, loratadine, loroxicam, losartan, lovastatin, lusutrombopag, meclizine, meloxicam, mercaptopurine, methadone, methotrexate, metoclopramide, metoprolol, mirabegron, mirtazapine, mivacurium, moclobemide, modafinil, nebivolol, nefazodone, nevirapine, nilotinib, nortriptyline, olanzapine, oliceridine, ondansetron, oxycodone, paliperidone, palonosetron, paroxetine, pazopanib, perphenazine, phenprocoumon, phentytoin, pimozide, pioglitazone, piroxicam, pitavastatin, pitolisant, prasugrel, pravastatin, propafenone, propranolol, protriptyline, quetiapine, rabeprazole, raltegravir, ranolazine, rimegepant, risperidone, romiplostim, rosiglitazone, rosuvastatin, rucaparib, sacituzumab govitecan, sertindole, sertraline, simeprevir, simvastatin, sofosbuvir, synthetic conjugated estrogens, tacrolimus, tamoxifen, tamsulosin, tegafur, tenoxicam, terbinafine, thioguanine, thioridazine, tibolone, ticagrelor, tolterodine, tramadol, trimipramine, tropisetron, umeclidinium, upadacitinib, valbenazine, venlafaxine, voriconazole, vortioxetine, zuclopentixol

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## 1. Introduction

This is the report of your pharmacogenetic test results. The report contains information on the tested genetic variants and their effects on the safety and efficacy of medications. **This report should not be used to change medications without guidance from a physician. Always consult your physician before making any changes to your medications.**

## 2. How to read this report

First, here is a short list of terms to understand the report better:

- variant = a genetic alteration which deviates from the common form
- genotype = the composition of your genetic variants for a gene
- phenotype = a property or function caused by a genotype, e.g. “rapid metabolizer” or “increased risk”

The report is divided into three major sections: gene-specific recommendations for medications, detailed genotype results and the raw data of your variants.

It is vital to remember that drug responses may be affected by other genetic variants not included in this report. Additionally, many other individual factors, e.g. age, body weight, allergies or hypersensitivities, other drugs, foods and natural products, kidney and liver function and disease states affect the drug responses. Even though a gene might be stated here as having a normal genotype and phenotype (i.e. no variants with aberrant functionality detected), a possibility of having a deviant genotype exists e.g. due to rare non-detectable variants or technical error. Scientific knowledge also changes over time and thus it is important to check most recent version of the recommendations from GeneAccount

Some of the genes are shown as affecting medications significantly, although their genotypes and phenotypes were normal. This confusing listing is due to the fact, that for some medications there are highly significant drug recommendations even though the genotype is normal. In these cases, the normal genotype should also be regarded when prescribing and dosing the medication. This stands for e.g. genes *CYP2C9* and *VKORC1* (recommendation for warfarin) and *CYP2D6* (recommendations for eliglustat and atomoxetine). On the other hand, for gene *CYP3A5*, the most common phenotype in the white populations is “poor metabolizer” and common drug dosages stated in drug labels apply to this group. Therefore, *CYP3A5* is shown in the list of significant gene results for individuals with “normal metabolizers” phenotype for *CYP3A5*, as this genotype / phenotype alters the dosing of certain medications significantly.

### 3. Classification of drug recommendations



Pharmacogenetic variation affects drug effectiveness or adverse reactions with significant clinical relevance. A genetic test is recommended. Check existing test results before prescribing the drug. Check dosing and administration based on test results.



Pharmacogenetic variation affects drug effectiveness or adverse reactions with some clinical relevance. If genetic test results are available, consider changing drug or dosing based on results. If genetic testing has not been conducted, consider ordering a test.



Pharmacogenetic variation may affect drug effectiveness or adverse reactions, but with minor clinical significance in most patients. Monitor drug response and possible adverse reactions. If genetic test results are available, consider changing drug or dosing based on results.



Pharmacogenetic variation does not significantly affect drug effectiveness or adverse reactions.

## 4. Therapeutic area

### Alimentary tract and metabolism

Active ingredient	CYP2C9 NM Normal metabolizer (Activity score 2)	CYP2D6 NM Normal metabolizer	G6PD G6PD deficient	NAT2 Slow acetylator	VKORC1 Normal expression
ascorbic acid			C		
chlorpropamide			C		
eliglustat		D			
glibenclamide			C		
glimepiride			C		
glipizide			C		
sulfasalazine			C		
tolazamide			C		
tolbutamide			C		

### Blood and blood forming organs

Active ingredient	CYP2C9 NM Normal metabolizer (Activity score 2)	CYP2D6 NM Normal metabolizer	G6PD G6PD deficient	NAT2 Slow acetylator	VKORC1 Normal expression
warfarin	C				C

### Cardiovascular system

Active ingredient	CYP2C9 NM Normal metabolizer (Activity score 2)	CYP2D6 NM Normal metabolizer	G6PD G6PD deficient	NAT2 Slow acetylator	VKORC1 Normal expression
lidocaine			C		

## Dermatologicals

Active ingredient	CYP2C9 NM Normal metabolizer (Activity score 2)	CYP2D6 NM Normal metabolizer	G6PD G6PD deficient	NAT2 Slow acetylator	VKORC1 Normal expression
mafenide			C		

## General antiinfectives for systemic use

Active ingredient	CYP2C9 NM Normal metabolizer (Activity score 2)	CYP2D6 NM Normal metabolizer	G6PD G6PD deficient	NAT2 Slow acetylator	VKORC1 Normal expression
dapsone			D		
nalidixic acid			C		
nitrofurantoin			D		
sulfadiazine			D		
sulfamethoxazole			C		
sulfisoxazole			C		

## Antineoplastic and immunomodulating agents

Active ingredient	CYP2C9 NM Normal metabolizer (Activity score 2)	CYP2D6 NM Normal metabolizer	G6PD G6PD deficient	NAT2 Slow acetylator	VKORC1 Normal expression
dabrafenib			C		
flutamide			C		
siponimod	D				

## Musculo-skeletal system

Active ingredient	CYP2C9 NM Normal metabolizer (Activity score 2)	CYP2D6 NM Normal metabolizer	G6PD G6PD deficient	NAT2 Slow acetylator	VKORC1 Normal expression
pegloticase			D		
probenecid			C		

## Nervous system

Active ingredient	CYP2C9 NM Normal metabolizer (Activity score 2)	CYP2D6 NM Normal metabolizer	G6PD G6PD deficient	NAT2 Slow acetylator	VKORC1 Normal expression
amifampridine				D	
amifampridine phosphate				D	
articaine			C		
atomoxetine		C			
bupivacaine			C		
chloroprocaine			C		
mepivacaine			C		
prilocaine			C		
ropivacaine			C		
tetrabenazine		D			
tetracaine			C		

## Antiparasitic products

Active ingredient	CYP2C9 NM Normal metabolizer (Activity score 2)	CYP2D6 NM Normal metabolizer	G6PD G6PD deficient	NAT2 Slow acetylator	VKORC1 Normal expression
chloroquine			C		
hydroxychloroquine			C		
primaquine			D		
quinine			D		
tafenoquine			D		

## Various

Active ingredient	CYP2C9 NM Normal metabolizer (Activity score 2)	CYP2D6 NM Normal metabolizer	G6PD G6PD deficient	NAT2 Slow acetylator	VKORC1 Normal expression
methylthioninium			D		
rasburicase			D		
sodium nitrite			C		

## 5. Summary of tested genes and their predicted phenotypes

Gene	Diplotype	Phenotype
ABCB1	WT/WT	Likely low expression
ABCG2	WT/WT	Normal function
ALDH2	*1/*1	Normal activity
BCHE	WT/WT	Normal activity
CACNA1S	WT/WT	Uncertain susceptibility to malignant hyperthermia
CYP1A2	*1C/*1F	IM Intermediate metabolizer
CYP2B6	*1/*1	NM Normal metabolizer
CYP2C19	*1/*1	NM Normal metabolizer
CYP2C8	*1/*1	Normal metabolizer
CYP2C9	*1/*1	NM Normal metabolizer (Activity score 2), activity score 2
CYP2C_rs12777823	G/G	Normal warfarin dosing
CYP2D6	*1/*1	NM Normal metabolizer, activity score 2
CYP3A4	*1/*1	NM Normal metabolizer
CYP3A5	*3/*3	PM Poor metabolizer
CYP4F2	*1/*1	Normal metabolizer
DPYD	WT/WT	NM Normal metabolizer, activity score 2
F2	WT/WT	No increased risk of venous thromboembolism
F5	WT/WT	No increased risk of venous thromboembolism
G6PD	Canton/Canton	G6PD deficient
GRIK4	T/T	Poor responder (homozygous)
IFNL3	WT/WT	Favorable response genotype
MTHFR	WT/WT	Normal activity
NAT2	*5/*16	Slow acetylator
NFIB	WT/WT	Normal metabolizer
NUDT15	*1/*1	NM Normal metabolizer
SLCO1B1	*1/*14	Normal function

TPMT	*1/*1	NM Normal metabolizer
UGT1A1	*1/*1	NM Normal metabolizer
VKORC1	*1/*1	Normal expression

## 6. Drug-specific recommendations

### Acenocoumarol

- A** **CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.
- A** **VKORC1: Normal expression:** Label-recommended dosing and administration.

### Alcohol

- A** **ALDH2: Normal activity:** Minor or no flushing reaction to alcohol.

### Allopurinol

- A** **ABCG2: Normal function:** Label-recommended dosing and administration.

### Amifampridine

**D** **NAT2: Slow acetylator:** With this genotype, the acetylation rate of this medication is potentially significantly reduced. According to the label approved by the U.S. Food and Drug Administration (FDA) poor metabolizers, also referred to as "slow acetylators" (i.e., carriers of two reduced function alleles), had higher average plasma amifampridine concentrations than intermediate metabolizers, also referred to as "intermediate acetylators" (i.e., carriers of one reduced and one normal function alleles), and normal metabolizers, also referred to as "fast/rapid acetylators" (i.e., carriers of two normal function alleles). In the TQT study, poor metabolizers (N=19) had 1.1 to 3.7 times higher AUC0-4h and 1.3 to 3.7 times higher Cmax than intermediate metabolizers (N=21), following the first dose. Poor metabolizers had 6.0 to 8.5 times higher AUC0-4h and 6.1 to 7.6 times higher Cmax than normal metabolizers (N=3), following the first dose. The recommended starting dosage in pediatric patients weighing 45 kg or more who are known NAT2 poor metabolizers is 15 mg daily taken orally in divided doses. The recommended starting dosage in pediatric patients weighing less than 45 kg who are known NAT2 poor metabolizers is 7.5 mg daily taken orally in divided doses.

