PharmaDNA
Be sure

TEST SUMMARY

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You were tested for 11 genes, which 4 may affect the efficacy or safety of your medication: **CYP2C19, CYP2C9, CYP2D6, VKORC1**

Your genetic factors may affect the efficacy or safety of 72 drugs.

DRUGS WITH GENETIC VARIATION OF SIGNIFICANT CLINICAL RELEVANCE

amitriptyline, codeine, metoprolol, nortriptyline, paroxetine, propafenone

DRUGS WITH GENETIC VARIATION OF SOME CLINICAL RELEVANCE

clopidogrel, eliglustat, haloperidol, ondansetron, risperidone, tramadol, tropisetron, voriconazole, warfarin

DRUGS WITH GENETIC VARIATION OF MINOR CLINICAL RELEVANCE

acenocoumarol, arformoterol, aripiprazole, atomoxetine, brexpiprazole, brivaracetam, caffeine, carisoprodol, carvedilol, cevimeline, clobazam, clomipramine, clozapine, darifenacin, desipramine, deutetrabenazine, dextromethorphan, diazepam, doxepin, duloxetine, escitalopram, fesoterodine, flecainide, flibanserin, fluoxetine, flupenthixol, fluvoxamine, galantamine, gefitinib, iloperidone, imipramine, lacosamide, mirtazapine, modafinil, nebivolol, nefazodone, olanzapine, oxycodone, palonosetron, perphenazine, phenprocoumon, pimozide, primaquine, propranolol, protriptyline, quinidine, ranolazine, sertindole, terbinafine, tetrabenazine, tolterodine, trimipramine, valbenazine, venlafaxine, vincristine, vortioxetine, zuclopenthixol

DRUGS WITH NO CLINICALLY RELEVANT GENETIC VARIATION

atorvastatin, celecoxib, citalopram, desvenlafaxine, diclofenac, donepezil, dronabinol, efavirenz, eltrombopag, esomeprazole, estradiol, estriol, ethinylestradiol, flurbiprofen, fluvastatin, fosphenytoin, glibenclamide, glimepiride, irbesartan, lansoprazole, lesinurad, losartan, lovastatin, mirabegron, moclobemide, nevirapine, omeprazole, pantoprazole, phenytoin, piroxicam, prasugrel, pravastatin, rabeprazole, romiplostim, rosuvastatin, rucaparib, sertraline, simvastatin, tacrolimus, tamoxifen, thioridazine, tibolone, ticagrelor, umeclidinium

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.



High inducibility

*1F/*1F

30.11.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 5 of 5 single nucleotide polymorphisms (SNP).

Drug safety and efficacy (CYP2B6)

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



Normal metabolism

*1/*1

30.11.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 3 of 3 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.



IM Intermediate Metabolizer

*1/*2

30.11.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 10 of 10 single nucleotide polymorphisms (SNP).

Drug safety and efficacy (CYP2C9)

CYP2C9 is a hepatic enzyme which mediates metabolism of several drugs, including warfarin and phenytoin. There is genetic variation concerning CYP2C9, and due to this the speed of metabolism by the enzyme in an individual can be slower than average. This increases efficacy of certain drugs. 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.



NM Normal Metabolizer

*1/*1

30.11.2016 YHTYNEET MEDIX LABORATORIOT

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.



UM Ultrarapid Metabolizer

(*1/*2)x3

30.11.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 13 of 13 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 metabolism

*1/*1

30.11.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 6 of 6 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 white people are poor CYP3A5 metabolizers. This alters the needed doses of certain drugs between individuals.



PM Poor metabolizer

*3/*3

30.11.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 7 of 7 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

WT/WT

30.11.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

Blood coagulation factor V (F5 Leiden)

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

NORMAL	RISK	HIGHRISK

No increased risk of venous thromboembolism

WT/WT

30.11.2016 YHTYNEET MEDIX LABORATORIOT

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 statins from the plasma. One variant allele of the gene (C allele) decreases the transport function of the protein and thus leads to accumulation of statins in the plasma and increased risk for myopathy. The risk for myopathy has been shown to be associated to the use of simvastatin in allele C carriers, especially in homozygotes (CC) but also in heterozygotes (CT). There may also be association 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.

NORMAL	DECREASED	POOR

Normal function

*1/*1

30.11.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 1 of 1 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.



