GeneAccount

TEST SUMMARY

LASTNAME, FIRSTNAME DEMOSAMPLE2

You were tested for 29 genes, out of which 6 may affect the efficacy or safety of your medication: **CYP2C19, CYP2C9, CYP2D6, IFNL3, SLCO1B1, VKORC1**

Your genetic factors may affect the efficacy or safety of 66 drugs.

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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.**

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.

DRUGS WITH GENETIC VARIATION OF SIGNIFICANT CLINICAL RELEVANCE

boceprevir, clopidogrel, eliglustat, peginterferon alfa-2a, peginterferon alfa-2b, ribavirin, simvastatin, siponimod, telaprevir, tetrabenazine

DRUGS WITH GENETIC VARIATION OF SOME CLINICAL RELEVANCE

atomoxetine, atorvastatin, citalopram, escitalopram, fluvastatin, lovastatin, pitavastatin, pravastatin, rosuvastatin, voriconazole, warfarin

DRUGS WITH GENETIC VARIATION OF MINOR CLINICAL RELEVANCE

acenocoumarol, brivaracetam, carisoprodol, clobazam, clomipramine, dapsone, desflurane, dexlansoprazole, diazepam, digoxin, doxepin, enflurane, flibanserin, halothane, imipramine, isoflurane, isoniazid, lacosamide, lansoprazole, methotrexate, methoxyflurane, methylthioninium, mivacurium, moclobemide, nitrofurantoin, omeprazole, ondansetron, pantoprazole, pegloticase, phenprocoumon, phenytoin, primaquine, quinidine, quinine, rasburicase, sevoflurane, simeprevir, sofosbuvir, sulfadiazine, suxamethonium, tafenoquine, tetracaine, trimipramine, venlafaxine, vincristine

DRUGS WITH NO CLINICALLY RELEVANT GENETIC VARIATION

agomelatine, alcohol, allopurinol, amifampridine, amifampridine phosphate, amitriptyline, amoxapine, amphetamine, arformoterol, aripiprazole, aripiprazole lauroxil, articaine, ascorbic acid, atazanavir, atenolol, avatrombopag, azathioprine, belinostat, binimetinib , bisoprolol, brexpiprazole, bupivacaine, bupropion, cabotegravir, caffeine, capecitabine, cariprazine, carvedilol, celecoxib, cevimeline, chloroprocaine, chloroquine, chlorpropamide, ciprofloxacin, cisplatin, clozapine, codeine, dabrafenib, daclatasvir, darifenacin, desipramine, desvenlafaxine, deutetrabenazine, dexamfetamine, dextromethorphan, diclofenac, dolutegravir, donepezil, dronabinol, duloxetine, efavirenz, elagolix, eltrombopag, erdafitinib, erlotinib, esomeprazole, estradiol, estriol, ethinylestradiol, fesoterodine, flecainide, flucytosine, fluorouracil, fluoxetine, flupentixol, flurbiprofen, flutamide, fluvoxamine, folic acid, fosphenytoin, galantamine, gefitinib, glibenclamide, glimepiride, glipizide, glyceryl trinitrate, govitecan, haloperidol, hydralazine, hydrocodone, hydroxychloroquine, ibuprofen, iloperidone, indacaterol, irbesartan, irinotecan, lesinurad, levofloxacin, lidocaine, lisdexamfetamine, lofexidine, loratadine, lornoxicam, losartan, lusutrombopag, mafenide, meclizine, meloxicam, mepivacaine, mercaptopurine, methadone, metoclopramide, metoprolol, mirabegron, mirtazapine, modafinil, moxifloxacin, nalidixic acid, nebivolol, nefazodone, nevirapine, nilotinib, norfloxacin, nortriptyline, olanzapine, oliceridine, oxycodone, paliperidone, palonosetron, paroxetine, pazopanib, perphenazine, pimozide, pioglitazone, piroxicam, pitolisant, prasugrel, prilocaine, probenecid, propafenone, propranolol, protriptyline, quetiapine, rabeprazole, raltegravir, ranolazine, rimegepant, risperidone, romiplostim, ropivacaine, rosiglitazone, rucaparib, sacituzumab govitecan, sertindole, sertraline, sodium nitrite, sulfamethoxazole, sulfasalazine, sulfisoxazole, synthetic conjugated estrogens, tacrolimus, tamoxifen, tamsulosin, tegafur, tenoxicam, terbinafine, thioguanine, thioridazine, tibolone, ticagrelor, tolazamide, tolbutamide, tolterodine, tramadol, tropisetron, umeclidinium, upadacitinib, valbenazine, vortioxetine, zuclopenthixol

CLASSIFICATION OF DRUG RECOMMENDATIONS

D — 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.

C — 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.

B — 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.

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

CUT AWAY THIS INFORMATION AND STORE IT IN A SAFE PLACE FOR LATER REFERENCE.

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.

Login to the GeneAccount web service with your mobile or desktop device to see your test results and up-to-date report. Via the service, you can print or send your test results to your doctor.