### Amifampridine phosphate

- D** **NAT2: Slow acetylator:** With this genotype, the acetylation rate of this medication is potentially significantly reduced. According to the label approved by the U.S. Food and Drug Administration (FDA) poor metabolizers, also referred to as "slow acetylators" (i.e., carriers of two reduced function alleles), have 3.5- to 4.5-fold higher Cmax, and 5.6- to 9 fold higher AUC than normal metabolizers, also referred to as "fast/rapid acetylators" (i.e., carriers of two normal function alleles). Treatment should be initiated at the lowest recommended starting dosage (15 mg/day (taken orally in 3 divided doses)) in known NAT2 poor metabolizers, and such patients should be closely monitored for adverse reactions.

### Amitriptyline

- A** **CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.
- A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

### Amoxapine

- A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

### Amphetamine

- A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

### Arformoterol

- A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.
- A** **UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

### Aripiprazole

- A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Aripiprazole lauroxil

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Articaine

C

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer, patients with G6PD deficiency are at increased risk for methaemoglobinemia when using the product. If use of product is required in patients with this genotype, close monitoring for symptoms and signs of methaemoglobinemia (shortness of breath, high pulse, cyanosis, or seizures) is recommended.

## Ascorbic acid

C

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug may be at risk of severe haemolytic reactions. Normal doses of vitamin C are considered safe but haemolysis has been reported in patients consuming 3-4 grams of vitamin C during 4-6 hours. In some cases, hospitalization after severe haemolysis has been required. The product should be used with caution, especially G6PD deficiency patients with an active infection, with a history of hemolysis, or taking concomitant medications known to precipitate hemolytic reactions

## Atazanavir

A

**UGT1A1: NM Normal metabolizer:** With this genotype the risk of jaundice caused by atazanavir is not increased. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): There is no need to avoid prescribing of atazanavir based on UGT1A1 genetic test result. Inform the patient that some patients stop atazanavir because of jaundice (yellow eyes and skin) but this patient's genotype makes this unlikely (less than about a one in 20 chance of stopping atazanavir because of jaundice).

## Atenolol

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Atomoxetine

C

**CYP2D6: NM Normal metabolizer:** With this genotype, the exposure to the drug is potentially decreased as compared to poor metabolizers which may lead to insufficient efficacy. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): FOR ADULTS: Initiate with a dose of 40 mg/day and increase to 80 mg/day after 3 days. If no clinical response and in the absence of adverse events after 2 weeks, consider increasing dose to 100 mg/day. If no clinical response observed after 2 weeks, consider obtaining a peak plasma concentration (1-2 hours after dose administered). If < 200 ng/ml, consider a proportional increase in dose to approach 400 ng/ml. Dosages > 100 mg/day may be needed to achieve target concentrations. FOR CHILDREN: Initiate with a dose of 0.5 mg/kg and increase to 1.2 mg/kg/day after 3 days. If no clinical response and in the absence of adverse events after 2 weeks, consider obtaining a peak plasma concentration (1-2 hours after dose administered). If < 200 ng/ml, consider a proportional increase in dose to approach 400 ng/ml.

## Atorvastatin

A

**ABCG2: Normal function:** Label-recommended dosing and administration.

A

**CYP3A4: NM Normal metabolizer:** Label-recommended dosing and administration.

A

**SLCO1B1: Normal function:** Typical risk for myopathy and exposure for statins. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe desired starting dose and adjust doses based on disease- specific guidelines.

## Avatrombopag

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

A

**F2 (prothrombin): No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

A

**F5: No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

## Azathioprine

A

### NUDT15: NM Normal metabolizer:

Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Start with normal starting dose (e.g. 2-3 mg/kg/day) and adjust dosing based on disease-specific guidelines. Allow 2 weeks to reach steady-state after each dose adjustment. Note that also TPMT genotype affects the risk for thiopurine-induced adverse reactions. See if TPMT test result is available and treat according to the recommendation for more severe phenotype for either TPMT or NUDT15 gene (e.g. if NUDT15 phenotype is normal and TPMT phenotype is poor metabolizer, treat according to the TPMT poor metabolizer guideline).

A

**TPMT: NM Normal metabolizer:** Start with normal starting dose and adjust doses of azathioprine based on disease-specific guidelines. Allow 2 weeks to reach steady state after each dose adjustment. Note that also NUDT15 genotype affects the risk for thiopurine-induced adverse reactions. See if NUDT15 test result is available and treat according to the recommendation for more severe phenotype for either TPMT or NUDT15 gene (e.g. if TPMT phenotype is normal and NUDT15 phenotype is poor metabolizer, treat according to the NUDT15 poor metabolizer guideline).

## Belinostat

A

**UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

## Binimetinib

A

**UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

## Bisoprolol

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Boceprevir

B

### IFNL3: Favorable response genotype:

This genotype is associated with a favorable response of hepatitis C virus (genotype 1) treatment with combination of peginterferon alpha 2 (PEG-IFN alpha) and ribavirin (RBV). According to a recommendation by an international board of experts (Clinical Pharmacogenetics Implementation Consortium) with this genotype there is approximately 70% chance for sustained virologic response after 48 weeks of treatment when treated with combination of PEG-IFN alpha and RBV. Consider implications before initiating PEG-IFN alpha and RBV containing regimens. Additionally, there is approximately 90% chance for sustained virologic response after 24-48 weeks of treatment when treated with combination of PEG-IFN alpha, RBV and protease inhibitor and approximately 80-90% of patients are eligible for shortened therapy (24-28 weeks instead of 48 weeks). This genotype weighs in favor of using PEG-IFN alpha and RBV containing regimens.

## Brexipiprazole

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Brivaracetam

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

## Bupivacaine

C

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer, patients with G6PD deficiency are at increased risk for methaemoglobinemia when using the product. If use of product is required in patients with this genotype, close monitoring for symptoms and signs of methaemoglobinemia (shortness of breath, high pulse, cyanosis, or seizures) is recommended.

## Bupropion

A

**CYP2B6: NM Normal metabolizer:** Label-recommended dosage and administration.

## Cabotegravir

A

**UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

## Capecitabine

A

**DYPD: NM Normal metabolizer:** Normal dihydropyrimidine dehydrogenase activity and no increased risk for fluoropyrimidine toxicity. Label-recommended dosage.

## Cariprazine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Carisoprodol

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

## Carvedilol

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Celecoxib

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Cevimeline

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Chlorprocaine

C

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer, patients with G6PD deficiency are at increased risk for methaemoglobinemia when using the product. If use of product is required in patients with this genotype, close monitoring for symptoms and signs of methaemoglobinemia (shortness of breath, high pulse, cyanosis, or seizures) is recommended.

## Chloroquine

C

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug may be at risk of severe haemolytic reactions. According to the summary of product characteristics the drug should be administered with caution to patients with G6PD deficiency. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

## Chlorpropamide

C

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer use of chlorpropamide can lead to haemolytic anaemia in patients with G6PD deficiency. Caution should be used in patients with G6PD deficiency and a non-sulfonylurea alternative should be considered.

## Ciprofloxacin

B

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer haemolytic reactions have been reported with ciprofloxacin in patients with glucose-6-phosphate dehydrogenase deficiency. Ciprofloxacin should be avoided in these patients unless the potential benefit is considered to outweigh the possible risk. In this case, potential occurrence of haemolysis should be monitored.

## Cisplatin

A

**TPMT: NM Normal metabolizer:** Label-recommended dosing and administration.

## Citalopram

B

**GRIK4: Poor responder (homozygous):** Label-recommended dosage. Patients with this genotype may be less likely to respond to antidepressant treatment as compared to high response genotype.

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Clobazam

**A** **CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

## Clomipramine

**A** **CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Clopidogrel

**A** **CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

**A** **CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Clozapine

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

**A** **NFIB: Normal metabolizer:** Label-recommended dosing and administration.

## Codeine

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Dabrafenib

**C** **G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug may be at risk of severe haemolytic reactions. The warnings and precautions of the summary of product characteristics approved by the U.S. Food and Drug Administration (FDA): Closely observe patients with G6PD deficiency for signs of haemolytic anaemia. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

## Daclatasvir

**A** **IFNL3: Favorable response genotype:** According to the summary of product characteristics provided by the manufacturer IFNL3 genotype was not associated with treatment response when treating patients coinfected with hepatitis C and HIV with combination of daclatasvir and sofosbuvir.

## Dapsone

**D** **G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug orally are at risk of moderate to severe haemolytic reactions. According to the summary of product characteristics the use of the drug orally is contraindicated in patients with G6PD deficiency. Topical administration is not contraindicated, but it may cause hemolysis. According to the summary of product characteristics there is no evidence of progress of clinically significant hemolysis in topical use. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

**B** **NAT2: Slow acetylator:** With this genotype, the acetylation rate of this medication is potentially significantly reduced. This potentially predisposes to increased risk of hemolysis or methemoglobinemia, although the published literature regarding this association is scarce.

## Darifenacin

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Desflurane

B

**CACNA1S: Uncertain susceptibility to malignant hyperthermia:** No malignant hyperthermia (MH)-causative variants were detected. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): These results do not eliminate the chance that this patient is susceptible to MH. The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown. Clinical findings, family history, further genetic testing, and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants. It should be noted that individuals with muscle diseases caused by, or associated with, genetic abnormalities in RYR1 receptors (or less often the dihydropyridine receptor) should be treated as MH-susceptible and should be managed by the anesthesiologist in consultation with an expert in these rare neuromuscular diseases.

## Dexlansoprazole

B

**CYP2C19: NM Normal metabolizer:**

Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of *H. pylori* infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.