Remarkably reduced expression of the enzyme

*2/*2

30.11.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

CLASSIFICATION OF RECOMMENDATIONS

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

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.

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.

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.

RECOMMENDATIONS

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): Check INR more frequently.

VKORC1: Remarkably reduced expression of the enzyme

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

amitriptyline

D Efficacy of amitriptyline is potentially lower than normal with this genotype and therefore its use should be avoided. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider titrating to a higher target dose (compared to normal metabolizers). Utilize therapeutic drug monitoring to guide dose adjustments. This recommendation applies to higher initial doses for treatment of conditions such as depression (and not for treatment of e.g. neuropathic pain; however, monitor the patients closely for response or consider alternative agents).

CYP2D6: UM Ultrarapid Metabolizer

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

CYP2C19: IM Intermediate Metabolizer

arformoterol

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

aripiprazole

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

atomoxetine

atorvastatin

B With this genotype the exposure to atomoxetine is potentially reduced. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Insufficient data to allow calculation of dose adjustment. Be alert to reduced efficacy or select alternative drug (e.g., methylphenidate, clonidine).

CYP2D6: UM Ultrarapid Metabolizer

brexpiprazole

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

caffeine

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

CYP1A2: High inducibility

carvedilol

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

cevimeline

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

clobazam

B Label-recommended dosing and administration.

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP3A4: Normal metabolism

A Label-recommended dosing and administration.

SLCO1B1: Normal function

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

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

citalopram

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

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

clomipramine

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

CYP2C19: IM Intermediate Metabolizer

B Efficacy of clomipramine is potentially lower than normal with this genotype and therefore its use should be avoided. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Since tricyclic antidepressants have comparable pharmacokinetic properties, it may be reasonable to apply the dosing guideline for amitriptyline/nortriptyline and CYP2D6 to other tricyclics including clomipramine: Avoid tricyclic use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider titrating to a higher target dose (compared to normal metabolizers). Utilize therapeutic drug monitoring to guide dose adjustments. This recommendation applies to higher initial doses for treatment of conditions such as depression (and not for treatment of e.g. neuropathic pain; however, monitor the patients closely for response or consider alternative agents).

CYP2D6: UM Ultrarapid Metabolizer

clopidogrel

C 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): Alternative antiplatelet therapy (if not contraindicated), e.g. prasugrel or ticagrelor, is recommended. This recommendation is mainly to be considered for patients with acute coronary syndrome treated with PCI and stenting, for which prasugrel and ticagrelor are also indicated.

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

clozapine

B Label-recommended dosage. Monitor the drug response. With this genotype the activity of CYP1A2 is potentially increased (especially in smokers) and thus the exposure to clozapine may be decreased. On the other hand, the seizure risk related to the use of clozapine is potentially increased but scientific evidence about this is limited. Several other genetic and behavioral factors, such as smoking, also affect the metabolism.

CYP1A2: High inducibility

A Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

codeine

D With this genotype the metabolism of codeine to morphine is increased. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Avoid codeine use due to potential for toxicity. Alternatives that are not affected by this CYP2D6 genotype include morphine and non-opioid analgesics. Tramadol, and to a lesser extent hydrocodone and oxycodone, are not good alternatives because their metabolism is affected by CYP2D6 activity.

CYP2D6: UM Ultrarapid Metabolizer

darifenacin

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

desipramine

B Efficacy of desipramine is potentially lower than normal with this genotype and therefore its use should be avoided. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Since tricyclic antidepressants have comparable pharmacokinetic properties, it may be reasonable to apply the dosing guideline for amitriptyline/nortriptyline and CYP2D6 to other tricyclics including desipramine: Avoid tricyclic use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider titrating to a higher target dose (compared to normal metabolizers). Utilize therapeutic drug monitoring to guide dose adjustments. This recommendation applies to higher initial doses for treatment of conditions such as depression (and not for treatment of e.g. neuropathic pain; however, monitor the patients closely for response or consider alternative agents).

CYP2D6: UM Ultrarapid Metabolizer

desvenlafaxine

A Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

deutetrabenazine

B 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: UM Ultrarapid Metabolizer

dextromethorphan

B Half-life of dextrometorphane may be shorter in ultrarapid metabolizers than in normal metabolizers. Monitor the patient's drug response.

CYP2D6: UM Ultrarapid Metabolizer

diazepam

B Label-recommended dosing and administration.