GO TO

my.geneaccount.com/[redacted]

OR SCAN QR CODE

YOUR PIN CODE

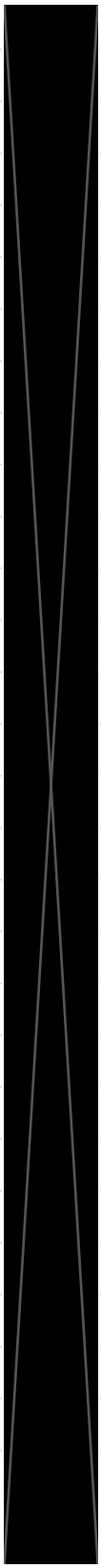
[redacted]

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

HIGHLY AFFECTED MEDICATIONS ORDERED BY THERAPEUTIC AREA

Therapeutic area		Active ingredient	Phenotype	Classification
Alimentary Tract And Metabolism	Other Alimentary Tract And Metabolism Products	eliglustat	CYP2D6 NM Normal Metabolizer	D
Blood And Blood Forming Organs	Antithrombotic Agents	clopidogrel	CYP2C19 IM Intermediate Metabolizer	D
		warfarin	CYP2C9 NM Normal Metabolizer (Activity score 2)	C
		warfarin	VKORC1 Reduced expression of the enzyme	C
Cardiovascular System	Lipid Modifying Agents, Plain	atorvastatin	SLCO1B1 Decreased function	C
		fluvastatin	SLCO1B1 Decreased function	C
		pitavastatin	SLCO1B1 Decreased function	C
		pravastatin	SLCO1B1 Decreased function	C
		rosuvastatin	SLCO1B1 Decreased function	C
		simvastatin	SLCO1B1 Decreased function	D
	Lipid Modifying Agents, Combinations	atorvastatin	SLCO1B1 Decreased function	C
		rosuvastatin	SLCO1B1 Decreased function	C
General Antiinfectives For Systemic Use	Antimycotics For Systemic Use	voriconazole	CYP2C19 IM Intermediate Metabolizer	C
	Agents Affecting The Virus Directly	boceprevir	IFNL3 Unfavorable response genotype	D
		ribavirin	IFNL3 Unfavorable response genotype	D
		telaprevir	IFNL3 Unfavorable response genotype	D
Antineoplastic And Immunomodulating Agents	Immunostimulating Agents	peginterferon alfa-2a	IFNL3 Unfavorable response genotype	D
		peginterferon alfa-2b	IFNL3 Unfavorable response genotype	D
	Immunosuppressive Agents	siponimod	CYP2C9 NM Normal Metabolizer (Activity score 2)	D
Nervous System	Antidepressants	citalopram	CYP2C19 IM Intermediate Metabolizer	C
		escitalopram	CYP2C19 IM Intermediate Metabolizer	C
	Psychostimulants	atomoxetine	CYP2D6 NM Normal Metabolizer	C
	Other Nervous System Drugs	tetrabenazine	CYP2D6 NM Normal Metabolizer	D

SUMMARY OF TESTED GENES AND THEIR PREDICTED PHENOTYPES

Gene	Diplotype	Phenotype
ABCB1		Possibly high expression of P-GP (homozygous)
ABCG2		Normal function
ALDH2		Normal enzyme activity
BCHE		Decreased enzyme activity
CACNA1S		Uncertain susceptibility to malignant hyperthermia
CYP1A2		Normal metabolism
CYP2B6		NM Normal metabolism
CYP2C19		IM Intermediate Metabolizer
CYP2C8		Normal metabolism
CYP2C9		NM Normal Metabolizer (Activity score 2), activity score 2
CYP2C_rs12777823		Decreased warfarin dose requirement
CYP2D6		NM Normal Metabolizer, activity score 2
CYP3A4		Normal metabolism
CYP3A5		PM Poor metabolizer
CYP4F2		Normal metabolizer
DPYD		NM Normal metabolizer, activity score 2
F2		No increased risk of venous thromboembolism
F5		No increased risk of venous thromboembolism
G6PD		No detected G6PD deficiency
GRIK4		Poor responder (heterozygous)
IFNL3		Unfavorable response genotype
MTHFR		Decreased enzyme activity
NAT2		Rapid acetylator
NFIB		Normal metabolizer
NUDT15		Normal metabolizer
SLCO1B1		Decreased function
TPMT		NM Normal metabolizer
UGT1A1		NM Normal Metabolizer
VKORC1		Reduced expression of the enzyme

acenocoumarol

B Label-recommended dosing and administration. With this genotype the sensitivity to acenocoumarol is potentially increased. There are several published genetically guided dosing algorithms (for CYP2C9 and VKORC1 genotypes) but, however, there is no consistent scientific evidence, whether they help in finding appropriate dose. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): No action is needed for this gene-drug interaction. The genetic variation results in a reduction of the required dose, but with the current practice of initiating or reviewing treatment this results in little or no increased risk of bleeding or excessive anticoagulation.

VKORC1: Reduced expression of the enzyme

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

agomelatine

A Label-recommended dosing and administration.

CYP1A2: Normal metabolism

alcohol

A Minor or no flushing reaction to alcohol.

ALDH2: Normal enzyme activity

allopurinol

A Label-recommended dosing and administration.

ABCG2: Normal function

amifampridine

A Label-recommended dosing and administration.

NAT2: Rapid acetylator

amifampridine phosphate

A Label-recommended dosing and administration.

NAT2: Rapid acetylator

amitriptyline

A Label-recommended dosing and administration. With this genotype, the metabolism of amitriptyline is decreased.

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

amoxapine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

amphetamine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

arformoterol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

aripiprazole

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

aripiprazole lauroxil

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

articaine

A Label-recommended dosing. The drug should be discontinued if signs of methaemoglobinaemia occur (shortness of breath, high pulse, cyanosis, or seizures).

G6PD: No detected G6PD deficiency

ascorbic acid

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

atazanavir

A 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

atenolol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

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).

UGT1A1: NM Normal Metabolizer

atomoxetine

C 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.

CYP2D6: NM Normal Metabolizer

atorvastatin

C In patients with this genotype exposure for atorvastatin is increased compared to normal function which may translate to increased risk for myopathy. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe ≤40mg as a starting dose and adjust doses of atorvastatin based on disease-specific guidelines. Prescriber should be aware of possible increased risk for myopathy especially for 40mg dose. If dose >40mg needed for desired efficacy, consider combination therapy.

SLCO1B1: Decreased function

A Label-recommended dosing and administration.

ABCG2: Normal function

A Label-recommended dosing and administration.

CYP3A4: Normal metabolism

avatrombopag

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

A Label-recommended dosing and administration.