## Dextromethorphan

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Diazepam

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

## Diclofenac

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Digoxin

B

**ABCB1: Likely low expression:** Label-

recommended dosing. With this genotype, exposure to digoxin is potentially increased. Be alert for increased digoxin concentrations. Scientific evidence for this is inconsistent, though. Pay attention to concomitant use of drugs inhibiting P-glycoprotein, which seem to affect the digoxin concentrations more significantly than the genotype.

## Dolutegravir

A

**UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

## Donepezil

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Desipramine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Desvenlafaxine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Deutetrabenazine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration. A clinically relevant QT prolongation may occur in some patients treated with deutetrabenazine who are co-administered a strong CYP2D6 inhibitor.

## Dexamfetamine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Doxepin

- A** **CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.
- A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Dronabinol

- A** **CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Duloxetine

- A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Efavirenz

- A** **CYP2B6: NM Normal metabolizer:** Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC) for adults and children who weigh more than 40 kg: Initiate efavirenz with standard dose of 600 mg/day. CPIC does not recommend use of efavirenz in children aged 3 months to < 3 years, except in special circumstances, such as tuberculosis coinfection. In such circumstances, weight-guided dosing is recommended. For patients with this genotype, the weight groups and dosing are as follows: 5-7 kg = 300 mg; 7-14 kg = 400 mg; 14-17 kg = 500 mg; > 17 kg = 600 mg. Measuring efavirenz concentration after 2 weeks of initiation is recommended in this age group. There is not yet enough data available to recommend genotype-guided dosing in children older than 3 years but weighing less than 40 kg. Therapeutic drug monitoring, where available and accessible, could help guide dosing adjustments in this age/weight group, especially in a setting of potential drug-related toxicity, virologic rebound, or lack of response in an adherent patient.

## Elagolix

- A** **SLCO1B1: Normal function:** Label-recommended dosing and administration.

## Eliglustat

- D** **CYP2D6: NM Normal metabolizer:** According to the summary of product characteristics provided by the manufacturer: For normal CYP2D6 metabolizers the dose is 84 mg twice daily. See drug label or summary of product characteristics for specific dosing or contraindications when used concomitantly with strong or moderate CYP2D6 inhibitors (e.g. paroxetine, fluoxetine, duloxetine, terbinafine) or strong or moderate CYP3A inhibitors (e.g. clarithromycin, ketoconazole, erythromycin, ciprofloxacin, fluconazole).

## Eltrombopag

- A** **F2 (prothrombin): No increased risk of venous thromboembolism:** Label-recommended dosing and administration.
- A** **F5: No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

## Enflurane

- B** **CACNA1S: Uncertain susceptibility to malignant hyperthermia:** No malignant hyperthermia (MH)-causative variants were detected. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): These results do not eliminate the chance that this patient is susceptible to MH. The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown. Clinical findings, family history, further genetic testing, and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants. It should be noted that individuals with muscle diseases caused by, or associated with, genetic abnormalities in RYR1 receptors (or less often the dihydropyridine receptor) should be treated as MH-susceptible and should be managed by the anesthesiologist in consultation with an expert in these rare neuromuscular diseases.

## Erdafitinib

- A** **CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Erlotinib

**A** **UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

## Escitalopram

**B** **GRIK4: Poor responder (homozygous):** Label-recommended dosage. Patients with this genotype may be less likely to respond to antidepressant treatment as compared to high response genotype.

**A** **CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Esomeprazole

**A** **CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

## Estradiol

**A** **F2 (prothrombin): No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

**A** **F5: No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

## Estriol

**A** **F2 (prothrombin): No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

**A** **F5: No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

## Ethinylestradiol

**A** **F2 (prothrombin): No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

**A** **F5: No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

## Fesoterodine

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Flecainide

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Flibanserin

**A** **CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

**A** **CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Flucytosine

**A** **DPYD: NM Normal metabolizer:** Normal dihydropyrimidine dehydrogenase activity and no increased risk for fluoropyrimidine toxicity. Label-recommended dosage.

## Fluorouracil

**A** **DPYD: NM Normal metabolizer:** Normal dihydropyrimidine dehydrogenase activity and no increased risk for fluoropyrimidine toxicity. Label-recommended dosage.

## Fluoxetine

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Flupentixol

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Flurbiprofen

**A** **CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Flutamide

**C** **G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer, patients with G6PD deficiency are at increased risk for methaemoglobinemia when using the product. Monitoring of methaemoglobin levels should be considered.

## Fluvastatin

**A** **CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration. Check also if dosing guidelines for SLCO1B1 are available.

**A** **SLCO1B1: Normal function:** Typical risk for myopathy and exposure for statins. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe desired starting dose and adjust doses based on disease-specific guidelines. Check also if CYP2C9 phenotype is available. If CYP2C9 phenotype is intermediate metabolizer, prescribe  $\leq 40$ mg per day as a starting dose and adjust doses of fluvastatin based on disease-specific guidelines. If dose  $> 40$ mg needed for desired efficacy, consider an alternative statin or combination therapy. If CYP2C9 phenotype is poor metabolizer, prescribe  $\leq 20$ mg per day as a starting dose and adjust doses of fluvastatin based on disease-specific guidelines. If dose  $> 20$ mg needed for desired efficacy, consider an alternative statin or combination therapy.

## Fluvoxamine

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Folic acid

**A** **MTHFR: Normal activity:** Label-recommended dosing and administration.

## Fosphenytoin

**A** **CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Galantamine

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Gefitinib

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Glibenclamide

**C** **G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug may be at risk of severe haemolytic reactions. The warnings and precautions of the summary of product characteristics approved by the U.S. Food and Drug Administration (FDA): "Caution should be used in patients with G6PD deficiency and a non-sulfonylurea alternative should be considered." The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in hemoglobin concentration or erythrocyte count occurs.

**A** **CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Glimepiride

**C** **G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug may be at risk of severe haemolytic reactions. The warnings and precautions of the summary of product characteristics approved by the U.S. Food and Drug Administration (FDA): "Caution should be used in patients with G6PD deficiency and a non-sulfonylurea alternative should be considered." The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in hemoglobin concentration or erythrocyte count occurs.

**A** **CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Glipizide

C

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug may be at risk of severe haemolytic reactions. The warnings and precautions of the summary of product characteristics approved by the U.S. Food and Drug Administration (FDA): "Caution should be used in patients with G6PD deficiency and a non-sulfonylurea alternative should be considered." The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in hemoglobin concentration or erythrocyte count occurs.

## Glyceryl trinitrate

A

**ALDH2: Normal activity:** Label-recommended dosing and administration.

## Govitecan

A

**UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

## Haloperidol

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Halothane

B

**CACNA1S: Uncertain susceptibility to malignant hyperthermia:** No malignant hyperthermia (MH)-causative variants were detected. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): These results do not eliminate the chance that this patient is susceptible to MH. The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown. Clinical findings, family history, further genetic testing, and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants. It should be noted that individuals with muscle diseases caused by, or associated with, genetic abnormalities in RYR1 receptors (or less often the dihydropyridine receptor) should be treated as MH-susceptible and should be managed by the anesthesiologist in consultation with an expert in these rare neuromuscular diseases.

## Hydralazine

B

**NAT2: Slow acetylator:** With this genotype, the acetylation rate of this medication is potentially significantly reduced. This predisposes to higher concentrations of the medication and thus the drug response may be better. On the other hand, the risk for adverse effects is potentially higher.

## Hydrocodone

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Hydroxychloroquine

C

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug may be at risk of severe haemolytic reactions. According to the summary of product characteristics the drug should be administered with caution to patients with G6PD deficiency. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

## Ibuprofen

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Iloperidone

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Imipramine

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Indacaterol

A

**UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

## Irbesartan

**A** **CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Irinotecan

**A** **UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

## Isoflurane

**B** **CACNA1S: Uncertain susceptibility to malignant hyperthermia:** No malignant hyperthermia (MH)-causative variants were detected. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): These results do not eliminate the chance that this patient is susceptible to MH. The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown. Clinical findings, family history, further genetic testing, and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants. It should be noted that individuals with muscle diseases caused by, or associated with, genetic abnormalities in RYR1 receptors (or less often the dihydropyridine receptor) should be treated as MH-susceptible and should be managed by the anesthesiologist in consultation with an expert in these rare neuromuscular diseases.

## Isoniazid

**B** **NAT2: Slow acetylator:** With this genotype, the acetylation rate of this medication is potentially significantly reduced. This predisposes to higher concentrations of the medication and increases its hepatotoxicity risk. In one study, reduction of the standard dose by 50 % in slow acetylator patients reduced the risk of hepatotoxicity.

## Lacosamide

**A** **CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

## Lansoprazole

**B** **CYP2C19: NM Normal metabolizer:** Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of *H. pylori* infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.

## Lesinurad

**A** **CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Levofloxacin

**B** **G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer haemolytic reactions have been reported with levofloxacin in patients with glucose-6-phosphate dehydrogenase deficiency. Levofloxacin should be avoided in these patients unless the potential benefit is considered to outweigh the possible risk. In this case, potential occurrence of haemolysis should be monitored.

## Lidocaine

**C** **G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer, patients with G6PD deficiency are at increased risk for methaemoglobinemia when using the product. If use of product is required in patients with this genotype, close monitoring for symptoms and signs of methaemoglobinemia (shortness of breath, high pulse, cyanosis, or seizures) is recommended.

## Lisdexamfetamine

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Lofexidine

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Loratadine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Lornoxicam

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Losartan

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Lovastatin

A

**SLCO1B1: Normal function:** Typical risk for myopathy and exposure for statins.

Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe desired starting dose and adjust doses based on disease- specific guidelines.

## Lusutrombopag

A

**F2 (prothrombin): No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

A

**F5: No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

## Mafenide

C

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer fatal haemolytic anaemia and disseminated intravascular coagulation have been reported during treatment with this drug. These adverse events are presumably linked to G6PD deficiency

## Meclizine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Meloxicam

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Mepivacaine

C

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer, patients with G6PD deficiency are at increased risk for methaemoglobinemia when using the product. If use of product is required in patients with this genotype, close monitoring for symptoms and signs of methaemoglobinemia (shortness of breath, high pulse, cyanosis, or seizures) is recommended.