CYP2C19: IM Intermediate Metabolizer

diclofenac

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

donepezil

A Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

doxepin

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

CYP2C19: IM Intermediate Metabolizer

B Efficacy of doxepin is potentially lower than normal with this genotype and therefore its use should be avoided. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Since tricyclic antidepressants have comparable pharmacokinetic properties, it may be reasonable to apply the dosing guideline for amitriptyline/nortriptyline and CYP2D6 to other tricyclics including doxepin: Avoid tricyclic use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider titrating to a higher target dose (compared to normal metabolizers). Utilize therapeutic drug monitoring to guide dose adjustments. This recommendation applies to higher initial doses for treatment of conditions such as depression (and not for treatment of e.g. neuropathic pain; however, monitor the patients closely for response or consider alternative agents).

CYP2D6: UM Ultrarapid Metabolizer

dronabinol

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

duloxetine

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

efavirenz

A Label-recommended dosing and administration.

CYP2B6: Normal metabolism

eliglustat

C With this genotype the patient may not achieve adequate concentrations of eliglustat to achieve a therapeutic effect.

CYP2D6: UM Ultrarapid Metabolizer

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

escitalopram

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

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

CYP2C19: IM Intermediate Metabolizer

esomeprazole

A Label-recommended dosing and administration. Exposure to and effect of esomeprazole are increased in intermediate metabolizers, which may even improve treatment.

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.

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

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid 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

A Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

flupenthixol

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

fluvastatin

A Label-recommended dosing and administration.

SLCO1B1: Normal function

fosphenytoin

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

gefitinib

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

F2 (prothrombin): No increased risk of venous thromboembolism

A Label-recommended dosing and administration.

F5: No increased risk of venous thromboembolism

flecainide

B With this genotype the exposure to flecainide is potentially reduced. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Record ECG and monitor plasma concentration or select alternative drug (e.g., sotalol, disopyramide, quinidine, amiodarone).

CYP2D6: UM Ultrarapid Metabolizer

fluoxetine

B With this genotype the proportions of active fluoxetine metabolites are altered. There are no dosage recommendations however, due to lack of evidence on how it affects the outcome or the safety of the treatment. It may be reasonable to monitor these patients more closely if they are prescribed fluoxetine or to select an alternative SSRI not normal metabolized by CYP2D6.

CYP2D6: UM Ultrarapid Metabolizer

flurbiprofen

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

fluvoxamine

B Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): With this genotype there are no dosage recommendations due to lack of evidence on how ultrarapid metabolizer type affects fluvoxamine treatment. It may be reasonable, though, to select an alternative SSRI not normal metabolized by CYP2D6.

CYP2D6: UM Ultrarapid Metabolizer

galantamine

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

glibenclamide

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

glimepiride

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

haloperidol

C With this genotype the exposure to haloperidol is potentially decreased. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Insufficient data to allow calculation of dose adjustent. Be alert to decreased haloperidol plasma concentration and adjust maintenance dose in response to haloperidol plasma concentration or select alternative drug (e.g., pimozide, flupenthixol, fluphenazine, quetiapine, olanzapine, clozapine).

CYP2D6: UM Ultrarapid Metabolizer

iloperidone

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

imipramine

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

CYP2C19: IM Intermediate Metabolizer

B Efficacy of imipramine is potentially lower than normal with this genotype and therefore its use should be avoided. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Since tricyclic antidepressants have comparable pharmacokinetic properties, it may be reasonable to apply the dosing guideline for amitriptyline/nortriptyline and CYP2D6 to other tricyclics including imipramine: Avoid tricyclic use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider titrating to a higher target dose (compared to normal metabolizers). Utilize therapeutic drug monitoring to guide dose adjustments. This recommendation applies to higher initial doses for treatment of conditions such as depression (and not for treatment of e.g. neuropathic pain; however, monitor the patients closely for response or consider alternative agents).

CYP2D6: UM Ultrarapid Metabolizer

irbesartan

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

lacosamide

B Label-recommended dosing and administration.

CYP2C19: IM Intermediate Metabolizer

lansoprazole

A Label-recommended dosage. Exposure to and effect of lansoprazole are increased in intermediate metabolizers, which may even improve treatment efficacy.

CYP2C19: IM Intermediate Metabolizer

lesinurad

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

losartan

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

lovastatin

A Label-recommended dosing and administration.