F2 (prothrombin): No increased risk of venous thromboembolism

A Label-recommended dosing and administration.

F5: No increased risk of venous thromboembolism

azathioprine

A 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).

NUDT15: Normal metabolizer

A 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).

TPMT: NM Normal metabolizer

belinostat

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

binimetinib

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

bisoprolol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

boceprevir

D This genotype is associated with an unfavorable 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 30% 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 60% 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 50% of patients are eligibile for shortened therapy (24–28 weeks instead of 48 weeks). Consider implications before initiating PEG-IFN alpha and RBV containing regimens.

IFNL3: Unfavorable response genotype

brexpiprazole

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

brivaracetam

B With this genotype the exposure to brivaracetam is potentially increased. According to the drug label approved by U.S. Food and Drug Administration (FDA), a reduced dose may be required.

CYP2C19: IM Intermediate Metabolizer

bupivacaine

A Label-recommended dosing. The drug should be discontinued if signs of methaemoglobinaemia occur (shortness of breath, high pulse, cyanosis, or seizures).

G6PD: No detected G6PD deficiency

bupropion

A Label-recommended dosage and administration.

CYP2B6: NM Normal metabolism

cabotegravir

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

capecitabine

A Normal dihydropyrimidine dehydrogenase activity and no increased risk for fluoropyrimidine toxicity. Label-recommended dosage.

DPYD: NM Normal metabolizer

carisoprodol

B With this genotype the exposure to carisoprodol is potentially increased. Use carisoprodol with caution.

CYP2C19: IM Intermediate Metabolizer

celecoxib

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

chloroprocaine

A Label-recommended dosing. The drug should be discontinued if signs of methaemoglobinaemia occur (shortness of breath, high pulse, cyanosis, or seizures).

G6PD: No detected G6PD deficiency

chlorpropamide

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

cisplatin

A Label-recommended dosing and administration.

TPMT: NM Normal metabolizer

clobazam

B Label-recommended dosing and administration.

CYP2C19: IM Intermediate Metabolizer

caffeine

A With this genotype the metabolism of caffeine by CYP1A2 is normal. In addition to genetic factors, the activity of CYP1A2 is affected significantly by daily habits, e.g. smoking.

CYP1A2: Normal metabolism

cariprazine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

carvedilol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

cevimeline

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

chloroquine

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

ciprofloxacin

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

citalopram

C With this genotype the metabolism of citalopram is reduced. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): The risk of QT prolongation and therefore also the theoretical risk of torsades de pointes is increased as the gene variation leads to an increased citalopram plasma concentration. If you follow the dose recommendation below, the increased plasma concentration and the increased risk of QT prolongation will be offset. Do not exceed the following daily doses: 1. Adults up to 65 years: 30 mg as tablets or 22 mg as drops. 2. Adults 65 years or older: 15 mg as tablets or 10 mg as drops.

CYP2C19: IM Intermediate Metabolizer

B Label-recommended dosage. Patients with this genotype may be less likely to respond to antidepressant treatment as compared to high response genotype.

GRIK4: Poor responder (heterozygous)

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

clomipramine

B Label-recommended dosing and administration. With this genotype, the metabolism of clomipramine is decreased.

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

clopidogrel

D With this genotype the metabolism of clopidogrel to active metabolites is reduced. The effect of clopidogrel in preventing thrombocyte aggregation is probably low. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): For patients with acute coronary syndrome and/or undergoing PCI: Avoid standard dose clopidogrel (75 mg) if possible. Use prasugrel or ticagrelor at standard dose if no contraindication (strong recommendation; no recommendation for other cardiovascular indications (including peripheral arterial disease and stable coronary artery disease following a recent myocardial infarction outside the setting of PCI)). For neurovascular indications (including acute ischemic stroke or TIA, secondary prevention of stroke or prevention of thromboembolic events following neurointerventional procedures, such as carotid artery stenting and stent-assisted coiling of intracranial aneurysms): Consider an alternative P2Y12 inhibitor at standard dose if clinically indicated and no contraindication (moderate recommendation). Alternative P2Y12 inhibitors not impacted by CYP2C19 genetic variants include ticagrelor and ticlopidine. Prasugrel is contraindicated in patients with a history of stroke or TIA.

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

clozapine

A Label-recommended dosing and administration.

CYP1A2: Normal metabolism

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

A Label-recommended dosing and administration.

NFIB: Normal metabolizer

codeine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

dabrafenib

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

daclatasvir

A 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.

IFNL3: Unfavorable response genotype

dapsone

B There was no detected G6PD deficiency with this gene test. However, due to possible nonfunctional alleles not included in this test, G6PD deficiency is possible. In populations at high risk for G6DP deficiency measuring the G6DP enzyme activity is recommended before initiation of the drug (e.g. those of African or Mediterranean ancestry). The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

A Label-recommended dosing and administration.

NAT2: Rapid acetylator

darifenacin

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

desflurane

B 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.

CACNA1S: Uncertain susceptibility to malignant hyperthermia

desipramine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

desvenlafaxine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

deutetrabenazine

A 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.

CYP2D6: NM Normal Metabolizer

dexamfetamine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

dexlansoprazole

dextromethorphan

B With this genotype the exposure to dexlansoprazole is potentially increased. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Initiate standard starting daily dose. For chronic therapy (>12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy.

CYP2C19: IM Intermediate Metabolizer

diazepam

B Label-recommended dosing and administration.

CYP2C19: IM Intermediate Metabolizer

digoxin

B Label-recommended dosing. Pay attention to concomitant use of P-glycoprotein inhibitors, which seem to affect the digoxin concentrations more significantly than the genotype.

ABCB1: Possibly high expression of P-GP (homozygous)

donepezil

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

dronabinol

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

efavirenz

A 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.

CYP2B6: NM Normal metabolism

eliglustat

D 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).