## Mercaptopurine

A

**NUDT15: NM Normal metabolizer:**

Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Start with normal starting dose (e.g. 75 mg/m<sup>2</sup>/day or 1.5 mg/kg/day) and adjust doses of mercaptopurine (and of any other myelosuppressive therapy) without any special emphasis on mercaptopurine compared to other agents. Allow at least 2 weeks to reach steady state after each dose adjustment. Note that also TPMT genotype affects the risk for thiopurine-induced adverse reactions. See if TPMT test result is available and treat according to the recommendation for more severe phenotype for either TPMT or NUDT15 gene (e.g. if NUDT15 phenotype is normal and TPMT phenotype is poor metabolizer, treat according to the TPMT poor metabolizer guideline).

A

**TPMT: NM Normal metabolizer:** Start with normal starting dose and adjust doses of mercaptopurine (and of any other myelosuppressive therapy) without any special emphasis on mercaptopurine compared to other agents. Allow 2 weeks to reach steady state after each dose adjustment. Note that also NUDT15 genotype affects the risk for thiopurine-induced adverse reactions. See if NUDT15 test result is available and treat according to the recommendation for more severe phenotype for either TPMT or NUDT15 gene (e.g. if TPMT phenotype is normal and NUDT15 phenotype is poor metabolizer, treat according to the NUDT15 poor metabolizer guideline).

## Methadone

A

**CYP2B6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Methotrexate

A

**MTHFR: Normal activity:** Label-recommended dosing and administration.

A

**SLCO1B1: Normal function:** Label-recommended dosing and administration.

## Methoxyflurane

B

**CACNA1S: Uncertain susceptibility to malignant hyperthermia:** No malignant hyperthermia (MH)-causative variants were detected. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): These results do not eliminate the chance that this patient is susceptible to MH. The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown. Clinical findings, family history, further genetic testing, and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants. It should be noted that individuals with muscle diseases caused by, or associated with, genetic abnormalities in RYR1 receptors (or less often the dihydropyridine receptor) should be treated as MH-susceptible and should be managed by the anesthesiologist in consultation with an expert in these rare neuromuscular diseases.

## Methylthioninium

D

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug are at risk of severe haemolytic reactions. According to the summary of product characteristics the use of the drug is contraindicated in patients with G6PD deficiency.

## Metoclopramide

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Metoprolol

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Mirabegron

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Mirtazapine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Mivacurium

A

**BCHE: Normal activity:** Label-recommended dosing and administration.

## Moclobemide

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

## Modafinil

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Moxifloxacin

B

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer haemolytic reactions have been reported with moxifloxacin in patients with glucose-6-phosphate dehydrogenase deficiency. Moxifloxacin should be avoided in these patients unless the potential benefit is considered to outweigh the possible risk. In this case, potential occurrence of haemolysis should be monitored.

## Nalidixic acid

C

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer haemolytic anaemia is sometimes seen in association with G6DP deficiency during treatment with the drug. Caution should be used in patients with G6PD deficiency.

## Nebivolol

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Nefazodone

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Nevirapine

A

**CYP2B6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Nilotinib

A

**UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

## Nitrofurantoin

D

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug are at risk of moderate to severe haemolytic reactions. According to the summary of product characteristics the use of the drug is contraindicated in patients with G6PD deficiency.

## Norfloxacin

B

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer haemolytic reactions have been reported with norfloxacin in patients with glucose-6-phosphate dehydrogenase deficiency. Norfloxacin should be avoided in these patients unless the potential benefit is considered to outweigh the possible risk. In this case, potential occurrence of haemolysis should be monitored.

## Nortriptyline

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Olanzapine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Oliceridine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration. Note that according to the drug label approved by the U.S. Food and Drug Administration (FDA), in patients taking moderate or strong CYP2D6 inhibitors and/or moderate or strong CYP3A4 inhibitors (or discontinuing CYP3A4 inducers), increased plasma concentrations of oliceridine may occur, which may result in prolonged opioid adverse reactions and exacerbated respiratory depression. These patients may require less frequent dosing, and should be closely monitored for respiratory depression and sedation at frequent intervals. Subsequent doses should be based on the patient's severity of pain and response to treatment.

## Omeprazole

B

**CYP2C19: NM Normal metabolizer:**

Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of *H. pylori* infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.

## Ondansetron

A

**ABCB1: Likely low expression:** Label-recommended dosage. With this genotype, the anti-emetic efficacy of ondansetron is potentially better as compared to other genotypes. This considers especially chemotherapy-induced and post-operative nausea and vomiting in the early phase.

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Oxycodone

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Paliperidone

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Palonosetron

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Pantoprazole

B

**CYP2C19: NM Normal metabolizer:**

Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of *H. pylori* infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.

## Paroxetine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Pazopanib

A

**UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

## Peginterferon alfa-2a

B

**IFNL3: Favorable response genotype:** This genotype is associated with a favorable response of hepatitis C virus (genotype 1) treatment with combination of peginterferon alpha 2 (PEG-IFN alpha) and ribavirin (RBV). According to a recommendation by an international board of experts (Clinical Pharmacogenetics Implementation Consortium) with this genotype there is approximately 70% chance for sustained virologic response after 48 weeks of treatment when treated with combination of PEG-IFN alpha and RBV. Consider implications before initiating PEG-IFN alpha and RBV containing regimens. Additionally, there is approximately 90% chance for sustained virologic response after 24-48 weeks of treatment when treated with combination of PEG-IFN alpha, RBV and protease inhibitor and approximately 80-90% of patients are eligible for shortened therapy (24-28 weeks instead of 48 weeks). This genotype weighs in favor of using PEG-IFN alpha and RBV containing regimens.

## Peginterferon alfa-2b

B

**IFNL3: Favorable response genotype:** This genotype is associated with a favorable response of hepatitis C virus (genotype 1) treatment with combination of peginterferon alpha 2 (PEG-IFN alpha) and ribavirin (RBV). According to a recommendation by an international board of experts (Clinical Pharmacogenetics Implementation Consortium) with this genotype there is approximately 70% chance for sustained virologic response after 48 weeks of treatment when treated with combination of PEG-IFN alpha and RBV. Consider implications before initiating PEG-IFN alpha and RBV containing regimens. Additionally, there is approximately 90% chance for sustained virologic response after 24-48 weeks of treatment when treated with combination of PEG-IFN alpha, RBV and protease inhibitor and approximately 80-90% of patients are eligible for shortened therapy (24-28 weeks instead of 48 weeks). This genotype weighs in favor of using PEG-IFN alpha and RBV containing regimens.

## Pegloticase

D

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer pegloticase is contraindicated in patients with G6PD deficiency due to potentially life-threatening haemolytic reactions and methaemoglobinemia.

## Perphenazine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Phenprocoumon

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

A

**VKORC1: Normal expression:** Label-recommended dosing and administration.

## Phenytoin

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Pimozide

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Pioglitazone

A

**CYP2C8: Normal metabolizer:** Label-recommended dosing and administration.

## Piroxicam

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Pitavastatin

A

**SLCO1B1: Normal function:** Typical risk for myopathy and exposure for statins. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe desired starting dose and adjust doses based on disease- specific guidelines.

## Pitolisant

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Prasugrel

A

**CYP2B6: NM Normal metabolizer:** Label-recommended dosing and administration.

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

A

**CYP3A5: PM Poor metabolizer:** Label-recommended dosing and administration.

## Pravastatin

A

**SLCO1B1: Normal function:** Typical risk for myopathy and exposure for statins.

Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe desired starting dose and adjust doses based on disease- specific guidelines.

## Prilocaine

C

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer, patients with G6PD deficiency are at increased risk for methaemoglobinemia when using the product. If use of product is required in patients with this genotype, close monitoring for symptoms and signs of methaemoglobinemia (shortness of breath, high pulse, cyanosis, or seizures) is recommended.

## Primaquine

D

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug are at risk of moderate to severe haemolytic reactions. According to Guidelines for the Treatment of Malaria by WHO primaquine is contraindicated in patients with G6PD deficiency. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in hemoglobin concentration or leukocyte count occurs.

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Probenecid

C

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer haemolytic anaemia is sometimes seen in association with G6DP deficiency during treatment with the drug. Caution should be used in patients with G6PD deficiency.

## Propafenone

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Propranolol

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Protriptyline

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Quetiapine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Quinidine

B

**CYP2D6: NM Normal metabolizer:** Quinidine is a potent inhibitor of CYP2D6 enzyme, effectively turning normal metabolizers to poor metabolizers of CYP2D6 substrates, which should be taken into consideration when administered concomitantly with other drugs metabolized by CYP2D6.

## Quinine

D

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug are at risk of moderate to severe haemolytic reactions. According to the summary of product characteristics the use of the drug is contraindicated in patients with G6PD deficiency.

## Rabeprazole

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

## Raltegravir

A

**UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

## Ranolazine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Rasburicase

D

**G6PD: G6PD deficient:** According to the summary of product characteristics the use of the drug is contraindicated in patients with G6PD deficiency. Patients with G6PD deficiency who are treated with the drug are at risk of moderate to severe haemolytic reactions. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Using the drug is contraindicated; alternatives include allopurinol.

## Ribavirin

B

**IFNL3: Favorable response genotype:** This genotype is associated with a favorable response of hepatitis C virus (genotype 1) treatment with combination of peginterferon alpha 2 (PEG-IFN alpha) and ribavirin (RBV). According to a recommendation by an international board of experts (Clinical Pharmacogenetics Implementation Consortium) with this genotype there is approximately 70% chance for sustained virologic response after 48 weeks of treatment when treated with combination of PEG-IFN alpha and RBV. Consider implications before initiating PEG-IFN alpha and RBV containing regimens. Additionally, there is approximately 90% chance for sustained virologic response after 24-48 weeks of treatment when treated with combination of PEG-IFN alpha, RBV and protease inhibitor and approximately 80-90% of patients are eligible for shortened therapy (24-28 weeks instead of 48 weeks). This genotype weighs in favor of using PEG-IFN alpha and RBV containing regimens.