CYP2D6: NM Normal Metabolizer

enflurane

B 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 Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

diclofenac

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

dolutegravir

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

doxepin

B Label-recommended dosing and administration. With this genotype, the metabolism of doxepin is decreased.

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

duloxetine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

elagolix

A Label-recommended dosing and administration.

SLCO1B1: Decreased function

eltrombopag

A Label-recommended dosing and administration.

F2 (prothrombin): No increased risk of venous thromboembolism

A Label-recommended dosing and administration.

F5: No increased risk of venous thromboembolism

erdafitinib

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

CACNA1S: Uncertain susceptibility to malignant hyperthermia

erlotinib

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

escitalopram

C With this genotype the metabolism of escitalopram is reduced. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): The risk of QT prolongation and torsades de pointes is theoretically increased because the gene variation leads to an increased escitalopram plasma concentration. If you follow the dose recommendation below, the increased plasma concentration and the theoretically increased risk of QT prolongation will be offset. Do not exceed the following doses (75% of the standard maximum dose): Adults < 65 years: 15 mg/day. Adults ≥65 years: 7.5 mg/day.

CYP2C19: IM Intermediate Metabolizer

B Label-recommended dosage. Patients with this genotype may be less likely to respond to antidepressant treatment as compared to high response genotype.

GRIK4: Poor responder (heterozygous)

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

esomeprazole

A Label-recommended dosing and administration. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): No action is required for this gene-drug interaction. Although the genetic variation leads to a higher plasma concentration of esomeprazole, there is insufficient evidence to support an effect on the therapeutic effectiveness and side effects.

CYP2C19: IM Intermediate Metabolizer

estradiol

A Label-recommended dosing and administration.

F2 (prothrombin): No increased risk of venous thromboembolism

A Label-recommended dosing and administration.

F5: No increased risk of venous thromboembolism

estriol

A Label-recommended dosing and administration.

F2 (prothrombin): No increased risk of venous thromboembolism

A Label-recommended dosing and administration.

F5: No increased risk of venous thromboembolism

ethinylestradiol

A Label-recommended dosing and administration.

F2 (prothrombin): No increased risk of venous thromboembolism

A Label-recommended dosing and administration.

F5: No increased risk of venous thromboembolism

fesoterodine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

flecainide

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

flibanserin

B With this genotype the exposure to flibanserin is potentially increased. Monitor the patient for adverse effects (e.g. hypotension).

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

flucytosine

A Normal dihydropyrimidine dehydrogenase activity and no increased risk for fluoropyrimidine toxicity. Label-recommended dosage.

DPYD: NM Normal metabolizer

fluorouracil

A Normal dihydropyrimidine dehydrogenase activity and no increased risk for fluoropyrimidine toxicity. Label-recommended dosage.

DPYD: NM Normal metabolizer

fluoxetine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

flupentixol

flurbiprofen

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

flutamide

A Label-recommended dosing. The drug should be discontinued if signs of methaemoglobinaemia occur (shortness of breath, high pulse, cyanosis, or seizures).

G6PD: No detected G6PD deficiency

fluvoxamine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

fosphenytoin

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

gefitinib

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

glimepiride

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

glyceryl trinitrate

A Label-recommended dosing and administration.

ALDH2: Normal enzyme activity

haloperidol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

fluvastatin

C Patients with this genotype have increased fluvastatin exposure compared to patients with normal function. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe desired starting dose and adjust doses of fluvastatin based on disease-specific guidelines. Prescriber should be aware of possible increased risk for myopathy especially for doses > 40mg per day. Check also if CYP2C9 phenotype is available. If CYP2C9 phenotype is intermediate metabolizer, prescribe ≤ 20mg per day as a starting dose and adjust doses of fluvastatin based on disease- specific guidelines. If dose > 20mg needed for desired efficacy, consider an alternative statin or combination therapy. If CYP2C9 phenotype is poor metabolizer, prescribe an alternative statin depending on the desired potency.

SLCO1B1: Decreased function

A Label-recommended dosing and administration. Check also if dosing guidelines for SLCO1B1 are available.

CYP2C9: NM Normal Metabolizer (Activity score 2)

folic acid

A Label-recommended dosing and administration. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group), considering the most studied C677T variant (rs1801133): No action is required for this gene-drug interaction. The gene variation either has no effect or a positive effect on the treatment with folic acid. Treatment with folic acid decreases the reduction of folate concentrations caused by the gene variation.

MTHFR: Decreased enzyme activity

galantamine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

glibenclamide

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

glipizide

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

govitecan

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

halothane

B 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.

CACNA1S: Uncertain susceptibility to malignant hyperthermia

hydralazine

A Label-recommended dosing and administration.

NAT2: Rapid acetylator

hydrocodone

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

hydroxychloroquine

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

ibuprofen

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

iloperidone

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

imipramine

B Label-recommended dosing and administration. With this genotype, the metabolism of imipramine is decreased.

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

indacaterol

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

irbesartan

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

irinotecan

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

isoflurane

B 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.

CACNA1S: Uncertain susceptibility to malignant hyperthermia

isoniazid

B Label-recommended dosing and administration. With this genotype the drug exposure is potentially decreased as compared to slower acetylation speed genotypes. This predisposes to treatment failure. In one study it has been shown that increased dosing (7.5 mg/kg) reduces the risk of treatment failure.

NAT2: Rapid acetylator

lacosamide

B Label-recommended dosing and administration.

CYP2C19: IM Intermediate Metabolizer

lansoprazole

B With this genotype the exposure to lansoprazole is potentially increased. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Initiate standard starting daily dose. For chronic therapy (>12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy.

CYP2C19: IM Intermediate Metabolizer

lesinurad

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

levofloxacin

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

lidocaine

A Label-recommended dosing. The drug should be discontinued if signs of methaemoglobinaemia occur (shortness of breath, high pulse, cyanosis, or seizures).

G6PD: No detected G6PD deficiency

lisdexamfetamine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

loratadine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

losartan

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

lusutrombopag

A Label-recommended dosing and administration.

F2 (prothrombin): No increased risk of venous thromboembolism

A Label-recommended dosing and administration.

F5: No increased risk of venous thromboembolism

meclizine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

mepivacaine

A Label-recommended dosing. The drug should be discontinued if signs of methaemoglobinaemia occur (shortness of breath, high pulse, cyanosis, or seizures).

G6PD: No detected G6PD deficiency

methadone

A Label-recommended dosing and administration.

CYP2B6: NM Normal metabolism

G6PD: No detected G6PD deficiency

lofexidine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

lornoxicam

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

lovastatin

C In patients with this genotype exposure for lovastatin acid is increased compared to patients with normal function which may translate to increased risk for myopathy. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe an alternative statin depending on the desired potency. If lovastatin therapy is warranted, limit dose to ≤20mg/day.

SLCO1B1: Decreased function

mafenide

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

meloxicam

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

mercaptopurine

A Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Start with normal starting dose (e.g. 75 mg/m2/day or 1.5 mg/kg/day) and adjust doses of mercaptopurine (and of any other myelosuppressive therapy) without any special emphasis on mercaptopurine compared to other agents. Allow at least 2 weeks to reach steady state after each dose adjustment. 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).

NUDT15: Normal metabolizer

A 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).

TPMT: NM Normal metabolizer

methotrexate

B With this genotype the risk for methotrexate toxicity is potentially increased. However, the scientific evidence about this is limited and partly controversial.

MTHFR: Decreased enzyme activity

B Label-recommended dosing and administration. Patients with this genotype might have decreased clearance of methotrexate durnig high-dose methotexate treatment. Risk for gastrointestinal side-effects might be decreased.

SLCO1B1: Decreased function

methoxyflurane

B 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.

CACNA1S: Uncertain susceptibility to malignant hyperthermia

methylthioninium

B There was no detected G6PD deficiency with this gene test. However, due to possible nonfunctional alleles not included in this test, G6PD deficiency is possible. In populations at high risk for G6DP deficiency measuring the G6DP enzyme activity is recommended before initiation of the drug (e.g. those of African or Mediterranean ancestry). The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

metoclopramide

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

metoprolol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

mirabegron

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

mirtazapine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

mivacurium

B Label-recommended dosage and administration. With this phenotype the duration of neuromuscular blockade may be slightly longer than in patients with normal pseudocholinesterase activity. Neuromuscular blockade and recovery should be monitored appropriately.

BCHE: Decreased enzyme activity

moclobemide

B Label-recommended dosage. With this genotype the exposure moclobemide might be increased but there is no need for change of dose. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): No action is needed for this gene-drug interaction. Although the moclobemide plasma concentration may increase as a result of the decreased CYP2C19 activity, this does not lead to an increased incidence of side effects, in as far as is known.

CYP2C19: IM Intermediate Metabolizer

modafinil

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

moxifloxacin

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

nalidixic acid

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

nebivolol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

nefazodone

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

nevirapine

A Label-recommended dosing and administration.

CYP2B6: NM Normal metabolism

nilotinib

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

nitrofurantoin

B There was no detected G6PD deficiency with this gene test. However, due to possible nonfunctional alleles not included in this test, G6PD deficiency is possible. In populations at high risk for G6DP deficiency measuring the G6DP enzyme activity is recommended before initiation of the drug (e.g. those of African or Mediterranean ancestry). The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

norfloxacin

nortriptyline

A Label-recommended dosing and administration.

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

olanzapine

A Label-recommended dosing and administration.

CYP1A2: Normal metabolism

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

omeprazole

B With this genotype the exposure to omeprazole is potentially increased. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Initiate standard starting daily dose. For chronic therapy (>12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy.

CYP2C19: IM Intermediate Metabolizer

oxycodone

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

palonosetron

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

paroxetine

A Label-recommended dosing and administration.

CYP1A2: Normal metabolism

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

peginterferon alfa-2a

D This genotype is associated with an unfavorable 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 30% 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 60% 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 50% of patients are eligibile for shortened therapy (24–28 weeks instead of 48 weeks). Consider implications before initiating PEG-IFN alpha and RBV containing regimens.

IFNL3: Unfavorable response genotype

pegloticase

B There was no detected G6PD deficiency with this gene test. However, due to possible nonfunctional alleles not included in this test, G6PD deficiency is possible. In populations at high risk for G6DP deficiency measuring the G6DP enzyme activity is recommended before

CYP2D6: NM Normal Metabolizer

oliceridine

A 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.

CYP2D6: NM Normal Metabolizer

ondansetron

B Label-recommended dosage. With this genotype, the anti-emetic efficacy of ondansetron is potentially decreased. Monitor the drug response and use alternative medication if needed. This considers especially chemotherapy-induced and post-operational nausea and vomiting in the early phase.

ABCB1: Possibly high expression of P-GP (homozygous)

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

paliperidone

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

pantoprazole

B With this genotype the exposure to pantoprazole is potentially increased. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Initiate standard starting daily dose. For chronic therapy (>12 weeks) and efficacy achieved, consider 50% reduction in daily dose and monitor for continued efficacy.

CYP2C19: IM Intermediate Metabolizer

pazopanib

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

peginterferon alfa-2b

D This genotype is associated with an unfavorable 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 30% 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 60% 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 50% of patients are eligibile for shortened therapy (24–28 weeks instead of 48 weeks). Consider implications before initiating PEG-IFN alpha and RBV containing regimens.