## Rimegepant

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Risperidone

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Romiplostim

**A** **F2 (prothrombin): No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

**A** **F5: No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

## Ropivacaine

**C** **G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer, patients with G6PD deficiency are at increased risk for methaemoglobinemia when using the product. If use of product is required in patients with this genotype, close monitoring for symptoms and signs of methaemoglobinemia (shortness of breath, high pulse, cyanosis, or seizures) is recommended.

## Rosiglitazone

**A** **CYP2C8: Normal metabolizer:** Label-recommended dosing and administration.

## Rosuvastatin

**A** **ABCG2: Normal function:** Patients with this genotype have typical myopathy risk and rosuvastatin exposure. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe desired starting dose and adjust doses of rosuvastatin based on disease-specific and specific population guidelines. Check also if SLCO1B1 phenotype is available. If SLCO1B1 phenotype is decreased function or possible decreased function, the prescriber should be aware of possible increased risk for myopathy especially for doses > 20mg. If SLCO1B1 phenotype is poor function, prescribe ≤20mg as a starting dose and adjust doses of rosuvastatin based on disease-specific and specific population guidelines. If dose > 20mg needed for desired efficacy, consider combination therapy.

**A** **SLCO1B1: Normal function:** Typical risk for myopathy and exposure for statins. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe desired starting dose and adjust doses based on disease-specific guidelines. Check also if ABCG2 phenotype is available. If ABCG2 phenotype is poor function, prescribe ≤20mg as a starting dose and adjust doses of rosuvastatin based on disease-specific and specific population guidelines. If dose >20mg needed for desired efficacy, consider an alternative statin or combination therapy.

## Rucaparib

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Sacituzumab govitecan

**A** **UGT1A1: NM Normal metabolizer:** Label-recommended dosing and administration.

## Sertindole

**A** **CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Sertraline

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

## Sevoflurane

B

**CACNA1S: Uncertain susceptibility to malignant hyperthermia:** No malignant hyperthermia (MH)-causative variants were detected. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): These results do not eliminate the chance that this patient is susceptible to MH. The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown. Clinical findings, family history, further genetic testing, and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants. It should be noted that individuals with muscle diseases caused by, or associated with, genetic abnormalities in RYR1 receptors (or less often the dihydropyridine receptor) should be treated as MH-susceptible and should be managed by the anesthesiologist in consultation with an expert in these rare neuromuscular diseases.

## Simeprevir

A

**IFNL3: Favorable response genotype:** According to the summary of product characteristics provided by the manufacturer, this genotype is associated with favourable hepatitis C (genotypes 1) treatment response when treating treatment-naïve patients with combination of simeprevir, ribavirin, and peginterferon-alfa. Sustained virological response was achieved in 95 % of patients with this genotype compared to 61 % homozygous for unfavourable response genotype.

## Simvastatin

A

**CYP3A4: NM Normal metabolizer:** Label-recommended dosing and administration.

A

**SLCO1B1: Normal function:** Typical risk for myopathy and exposure for statins. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe desired starting dose and adjust doses based on disease- specific guidelines.

## Siponimod

D

**CYP2C9: NM Normal metabolizer (Activity score 2):** According to the summary of product characteristics or drug label, after treatment titration, with this genotype the recommended maintenance dosage is 2 mg taken orally once daily starting on day 6. Note also the potential effect of inducers and inhibitors of CYP3A4 and/or CYP2C9 (see drug label or summary of product characteristics for details).

## Sodium nitrite

C

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug may be at risk of severe haemolytic reactions. According to the summary of product characteristics provided by the manufacturer alternative therapeutic approaches should be considered. Patients with known or suspected G6PD deficiency should be monitored for acute drop in haematocrit. Exchange transfusion might be needed in G6PD deficient patients receiving sodium nitrite.

## Sofosbuvir

A

**IFNL3: Favorable response genotype:** According to the summary of product characteristics provided by the manufacturer, this genotype is associated with favourable hepatitis C (genotypes 1 and 4) treatment response when treating treatment-naïve patients with combination of sofosbuvir, ribavirin, and peginterferon-alfa for 12 weeks. Sustained virological response was achieved in 99 % of patients.

## Sulfadiazine

D

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug (orally or topically) are at risk of moderate to severe haemolytic reactions. According to the summary of product characteristics the use of the drug (orally) is contraindicated in patients with G6PD deficiency.

## Sulfamethoxazole

C

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug may be at risk of severe haemolytic reactions. The warnings and precautions of the summary of product characteristics approved by the U.S. Food and Drug Administration (FDA): "In glucose-6-phosphate dehydrogenase deficient individuals, hemolysis may occur. This reaction is frequently dose-related." Be alert to adverse effects. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in hemoglobin concentration or erythrocyte count occurs.

B

**NAT2: Slow acetylator:** With this genotype, the acetylation rate of this medication is potentially significantly reduced. This predisposes to higher concentrations of the medication and increases the risk for adverse effects (e.g. rash, hepatic impairment, Stevens-Johnson syndrome).

## Sulfasalazine

C

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug may be at risk of severe haemolytic reactions. According to the summary of product characteristics provided by the manufacturer patients with G6PD deficiency should be monitored closely for signs of haemolytic anaemia. The reaction is often dose-related.

B

**NAT2: Slow acetylator:** With this genotype, the acetylation rate of this medication is potentially significantly reduced. This predisposes to higher concentrations of the medication and increases the risk for adverse effects.

## Sulfisoxazole

C

**G6PD: G6PD deficient:** Haemolytic anaemia has been described in patients with G6PD deficiency during sulfisoxazole treatment. A still birth of G6PD deficient foetus with signs of haemolysis has been reported after sulfisoxazole use during third trimester in G6PD deficient mother. Alternative therapeutic approaches to sulfisoxazole are recommended.

## Suxamethonium

B

**CACNA1S: Uncertain susceptibility to malignant hyperthermia:** No malignant hyperthermia (MH)-causative variants were detected. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): These results do not eliminate the chance that this patient is susceptible to MH. The genetic cause of about half of all MH survivors, with MH susceptibility confirmed by contracture test, remains unknown. Clinical findings, family history, further genetic testing, and other laboratory data should guide use of halogenated volatile anesthetics or depolarizing muscle relaxants. It should be noted that individuals with muscle diseases caused by, or associated with, genetic abnormalities in RYR1 receptors (or less often the dihydropyridine receptor) should be treated as MH-susceptible and should be managed by the anesthesiologist in consultation with an expert in these rare neuromuscular diseases.

A

**BCHE: Normal activity:** Label-recommended dosing and administration.

## Synthetic conjugated estrogens

A

**F2 (prothrombin): No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

A

**F5: No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

## Tacrolimus

A

**CYP3A5: PM Poor metabolizer:** Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): In patients with this genotype, starting dose of tacrolimus is normal, mentioned in summary of product characteristics. Do further dose adjustments according to therapeutic drug monitoring. Note! This recommendation concerns those liver transplant recipients, whose donor's genotype is identical with recipient's genotype.

## Tafenoquine

D

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer use of drug is contraindicated in patients with G6PD deficiency due to potentially life-threatening haemolytic reactions.

## Tamoxifen

A

**CYP2D6: NM Normal metabolizer:**

Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Initiate therapy with recommended standard of care dosing (tamoxifen 20 mg/day). Avoid moderate and strong CYP2D6 inhibitors.

A

**F2 (prothrombin): No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

A

**F5: No increased risk of venous thromboembolism:**

Label-recommended dosing and administration.

## Tamsulosin

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Tegafur

A

**DPYD: NM Normal metabolizer:** Normal dihydropyrimidine dehydrogenase activity and no increased risk for fluoropyrimidine toxicity. Label-recommended dosage.

## Telaprevir

B

**IFNL3: Favorable response genotype:** This genotype is associated with a favorable response of hepatitis C virus (genotype 1) treatment with combination of peginterferon alpha 2 (PEG-IFN alpha) and ribavirin (RBV). According to a recommendation by an international board of experts (Clinical Pharmacogenetics Implementation Consortium) with this genotype there is approximately 70% chance for sustained virologic response after 48 weeks of treatment when treated with combination of PEG-IFN alpha and RBV. Consider implications before initiating PEG-IFN alpha and RBV containing regimens. Additionally, there is approximately 90% chance for sustained virologic response after 24-48 weeks of treatment when treated with combination of PEG-IFN alpha, RBV and protease inhibitor and approximately 80-90% of patients are eligible for shortened therapy (24-28 weeks instead of 48 weeks). This genotype weighs in favor of using PEG-IFN alpha and RBV containing regimens.

## Tenoxicam

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Terbinafine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Tetrabenazine

D

**CYP2D6: NM Normal metabolizer:** According to the U.S. Food and Drug Administration (FDA), with this genotype the dosing is as follows: At doses under 50 mg per day: The starting dose should be 12.5 mg per day given once in the morning. After one week, the dose should be increased to 25 mg per day given as 12.5 mg twice a day. The dose should be titrated up slowly at weekly intervals by 12.5 mg, to allow the identification of a dose that reduces chorea and is well tolerated. If a dose of 37.5 to 50 mg per day is needed, it should be given in a three times a day regimen. The maximum recommended single dose is 25 mg. At doses above 50 mg per day: The dose should be titrated up slowly at weekly intervals by 12.5 mg, to allow the identification of a dose that reduces chorea and is well tolerated. Doses above 50 mg per day should be given in a three times a day regimen. The maximum recommended daily dose is 100 mg and the maximum recommended single dose is 37.5 mg.

## Tetracaine

C

**G6PD: G6PD deficient:** According to the summary of product characteristics provided by the manufacturer, patients with G6PD deficiency are at increased risk for methaemoglobinemia when using the product. If use of product is required in patients with this genotype, close monitoring for symptoms and signs of methaemoglobinemia (shortness of breath, high pulse, cyanosis, or seizures) is recommended.

A

**BCHE: Normal activity:** Label-recommended dosing and administration.

## Thioguanine

A

**NUDT15: NM Normal metabolizer:**

Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Start with normal starting dose (40-60 mg/m<sup>2</sup>/day). Adjust dosing every two weeks without any special emphasis on thioguanine. Allow 2 weeks to reach steady-state after each dose adjustment. Note that also TPMT genotype affects the risk for thiopurine-induced adverse reactions. See if TPMT test result is available and treat according to the recommendation for more severe phenotype for either TPMT or NUDT15 gene (e.g. if NUDT15 phenotype is normal and TPMT phenotype is poor metabolizer, treat according to the TPMT poor metabolizer guideline).