IFNL3: Unfavorable response genotype

perphenazine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

initiation of the drug (e.g. those of African or Mediterranean ancestry). The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

phenprocoumon

B Label-recommended dosing and administration. With this genotype the sensitivity to phenprocoumon is potentially increased. There are several published genetically guided dosing algorithms (for CYP2C9 and VKORC1 genotypes) but, however, there is no consistent scientific evidence, whether they help in finding appropriate dose. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): No action is needed for this gene-drug interaction. The genetic variation results in a reduction of the required dose, but regular monitoring of patients ensures that this does not lead to a distinct increase in the risk of bleeding.

VKORC1: Reduced expression of the enzyme

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

phenytoin

B With this genotype the exposure to the drug is potentially increased which may predispose to adverse effects. According to the drug label approved by U.S. Food and Drug Administration (FDA) there may be wide interpatient variability in phenytoin serum levels with equivalent dosages. Unusually high levels result potentially from variant CYP2C19 alleles.

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

pimozide

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

pioglitazone

A Label-recommended dosing and administration.

CYP2C8: Normal metabolism

piroxicam

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

pitavastatin

C In patients with this genotype exposure for pitavastatin is increased compared to patients with normal function which may translate to increased risk for myopathy. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe ≤ 2mg as a starting dose and adjust doses of pitavastatin based on disease-specific guidelines. Prescriber should be aware of possible increased risk for myopathy especially for doses >1mg. If dose >2mg needed for desired efficacy, consider an alternative statin or combination therapy.

SLCO1B1: Decreased function

pitolisant

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

prasugrel

A Label-recommended dosing and administration.

CYP2B6: NM Normal metabolism

A Label-recommended dosing and administration.

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

A Label-recommended dosing and administration.

CYP3A5: PM Poor metabolizer

pravastatin

C In patients with this genotype exposure to pravastatin is increased compared to patients with normal function. Typical risk for myopathy with doses ≤ 40mg. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe desired starting dose and adjust doses of pravastatin based on disease-specific guidelines. Prescriber should be aware of possible increased risk for myopathy with pravastatin especially with doses >40mg per day.

SLCO1B1: Decreased function

prilocaine

A Label-recommended dosing. The drug should be discontinued if signs of methaemoglobinaemia occur (shortness of breath, high pulse, cyanosis, or seizures).

G6PD: No detected G6PD deficiency

primaquine

B There was no detected G6PD deficiency with this gene test. However, due to possible nonfunctional alleles not included in this test, G6PD deficiency is possible. In populations at high risk for G6DP deficiency measuring the G6DP enzyme activity is recommended before initiation of the drug (e.g. those of African or Mediterranean ancestry). The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

probenecid

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

propafenone

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

propranolol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

protriptyline

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

quetiapine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

quinidine

B 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.

CYP2D6: NM Normal Metabolizer

quinine

B There was no detected G6PD deficiency with this gene test. However, due to possible nonfunctional alleles not included in this test, G6PD deficiency is possible. In populations at high risk for G6DP deficiency measuring the G6DP enzyme activity is recommended before initiation of the drug (e.g. those of African or Mediterranean ancestry). The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

rabeprazole

A Label-recommended dosing and administration. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): No action is needed for this gene-drug interaction. The higher plasma concentration of rabeprazole does not result in an increase in side effects.

CYP2C19: IM Intermediate Metabolizer

raltegravir

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

ranolazine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

rasburicase

B There was no detected G6PD deficiency with this gene test. However, due to possible nonfunctional alleles not included in this test, G6PD deficiency is possible.To ascertain the G6PD metabolizer type, the enzyme activity of G6PD needs to be measured (phenotyping test). If the patient has ascertained normal G6PD activity: Label-recommended dosing and administration. No reason to withhold rasburicase based on G6PD status.

G6PD: No detected G6PD deficiency

ribavirin

D This genotype is associated with an unfavorable 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 30% 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 60% 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 50% of patients are eligibile for shortened therapy (24–28 weeks instead of 48 weeks). Consider implications before initiating PEG-IFN alpha and RBV containing regimens.

IFNL3: Unfavorable response genotype

rimegepant

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

risperidone

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

romiplostim

A Label-recommended dosing and administration.

F2 (prothrombin): No increased risk of venous thromboembolism

A Label-recommended dosing and administration.

F5: No increased risk of venous thromboembolism

ropivacaine

A Label-recommended dosing. The drug should be discontinued if signs of methaemoglobinaemia occur (shortness of breath, high pulse, cyanosis, or seizures).

rosiglitazone

A Label-recommended dosing and administration.

G6PD: No detected G6PD deficiency

CYP2C8: Normal metabolism

rosuvastatin

C In patients with this genotype exposure for rosuvastatin is increased compared to patients with normal function. Typical myopathy risk with doses ≤ 20mg. 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. Prescriber should be aware of possible increased risk for myopathy especially for doses >20mg. Check also if ABCG2 phenotype is available. If ABCG2 phenotype is poor function, prescribe ≤10mg as a starting dose and adjust doses of rosuvastatin based on disease-specific and specific population guidelines. If dose >10mg needed for desired efficacy, consider an alternative statin or combination therapy.

SLCO1B1: Decreased function

A 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.

ABCG2: Normal function

rucaparib

A Label-recommended dosing and administration.

CYP1A2: Normal metabolism

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

sacituzumab govitecan

A Label-recommended dosing and administration.

UGT1A1: NM Normal Metabolizer

sertindole

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

sertraline

A Label-recommended dosage. With this genotype the metabolism of sertraline is reduced.

CYP2C19: IM Intermediate Metabolizer

sevoflurane

B 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.

CACNA1S: Uncertain susceptibility to malignant hyperthermia

simeprevir

B According to the summary of product characteristics provided by the manufacturer, this genotype is associated with less favourable hepatitis C (genotypes 1) treatment response when treating treatment-naive patients with combination of simeprevir, ribavirin, and peginterferon-alfa. Sustained virological response was achieved in 61 % of patients homozygous for less favourable response genotype whereas corresponding number for heterozygotes was 78 % compared to 95 % in patients with favourable response genotype.

IFNL3: Unfavorable response genotype

simvastatin

D Patients with this genotype have increased simvastatin acid exposure as compared to normal function and increased risk for myopathy. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Prescribe an alternative statin depending on the desired potency. If simvastatin therapy is warranted, limit dose to < 20mg/day.

SLCO1B1: Decreased function

A Label-recommended dosing and administration.

CYP3A4: Normal metabolism

siponimod

D 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).

CYP2C9: NM Normal Metabolizer (Activity score 2)

sodium nitrite

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

sofosbuvir

B According to the summary of product characteristics provided by the manufacturer, this genotype is associated with less favourable hepatitis C (genotypes 1 and 4) treatment response when treating treatment-naive patients with combination of sofosbuvir, ribavirin, and peginterferon-alfa for 12 weeks. 87 % of patients with this genotyped achieved sustained virological response whereas 99 % of patients with favourable response genotype achieved sustained virological response.

IFNL3: Unfavorable response genotype

sulfadiazine

B There was no detected G6PD deficiency with this gene test. However, due to possible nonfunctional alleles not included in this test, G6PD deficiency is possible. In populations at high risk for G6DP deficiency measuring the G6DP enzyme activity is recommended before initiation of the drug (e.g. those of African or Mediterranean ancestry). The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

sulfamethoxazole

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

A Label-recommended dosing and administration.

NAT2: Rapid acetylator

sulfisoxazole

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

sulfasalazine

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

A Label-recommended dosing and administration.

NAT2: Rapid acetylator

suxamethonium

B Label-recommended dosage and administration. With this phenotype the duration of neuromuscular blockade may be slightly longer than in patients with normal pseudocholinesterase activity. Neuromuscular blockade and recovery should be monitored appropriately.

BCHE: Decreased enzyme activity

B 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.

CACNA1S: Uncertain susceptibility to malignant hyperthermia

synthetic conjugated estrogens

A Label-recommended dosing and administration.

F2 (prothrombin): No increased risk of venous thromboembolism

A Label-recommended dosing and administration.

F5: No increased risk of venous thromboembolism

tacrolimus

A 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.

CYP3A5: PM Poor metabolizer

tafenoquine

B According to the summary of product characteristics all patients must be tested for G6PD deficiency prior to prescribing of the product. There was no detected G6PD deficiency with this gene test. However, due to possible nonfunctional alleles not included in this test, G6PD deficiency is possible. In populations at high risk for G6DP deficiency measuring the G6DP enzyme activity is recommended before initiation of the drug (e.g. those of African or Mediterranean ancestry). The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs. Pregnancy test should be performed for all females with reproductive potential and in case of pregnancy the foetus should be screened for G6PD deficiency prior to initiating the product. G6PD-deficient infant may be at increased risk for hemolytic anaemia if exposed to product through breast feeding.

G6PD: No detected G6PD deficiency

tamoxifen

A 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.

CYP2D6: NM Normal Metabolizer

A Label-recommended dosing and administration.

F2 (prothrombin): No increased risk of venous thromboembolism

A Label-recommended dosing and administration.

F5: No increased risk of venous thromboembolism

tamsulosin

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

tegafur

A Normal dihydropyrimidine dehydrogenase activity and no increased risk for fluoropyrimidine toxicity. Label-recommended dosage.

DPYD: NM Normal metabolizer

telaprevir

D This genotype is associated with an unfavorable 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 30% 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 60% 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 50% of patients are eligibile for shortened therapy (24–28 weeks instead of 48

tenoxicam

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

weeks). Consider implications before initiating PEG-IFN alpha and RBV containing regimens.

IFNL3: Unfavorable response genotype

terbinafine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

tetrabenazine

D 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.

CYP2D6: NM Normal Metabolizer

tetracaine

B Label-recommended dosage and administration. According to FDA-approved summary of product characteristics patients with this phenotype are at increased risk for toxic plasma concentrations of the drug compared to patients with normal pseudocholinesterase activity. Monitor patients with pseudocholinesterase deficiency for signs of local anesthetic toxicity.

BCHE: Decreased enzyme activity

A Label-recommended dosing. The drug should be discontinued if signs of methaemoglobinaemia occur (shortness of breath, high pulse, cyanosis, or seizures).

G6PD: No detected G6PD deficiency

thioguanine

A Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Start with normal starting dose (40-60 mg/m2/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).

NUDT15: Normal metabolizer

A 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).

TPMT: NM Normal metabolizer

thioridazine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

tibolone

A Label-recommended dosing and administration.

F2 (prothrombin): No increased risk of venous thromboembolism

A Label-recommended dosing and administration.

F5: No increased risk of venous thromboembolism

ticagrelor

A Label-recommended dosing and administration.

CYP2C19: IM Intermediate Metabolizer

tolazamide

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

tolbutamide

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer (Activity score 2)

A Label-recommended dosing and administration. The drug should be discontinued immediately if marked darkening of the urine or sudden decrease in haemoglobin concentration or erythrocyte count occurs.

G6PD: No detected G6PD deficiency

tolterodine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

tramadol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

trimipramine

B Label-recommended dosing and administration. With this genotype, the metabolism of trimipramine is decreased.

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

tropisetron

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

umeclidinium

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

upadacitinib

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

valbenazine

A 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.

CYP2D6: NM Normal Metabolizer

venlafaxine

B Label-recommended dosing and administration. With this genotype the metabolism of venlafaxine is potentially decreased and exposure to venlafaxine and its active metabolite increased, especially in patients with decreased metabolic activity of CYP2D6. Scientific evidence on its association with adverse effects or efficacy is scarce, though.

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

vincristine

B 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.