A

**TPMT: NM Normal metabolizer:** Start with normal starting dose. Adjust doses of thioguanine and of other myelosuppressive therapy without any special emphasis on thioguanine. Allow 2 weeks to reach steady state after each dose adjustment. Note that also NUDT15 genotype affects the risk for thiopurine-induced adverse reactions. See if NUDT15 test result is available and treat according to the recommendation for more severe phenotype for either TPMT or NUDT15 gene (e.g. if TPMT phenotype is normal and NUDT15 phenotype is poor metabolizer, treat according to the NUDT15 poor metabolizer guideline).

## Thioridazine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Tibolone

A

**F2 (prothrombin): No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

A

**F5: No increased risk of venous thromboembolism:** Label-recommended dosing and administration.

## Ticagrelor

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

## Tolazamide

C

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug may be at risk of severe haemolytic reactions. The warnings and precautions of the summary of product characteristics approved by the U.S. Food and Drug Administration (FDA): "Caution should be used in patients with G6PD deficiency and a non-sulfonylurea alternative should be considered." The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in hemoglobin concentration or erythrocyte count occurs.

## Tolbutamide

C

**G6PD: G6PD deficient:** Patients with G6PD deficiency who are treated with the drug may be at risk of severe haemolytic reactions. The warnings and precautions of the summary of product characteristics approved by the U.S. Food and Drug Administration (FDA): "Caution should be used in patients with G6PD deficiency and a non-sulfonylurea alternative should be considered." The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in hemoglobin concentration or erythrocyte count occurs.

A

**CYP2C9: NM Normal metabolizer (Activity score 2):** Label-recommended dosing and administration.

## Tolterodine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Tramadol

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Trimipramine

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Tropisetron

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Umeclidinium

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Upadacitinib

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Valbenazine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration. A clinically relevant QT prolongation may occur in some patients treated with valbenazine who are co-administered a strong CYP2D6 inhibitor.

## Venlafaxine

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Vincristine

B

**CYP3A5: PM Poor metabolizer:** Label-recommended dosing and administration. With this genotype the metabolism vincristine is potentially reduced and thus the risk of drug-induced neurotoxicity increased. Scientific evidence of this is inconsistent, though.

## Voriconazole

A

**CYP2C19: NM Normal metabolizer:** Label-recommended dosing and administration.

## Vortioxetine

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## Warfarin

C

**CYP2C9: NM Normal metabolizer (Activity score 2):** Warfarin dosing is potentially benefited by use of a dosing algorithm which includes genotype information. For the use of algorithm, check the patient's detailed genotype from the gene test report. Recommendation for patients of non-african ancestry: Calculate a dose estimate using the algorithm available at [www.warfarindosing.org](http://www.warfarindosing.org) using the CYP2C9, CYP4F2 and VKORC1 genotype information. If the patient is a carrier of CYP2C9\*8 or \*11 variant alleles (not considered in the calculator), decrease the calculated dose by 15-30%. Recommendation for patients of african ancestry: Calculate a dose estimate using the algorithm available at [www.warfarindosing.org](http://www.warfarindosing.org) using the CYP2C9 and VKORC1 genotype information. If the patient is a carrier of CYP2C9\*8 or \*11 variant alleles (not considered in the calculator), decrease the calculated dose by 15-30%. If the patient has not been tested for CYP2C9\*5, \*6, \*8 or \*11 alleles, dose clinically. Additionally, if the patient is of African American ancestry and rs12777823 gene test has been made, decrease dose by 10-25% if the patient is a carrier of A allele. Recommendation for pediatric patients: If the patient is of European ancestry, use the dose calculation application (available at <http://www.warfarindoserevision.com>) which takes CYP2C9 and VKORC1 genotypes in consideration. Otherwise dose clinically.

C

**VKORC1: Normal expression:** Warfarin dosing is potentially benefited by use of a dosing algorithm which includes genotype information. For the use of algorithm, check the patient's detailed genotype from the gene test report. Recommendation for patients of non-african ancestry: Calculate a dose estimate using the algorithm available at [www.warfarindosing.org](http://www.warfarindosing.org) using the CYP2C9\*2 and \*3 and VKORC1 genotype information. If the patient is a carrier of CYP2C9\*5, \*6, \*8 or \*11 variant alleles, decrease the calculated dose by 15-30%. If the patient is a carrier of rs2108622 variant T allele of CYP4F2 gene, increase the calculated dose by 5-10%. Recommendation for patients of african ancestry: Calculate a dose estimate using the algorithm available at [www.warfarindosing.org](http://www.warfarindosing.org) using the CYP2C9\*2 and \*3 and VKORC1 genotype information. If the patient is a carrier of CYP2C9\*5, \*6, \*8 or \*11 variant alleles, decrease the calculated dose by 15-30%. If the patient has not been tested for CYP2C9\*5, \*6, \*8 or \*11 alleles, dose clinically. Additionally, if the patient is of African American ancestry and rs12777823 gene test has been made, decrease dose by 10-25% if the patient is a carrier of A allele. Recommendation for pediatric patients: If the patient is of European ancestry, use the dose calculation application (available at <http://www.warfarindoserevision.com>) which takes CYP2C9 and VKORC1 genotypes in consideration. Otherwise dose clinically.

A

**CYP2C rs12777823: Normal warfarin dosing:** Warfarin dosing is potentially benefited by use of a dosing algorithm which includes genotype information. See separate recommendations for CYP2C9, VKORC1 and CYP4F2 genes. With this CYP2C rs12777823 genotype, there's no need for further changes in warfarin dosing.

A

**CYP4F2: Normal metabolizer:** Warfarin dosing is potentially benefited by use of a dosing algorithm which includes genotype information. See separate recommendations for CYP2C9 and VKORC1 genes and CYP2C rs12777823 variant. With this CYP4F2 genotype, there's no need for further changes in warfarin dosing.

## Zuclopentixol

A

**CYP2D6: NM Normal metabolizer:** Label-recommended dosing and administration.

## 7. Gene-specific results and their predicted phenotypes

### Drug safety and efficacy (ABCB1)

ABCB1 gene encodes the P-glycoprotein (P-gp) which is a key cell membrane transporter. P-gp acts as a protective factor in several interfaces of organ systems (including the gut, the bile canaliculi and the blood-brain barrier) where it restricts the compounds entry and therefore affects the drug concentrations. P-gp activity is significantly affected by drugs which inhibit (e.g. atorvastatin, quinidine) or induce it (e.g. rifampin, carbamazepine). There are several known very common variants of the gene, but their effect on drug concentrations and responses are controversial in different studies. Other drugs affecting the activity of P-gp seem to be more significant factors in P-gp-related drug responses.

LOW	HIGH(HETEROZ)	HIGH(HOMOZ)
-----	---------------	-------------

#### Likely low expression

WT/WT

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

### Drug safety and efficacy (ABCG2)

ABCG2 gene encodes a cell membrane protein which transports several molecules, including drugs, across the cell membrane. The drugs transported by ABCG2 partially overlap with those transported by P-glycoprotein. In terms of pharmacogenetics, the frequency of two best characterised variant alleles is approximately 6-12% in Europeans. Variants in the gene affect e.g. pharmacokinetics of rosuvastatin, atorvastatin and allopurinol.

POOR	DECREASED	NORMAL
------	-----------	--------

#### Normal function

WT/WT

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (ALDH2)

Mitochondrial Aldehyde dehydrogenase enzyme oxidizes aldehydes to corresponding carboxylic acids. The function of the enzyme may be deficient due to genetic variation which manifests for example as intoxication symptoms after consumption of alcohol as acetaldehyde metabolite accumulates. Most Europeans have two major isozymes, while approximately 50% of Northeast Asians have one normal copy of the ALDH2 gene and one variant copy that encodes an inactive mitochondrial isoenzyme. The insufficient activity may also decrease the efficacy of glyceryl trinitrate used.

NORMAL	DECREASED	POOR
--------	-----------	------

### Normal activity

\*1/\*1

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (BCHE)

Butyrylcholinesterase (BCHE) also known as plasma cholinesterase and pseudocholinesterase is a nonspecific cholinesterase enzyme and it is very similar to the acetylcholinesterase. Over 60 single nucleotide polymorphisms (SNPs) in the BCHE gene have been reported. Butyrylcholinesterase deficiency is significant only when present in homozygous form, which occurs in approximately one in 2500 patients. Pseudocholinesterase deficiency results in delayed metabolism of only a few compounds of clinical significance, including succinylcholine, mivacurium and cocaine. The clinically most important substrate of these is the depolarizing neuromuscular blocking agent, succinylcholine (suxamethonium), which the BCHE enzyme hydrolyses to inactive metabolites. Genetic variants that impair the BCHE enzyme activity can be divided into two groups. The other variants affect the substrate affinity of the enzyme and the other variants affect the amount of the enzyme without affecting the substrate affinity. Both types of variants increase the patient's risk of prolonged apnea when using succinylcholine, but the duration of the apnea depends on the type and the number of variants present.

NORMAL	DECREASED	POOR
--------	-----------	------

### Normal activity

WT/WT

Analyzed 3 of 3 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (CACNA1S)

CACNA1S is a gene which encodes the alpha1 S subunit of the dihydropyridine receptor, expressed in the sarcoplasmic reticulum membrane of muscle cells. It activates the RYR1 calcium channel during membrane depolarization in contracting myocytes. Genetic variants of CACNA1S predispose to malignant hyperthermia, a potentially life-threatening state caused by halogenated volatile anesthetics (e.g. sevoflurane, enflurane, halothane) and depolarizing muscle relaxant suxamethonium (or succinylcholine). Symptoms of malignant hyperthermia include e.g. muscle rigidity, masseter spasm, tachycardia, arrhythmias, acidosis and hyperthermia. These agents used in anesthesia should be avoided in patients known to carry these variants. Prevalence of the genetic trait predisposing to malignant hyperthermia is approximately 1/2,000-1/3,000 and the state occurs in 1/10,000-1/250,000 anesthesias. It is good to notice that also variants in RYR1 gene predispose to malignant hyperthermia.