CYP3A5: PM Poor metabolizer

voriconazole

C With this genotype the exposure to voriconazole is potentially increased. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Initiate therapy with recommended standard of care dosing. Further dose adjustments or selection of alternative therapy may be necessary due to other clinical factors, such as drug interactions, hepatic function, renal function, species, site of infection, therapeutic drug monitoring, and comorbidities.

CYP2C19: IM Intermediate Metabolizer

vortioxetine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

warfarin

C 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 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 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.

CYP2C9: NM Normal Metabolizer (Activity score 2)

C 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 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 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.

VKORC1: Reduced expression of the enzyme

B Warfarin dosing is potentially benefited by use of a dosing algorithm which includes genotype information. See separate recommendations for CYP2C9, VKORC1 and CYP4F2 genes. In African American patients with this CYP2C rs12777823 genotype, decrease the calculated dose by 10 - 25%.

zuclopenthixol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

CYP2C rs12777823: Decreased warfarin dose requirement

A 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.

CYP4F2: Normal metabolizer

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.

TT	CT	**CC**

Possibly high expression of P-GP (homozygous)

15.01.2023 D.E.M.O LABORATORIES

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.

LOW	IM	**NORMAL**

Normal function

15.01.2023 D.E.M.O LABORATORIES

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	MISSING

Normal enzyme activity

15.01.2023 D.E.M.O LABORATORIES

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

Decreased enzyme activity

15.01.2023 D.E.M.O LABORATORIES

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 hyperthemia 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

15.01.2023 D.E.M.O LABORATORIES

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.

NORMAL	HIGH	LOW

Normal metabolism

15.01.2023 D.E.M.O LABORATORIES

Analyzed 4 of 4 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 metabolism

15.01.2023 D.E.M.O LABORATORIES

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**

Decreased warfarin dose requirement

15.01.2023 D.E.M.O LABORATORIES

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

IM Intermediate Metabolizer

15.01.2023 D.E.M.O LABORATORIES

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	LPM

Normal metabolism

15.01.2023 D.E.M.O LABORATORIES

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	IM AS15	**NM AS2**

NM Normal Metabolizer (Activity score 2)
Activity score: **2**

15.01.2023 D.E.M.O LABORATORIES

Analyzed 6 of 6 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**

15.01.2023 D.E.M.O LABORATORIES

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 substates. The combined metabolism of these enzymes may define the speed of metabolism of certain drugs better than that of CYP3A4 alone.

NORMAL	DECREASED

Normal metabolism

15.01.2023 D.E.M.O LABORATORIES

Analyzed 2 of 2 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	IM	NM	NM/IM

PM Poor metabolizer

15.01.2023 D.E.M.O LABORATORIES

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	DECREASED

Normal metabolizer

15.01.2023 D.E.M.O LABORATORIES

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	IM AS15	IM AS1	PM AS05	PM AS0

NM Normal metabolizer
Activity score: **2**

15.01.2023 D.E.M.O LABORATORIES

Analyzed 4 of 4 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 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

15.01.2023 D.E.M.O LABORATORIES

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

15.01.2023 D.E.M.O LABORATORIES

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	VARIABLE

No detected G6PD deficiency

15.01.2023 D.E.M.O LABORATORIES

Analyzed 7 of 7 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.

TT	CT	CC

Poor responder (heterozygous)

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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 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

Unfavorable response genotype

15.01.2023 D.E.M.O LABORATORIES

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

Decreased enzyme activity

15.01.2023 D.E.M.O LABORATORIES

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**

Rapid acetylator

15.01.2023 D.E.M.O LABORATORIES

Analyzed 4 of 4 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 aaram 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

15.01.2023 D.E.M.O LABORATORIES

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.

NORMAL	INTERMEDIATE	POOR	UNKNOWN

Normal metabolizer

15.01.2023 D.E.M.O LABORATORIES

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	**INTERMEDIATE**	POOR	POSDECR

Decreased function

15.01.2023 D.E.M.O LABORATORIES

Analyzed 2 of 2 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.

NORMAL	INTERMEDIATE	POOR	LIM

NM Normal metabolizer

15.01.2023 D.E.M.O LABORATORIES

Analyzed 4 of 4 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 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**

NM Normal Metabolizer

15.01.2023 D.E.M.O LABORATORIES

Analyzed 2 of 2 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

Reduced expression of the enzyme

15.01.2023 D.E.M.O LABORATORIES

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

RAW DATA

Gene	RS	Genotype
ABCB1	[redacted]	[redacted]
ABCG2		
ALDH2		
BCHE		
BCHE		
BCHE		
CACNA1S		
CACNA1S		
CYP1A2		
CYP1A2		
CYP1A2		
CYP1A2		
CYP2B6		
CYP2B6		
CYP2B6		
CYP2B6		
CYP2B6		
CYP2C19		
CYP2C19		
CYP2C19		
CYP2C19		
CYP2C19		
CYP2C8		
CYP2C8		
CYP2C8		
CYP2C9		
CYP2C9		
CYP2C9		
CYP2C9		
CYP2C9		
CYP2C9		
CYP2C_rs12777823		
CYP2D6		
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CYP2D6	[redacted]	[redacted]	
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CYP2D6			
CYP2D6			
CYP3A4			
CYP3A4			
CYP3A5			
CYP3A5			
CYP3A5			
CYP3A5			
CYP4F2			
DPYD			
DPYD			
DPYD			
DPYD			
F2			
F5			
G6PD			
G6PD			
G6PD			
G6PD			
G6PD			
G6PD			
G6PD			
GRIK4			
IFNL3			
MTHFR			
MTHFR			
NAT2			
NAT2			
NAT2			
NAT2			
NFIB			
NUDT15			
SLCO1B1			
SLCO1B1			

TPMT	[redacted]	[redacted]
TPMT		
TPMT		
TPMT		
UGT1A1		
UGT1A1		
VKORC1		