NORMAL	SUSCEPTIBLE	UNKNOWN
--------	-------------	---------

### Uncertain susceptibility to malignant hyperthermia

WT/WT

Analyzed 2 of 2 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (CYP1A2)

CYP1A2 is a hepatic enzyme which mediates metabolism of several drugs, caffeine and procarcinogens. Smoking, certain drugs and other exposures induce the expression of the enzyme. There is some genetic variation concerning CYP1A2, and due to this the speed of metabolism or the inducibility of the enzyme in an individual may be altered. This affects the efficacy of certain drugs. Environmental and drug exposures are likely more important factors altering the enzyme activity, though.

PM	IM	NM	HIGH
----	----	----	------

### IM Intermediate metabolizer

\*1C/\*1F

Analyzed 5 of 5 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (CYP2B6)

CYP2B6 is a hepatic enzyme that is responsible for the metabolism of HIV and cancer drugs as well as bupropion. There is genetic variation in the enzyme activity but there is no wide, coherent scientific evidence of the association between the variation and drug metabolism. The evidence is strongest for certain HIV drugs.

UM	RM	NM	IM	PM
----	----	----	----	----

### NM Normal metabolizer

\*1/\*1

Analyzed 5 of 5 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (CYP2C rs12777823)

CYP2C rs12777823 G>A is a genetic variant which is associated with lower warfarin doses in the African American population (approximately 10 - 25% lower doses than in non-carriers). The variant is located in the CYP2C gene cluster in chromosome 10.

NORMAL

DECREASED

### Normal warfarin dosing

G/G

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (CYP2C19)

CYP2C19 is a hepatic enzyme which mediates metabolism of several drugs. Drugs metabolized by it include e.g. psychotropic drugs and gastric acid pump blockers, and among the most important, drugs which prevent blood platelets from aggregating and thus from causing arterial blocks (clopidogrel, ticagrelor, prasugrel). There is genetic variation concerning CYP2C19, and due to this the speed of metabolism of the enzyme in an individual can be faster or slower than average. This either increases or decreases efficacy of different drugs. Frequencies of genotypes in different populations are dependent on ethnic background, and the variation of frequency for CYP2C19 genotypes is from a few percent to half of a population.

PM LPM IM LIM NM RM UM

### NM Normal metabolizer

\*1/\*1

Analyzed 5 of 5 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (CYP2C8)

CYP2C8 is a hepatic enzyme which mediates metabolism of several drugs. Drugs metabolized by it include e.g. antidiabetics, statins, pain medications and cancer therapeutics. There is genetic variation concerning CYP2C8, and due to this the speed of metabolism of the enzyme in an individual can be faster or slower than average. This either increases or decreases efficacy of different drugs. The effect of certain genotypes on metabolism depends on substrate which means that the same genotype may cause opposite effects on the metabolism rate of different drugs. Frequencies of genotypes in different populations are dependent on ethnic background, and the variation of frequency for CYP2C8 genotypes is from under one percent to tens of percents.

NM VM LDM

### Normal metabolizer

\*1/\*1

Analyzed 3 of 3 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (CYP2C9)

CYP2C9 is a hepatic enzyme which mediates metabolism of several drugs, including warfarin, phenytoin and NSAIDs. There is genetic variation concerning CYP2C9, and due to this the speed of metabolism of the enzyme in an individual can be slower than average. This potentially increases efficacy of certain drugs and may increase the risk of adverse effects. Altered alleles \*2 and \*3 of CYP2C9 gene are the most frequent and the most important functionally. They are shown to be linked to decreased enzymatic activity, slower metabolism and thus decreased required doses of certain drugs. In non-caucasian populations additional alleles, such as \*5, \*6, \*8 and \*11, are frequent and affect the enzyme activity significantly.

PM AS0 PM AS05 IM AS1 **NM AS2**

### NM Normal metabolizer (Activity score 2)

Activity score: **2**

\*1/\*1

Analyzed 7 of 7 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (CYP2D6)

CYP2D6 is a hepatic enzyme that is responsible for the metabolism of many pharmaceuticals. These include several antidepressants and pain medications, for example. There is genetic variation concerning CYP2D6, and due to this the speed of metabolism of the enzyme in an individual can be faster or slower than average. This either increases or decreases efficacy of different drugs, which alters the needed doses between individuals.

PM IM **NM** UM

### NM Normal metabolizer

Activity score: **2**

\*1/\*1

Analyzed 21 of 21 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (CYP3A4)

CYP3A4 is a hepatic enzyme which mediates metabolism of more drugs than any other human enzyme. Several drugs inhibit the activity or increase the expression of the enzyme. There is some genetic variation concerning CYP3A4, and due to this the speed of metabolism of the enzyme in an individual may be altered. This increases or decreases the efficacy of certain drugs. CYP3A4 and closely related CYP3A5 have some common substrates. The combined metabolism of these enzymes may define the speed of metabolism of certain drugs better than that of CYP3A4 alone.

**NM** IM PM

### NM Normal metabolizer

\*1/\*1

Analyzed 4 of 4 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (CYP3A5)

CYP3A5 is a hepatic enzyme that is responsible for the metabolism of many pharmaceuticals. The most important of these is tacrolimus. Due to genetic variation concerning CYP3A5 the speed of metabolism of the enzyme varies. The majority of people of European ancestry are poor CYP3A5 metabolizers. This alters the needed doses of certain drugs between individuals.



### PM Poor metabolizer

\*3/\*3

Analyzed 4 of 4 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (CYP4F2)

People fall into different categories according to CYP4F2 genotype. Genotype information is potentially helpful when predicting warfarin dose.



### Normal metabolizer

\*1/\*1

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (DPYD)

Dihydropyrimidine dehydrogenase (DPD) is a key enzyme catabolizing fluoropyrimidines, which are used as chemotherapeutics for various types of cancer. Due to genetic variation concerning DPYD, the gene encoding DPD, the speed of metabolism of the enzyme varies between individuals. DPD-deficient patients are in greater risk for adverse effects of fluoropyrimidines.



### NM Normal metabolizer

Activity score: 2

WT/WT

Analyzed 10 of 10 single nucleotide polymorphisms (SNP).

## Blood coagulation factor II (F2, prothrombin)

Occurrence of venous thromboembolic events is mediated by both hereditary and acquired risk factors. The most common reasons for dominantly inherited propensity for thrombotic events are point mutations in two genes encoding blood coagulation factors: factor V (F V) and factor II (prothrombin, FII). The mutation in prothrombin gene is the second most common genetic error after F V gene error predisposing to thrombotic events. Prothrombin, the precursor of thrombin, is a key enzyme involved in coagulation cascade. Thrombin transforms soluble fibrinogen to fibrin which forms the clot. It also activates thrombocytes. The point mutation in the prothrombin gene causes elevated levels of prothrombin in the plasma and thus advances the propensity for thrombotic events. The mutation is significantly more common in patients with venous thromboembolism than in normal population.

Appearance of the prothrombin mutation together with some other factor predisposing to thromboembolism increases the patients risk for thrombotic event.

NORMAL

RISK

HIGHRISK

### No increased risk of venous thromboembolism

WT/WT

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

## Blood coagulation factor V (F5 Leiden)

Occurrence of venous thromboembolic events is mediated by both hereditary and acquired risk factors. The most common reasons for dominantly inherited propensity for thrombotic events are point mutations in two genes encoding blood coagulation factors: factor V (F V) and factor II (prothrombin, FII). Resistance to activated protein C (APCR), which means the inability of protein C to degrade activated clotting factor V, occurs due to so called Leiden mutation in the gene encoding F V. It is over tenfold more common than any other known hereditary factor predisposing to clotting. Depending on experiment sample, frequency of APCR is between 21-60% in patients with venous thrombotic event, and between only 3-7% in control patients. Classic risk factor including surgery, fracture, severe infection, oral contraception, pregnancy and childbirth increase the risk for venous thrombosis.

NORMAL

RISK

HIGHRISK

### No increased risk of venous thromboembolism

WT/WT

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (G6PD)

Deficiency of glucose-6-phosphate dehydrogenase (G6PD) is an inherited enzyme defect which causes haemolytic anemia either continuously or under certain exposures (certain drugs, nutritional compounds or infections). A key compound produced by the enzyme protects erythrocytes from oxidative stress, and its significance is emphasized under circumstances where red blood cells are under unusually heavy oxidation. As oxidation increases, erythrocytes are broken up, i. e. hemolyzed. In some patients there is insufficient production of the enzyme and in some patients the enzyme is not active enough. The gene for this recessively inherited disease is located on the X chromosome, and thus the condition occurs mainly in men or boys, as females are normally asymptomatic. G6PD deficiency is the most common human enzyme defect, being present in more than 400 million people worldwide. More than 400 variations of the G6PD enzyme have been found. Severe G6PD deficiency appears in Mediterranean countries, Middle East and Asia, and milder forms in Africa. In populations of European descent the deficiency is rare. Even if G6PD deficiency wouldn't have been detected by a genetic test, it is however possible for the patient to have G6PD deficiency due to deficient variants not included in the genetic test. Therefore, the G6PD activity can only be fully ascertained with a phenotyping test (i.e. measurement of the enzyme activity) in patients with normal genotype.

NORMAL	DEFICIENT	CNSHA	VARIABLE
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### G6PD deficient

Can/Can

Analyzed 9 of 9 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (GRIK4)

Gene GRIK4 encodes a kainate receptor, a subtype of glutamate receptor. The receptor contributes to glutamatergic signalling. Glutamate is the major excitatory neurotransmitter in the central nervous system. Antidepressant treatment results in part in a correction of glutamate imbalance. A single nucleotide polymorphism in GRIK4 has been shown to be associated with decreased response to antidepressant therapy.

POOR(HOMOZ)	POOR(HETEROZ)	HIGH
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### Poor responder (homozygous)

T/T

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (IFNL3)

IFNL3 or IL28B gene encodes interferon lambda 3 which is a protein involved in immune reactions, triggered e.g. by virus infections. There are common genetic variants in this gene or its surroundings. They are the strongest predictors of the efficacy of hepatitis C virus (HCV) therapies with peginterferon alpha (PEG-IFN alpha) and ribavirin (RBV) alone or combined with protease inhibitors. These combination therapies last several months and produce a lot of adverse effects. Therefore, before initiating the treatment, it is necessary to consider the probability of treatment failure and other factors of the patient which may alter the outcome. The outcome is also dependent on the genotype of HCV itself, and the medication recommendations related to IFNL3 variation pertain especially to virus genotype I.

FAVOURABLE

UNFAVOURABLE

### Favorable response genotype

WT/WT

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (MTHFR)

MTHFR gene encodes the methylenetetrahydrofolate reductase enzyme which is critical for folate metabolism. It affects methylation and DNA synthesis pathways by reducing 5,10-methylenetetrahydrofolate (MTHF) to 5-methyltetrahydrofolate. 5-MTHF is used as a substrate for conversion of homocysteine to methionine which is subsequently used in methylation reactions. 5,10-MTHF is used in de novo purine synthesis. Several common genetic variants in the gene are characterized. Certain genetic variants decrease the enzyme activity of MTHFR which potentially affects outcome or adverse effects of e.g. antirheumatic and antineoplastic drugs, such as methotrexate, which target the DNA synthesis pathways. Associations between genetic variants of MTHFR and risk for cardiovascular diseases, Alzheimer disease, neural tube defects and cancer have been described but their scientific validity and reproducibility is low so far.

NORMAL

DECREASED

### Normal activity

WT/WT

Analyzed 2 of 2 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (NAT2)

Arylamine N-acetyltransferase 2 (NAT2) is an enzyme which acetylates and thus often detoxifies several foreign compounds. Partly, it also activates and generates certain carcinogens and its activity may thus have association to cancer risk (e.g. prostate or colorectal cancer). Evidence for these associations is however inconsistent. NAT2 is most prominently expressed in the liver and intestines. Several genetic variants in NAT2 gene have been described and their effect on the acetylation activity of the enzyme are varying. Acetylation and subsequent excretion of certain medications, e.g. isoniazide and hydralazine, are affected by the genetic variations of NAT2. Dose alterations may be warranted in patients carrying variants which slow down the NAT2 acetylation.

SA

IA

RA

### Slow acetylator

\*5/\*16

Analyzed 6 of 6 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (NFIB)

NFIB gene encodes a transcription factor which is expressed in many tissues. The gene is located in short arm of chromosome 9. Copy-number variants located in this region cause MACID syndrome (macrocephaly and impaired intellectual development). Variants within NFIB gene have been linked to clozapine metabolism. Individuals carrying rs28379954-C variant had clozapine concentration more likely below 300 nmol/l compared to wild-type (12.0% vs. 6.2%). The variant explained 7.6% of variation in clozapine concentration. The prevalence of the variant is 4.8% in non-Finnish Europeans.

NORMAL

RAPID

ULTRARAPID

### Normal metabolizer

WT/WT

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (NUDT15)

NUDT15 encodes nucleoside diphosphatase enzyme which converts metabolites which converts thiopurine drug metabolites to less cytotoxic form. The R139C variant (rs116855232; c.415C>T) was the first variant which was linked to increased thiopurine toxicity, leading to increased risk for thiopurine-induced bone marrow failure. Since then, additional variants from NUDT15 gene have been identified, some of which have resulted in decreased enzyme activity in vitro. Currently, the evidence from other variants than R139C is too weak to give treatment recommendations. Based on gnomAD data, the frequency of R139C variant allele in Europeans is 0.7% and in Eastern Asians 9%. Thiopurine drug metabolism is also affected by TPMT gene.

NM	IM	PM	UNKNOWN
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### NM Normal metabolizer

\*1/\*1

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (SLCO1B1)

OATP1B1 protein, which is encoded by SLCO1B1 gene, facilitates the hepatic uptake of several drugs, including statins from the plasma. Decreased transport function of the protein, caused by genetic variation, leads to accumulation of statins in the plasma and increases the risk for myopathy. The risk is especially related to simvastatin. There are also potential associations with other statins and the muscle toxicity and the size of the dose is also crucial: the higher the statin dose the greater the myopathy risk. The variation potentially affects certain other drugs also, such as methotrexate.

INCREASED	NORMAL	DECREASED	POOR	POSDECR
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### Normal function

\*1/\*14

Analyzed 4 of 4 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (TPMT)

Thiopurine methyltransferase (TPMT) is an enzyme responsible for the metabolism of thiopurine drugs (azathioprine, mercaptopurine and thioguanine). Approximately 0.3 % of the patients have inherited low enzyme activity of TPMT, which predisposes to adverse effects of these drugs (myelosuppression, pancytopenia and possible secondary malignancies). By adjusting the patient's thiopurine dose according to his/her TPMT activity, adverse effects may be avoided. Enzyme activity can be genetically determined.

NM	IM	PM	LIM
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### NM Normal metabolizer

\*1/\*1

Analyzed 7 of 7 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (UGT1A1)

UGT1A1 gene encodes the UDP-glucuronosyltransferase 1-1 enzyme which is responsible for elimination of certain drugs and bilirubin. It is also responsible for glucuronidation of the active metabolite of an anticancer drug irinotecan/CPT-11 and thus elimination of it. Using irinotecan in combination with poor UGT1A1 metabolism may lead to haematological or gastrointestinal adverse effects. Additionally, the development of hyperbilirubinemia during treatment with inhibitors of UGT1A1, such as atazanavir, has also been linked to poor UGT1A1 metabolizer phenotype. Evolving jaundice may cause early discontinuation of the causing drug.

PM	IM	NM
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### NM Normal metabolizer

\*1/\*1

Analyzed 4 of 4 single nucleotide polymorphisms (SNP).

## Drug safety and efficacy (VKORC1)

Warfarin treatment is used to prevent thrombotic disorders. In addition to numerous other factors, genetic factors have their role in individual determination of warfarin dose. VKORC1 enzyme (vitamin K epoxide reductase complex subunit 1), which takes part in activation of coagulation factors, has inherited variant forms that affect the required dose of warfarin. Taking this into consideration (together with variants of CYP2C9 enzyme) may help in finding the optimal warfarin dose.

NORMAL	REDUCED	SIGN.REDUCED
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### Normal expression

\*1/\*1

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

## 8. Raw data

Gene	rsID	Genotype	Reference
ABCB1	rs1045642	A/A	A
ABCG2	rs2231142	G/G	G
ALDH2	rs671	G/G	G
BCHE	rs1799807	T/T	T
	rs1803274	C/C	C
	rs28933390	C/C	C
CACNA1S	rs1800559	C/C	C
	rs772226819	G/G	G
CYP1A2	rs12720461	C/C	C
	rs2069514	G/A	G
	rs2069526	T/T	T
	rs35694136	T/T	T
	rs762551	C/A	C
CYP2B6	rs2279343	A/A	A
	rs28399499	T/T	T
	rs34223104	T/T	T
	rs36060847	G/G	G
	rs3745274	G/G	G
CYP2C19	rs12248560	C/C	C
	rs28399504	A/A	A
	rs41291556	T/T	T
	rs4244285	G/G	G
	rs4986893	G/G	G
CYP2C8	rs10509681	T/T	T
	rs11572080	C/C	C
	rs11572103	T/T	T

CYP2C9	rs1057910	A/A	A
	rs1799853	C/C	C
	rs28371685	C/C	C
	rs28371686	C/C	C
	rs72558189	G/G	G
	rs7900194	G/G	G
	rs9332131	A/A	A
CYP2C_rs12777823	rs12777823	G/G	G
CYP2D6	CNV	2	2
	rs1065852	G/G	G
	rs1135822	A/A	A
	rs1135840	C/C	C
	rs16947	G/G	G
	rs267608319	C/C	C
	rs28371706	G/G	G
	rs28371725	C/C	C
	rs35742686	T/T	T
	rs3892097	C/C	C
	rs5030655	A/A	A
	rs5030656	TCT/TCT	TCT
	rs5030865	C/C	C
	rs5030867	T/T	T
	rs59421388	C/C	C
	rs72549346	-/-	-
	rs72549347	G/G	G
	rs72549352	-/-	-
	rs72549356	-/-	-
	rs769258	C/C	C
	rs79292917	C/C	C
CYP3A4	rs2740574	T/T	C

	rs35599367	G/G	G
	rs4646438	-/-	-
	rs72552799	C/C	C
CYP3A5	rs10264272	C/C	C
	rs41303343	-/-	-
	rs55817950	G/G	G
	rs776746	C/C	T
CYP4F2	rs2108622	C/C	C
DPYD	rs112766203	G/G	G
	rs146356975	T/T	T
	rs186169810	A/A	A
	rs3918290	C/C	C
	rs55674432	C/C	C
	rs55886062	A/A	A
	rs56038477	C/C	C
	rs59086055	G/G	G
	rs67376798	T/T	T
	rs72549304	G/G	G
F2	rs1799963	G/G	G
F5	rs6025	C/C	C
G6PD	rs1050828	C/C	C
	rs1050829	T/T	T
	rs137852327	C/C	C
	rs137852339	C/C	C
	rs5030868	G/G	G
	rs5030869	C/C	C
	rs72554664	C/C	C
	rs72554665	A/A	C
	rs78478128	G/G	G
GRIK4	rs1954787	T/T	T

IFNL3	rs12979860	C/C	C
MTHFR	rs1801131	T/T	T
	rs1801133	G/G	G
NAT2	rs1208	G/A	G
	rs1799930	G/G	G
	rs1799931	G/G	G
	rs1801279	G/G	G
	rs1801280	C/C	T
	rs1805158	C/C	C
NFIB	rs28379954	T/T	T
NUDT15	rs116855232	C/C	C
SLCO1B1	rs11045819	C/A	C
	rs2306283	A/G	A
	rs4149056	T/T	T
	rs59502379	G/G	G
TPMT	rs1142345	T/T	T
	rs1800460	C/C	C
	rs1800462	C/C	C
	rs1800584	C/C	C
	rs267607275	A/A	A
	rs72552738	C/C	C
	rs759836180	-/-	-
UGT1A1	rs3064744	TA[7]/TA[7]	TA[7]
	rs35350960	C/C	C
	rs4148323	G/G	G
	rs887829	C/C	C
VKORC1	rs9923231	C/C	C