SLCO1B1: Normal function

metoprolol

D With this genotype the exposure to metoprolol is potentially decreased. If efficacy is insufficient, dosage recommendation by a Dutch group of experts (Dutch Pharmacogenetics Working Group) may be beneficial: Heart failure: select alternative drug (e.g., bisoprolol, carvedilol) or titrate dose to a maximum of 250% of the normal dose in response to efficacy and adverse drug effects (ADEs). Other indications: select alternative drug (e.g., atenolol, bisoprolol) or titrate dose to a maximum of 250% of the normal dose in response to efficacy and ADEs.

mirabegron

A Label-recommended dosing and administration. With this genotype the metabolism of mirabegron is potentially increased, but that doesn't seem to be clinically significant.

CYP2D6: UM Ultrarapid Metabolizer

CYP2D6: UM Ultrarapid Metabolizer

mirtazapine

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

modafinil

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

nefazodone

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

nortriptyline

D Efficacy of nortriptyline is potentially lower than normal with this genotype and therefore its use should be avoided. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider titrating to a higher target dose (compared to normal metabolizers). Utilize therapeutic drug monitoring to guide dose adjustments. This recommendation applies to higher initial doses for treatment of conditions such as depression (and not for treatment of e.g. neuropathic pain; however, monitor the patients closely for response or consider alternative agents).

CYP2D6: UM Ultrarapid Metabolizer

omeprazole

A Label-recommended dosage. Exposure to and effect of omeprazole are increased in intermediate metabolizers, which may even improve treatment efficacy.

CYP2C19: IM Intermediate Metabolizer

oxycodone

B With this genotype the speed of metabolism of oxycodone is increased but evidence of its significance in relation to efficacy or adverse drug effects is controversial. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Insufficient data to allow calculation of dose adjustment. Select alternate drug (NOT tramadol or codeine) or be alert to ADEs (e.g., nausea, vomiting, constipation, respiratory depression, confusion, urinary retention).

CYP2D6: UM Ultrarapid Metabolizer

pantoprazole

moclobemide

A Label-recommended dosing and administration.

CYP2C19: IM Intermediate Metabolizer

nebivolol

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

nevirapine

A Label-recommended dosing and administration.

CYP2B6: Normal metabolism

olanzapine

B Label-recommended dosage. Monitor the drug response. With this genotype the metabolism of CYP1A2 is potentially increased (especially in smokers) which may decrease the exposure to olanzapine. In addition, several other genetic and behavioral factors, such as smoking, also affect the metabolism.

CYP1A2: High inducibility

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

ondansetron

C With this genotype the metabolism of ondansetron is potentially increased which may lead to reduced efficacy. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Select an alternative drug not predominantly metabolized by CYP2D6 (i.e. granisetron).

CYP2D6: UM Ultrarapid Metabolizer

palonosetron

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

paroxetine

A Label-recommended dosing. Exposure to and effect of pantoprazole are increased in intermediate metabolizers, which may even improve treatment efficacy.

CYP2C19: IM Intermediate Metabolizer

D With this genotype the exposure to paroxetine is potentially decreased which may lead to insufficient efficacy. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Select alternative drug not predominantly metabolized by CYP2D6.

CYP2D6: UM Ultrarapid Metabolizer

B With this genotype the required dose of paroxetine may be higher than in normal metabolizers. In addition, several other genetic and behavioral factors, such as smoking, also affect the metabolism.

CYP1A2: High inducibility

perphenazine

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

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): Check INR more frequently.

VKORC1: Remarkably reduced expression of the enzyme

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

phenytoin

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

pimozide

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

piroxicam

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

prasugrel

A Label-recommended dosing and administration.

CYP2B6: Normal metabolism

A Label-recommended dosing and administration.

CYP2C19: IM Intermediate Metabolizer

A Label-recommended dosing and administration.

CYP2C9: NM Normal Metabolizer

A Label-recommended dosing and administration.

CYP3A5: PM Poor metabolizer

pravastatin

A Label-recommended dosing and administration.

SLCO1B1: Normal function

primaquine

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

propafenone

propranolol

D With this genotype the exposure to propafenone is potentially decreased. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Insufficient data to allow calculation of dose adjustment. Adjust dose in response to plasma concentration and record ECG or select alternative drug (e.g., sotalol, disopyramide, quinidine, amiodarone)

CYP2D6: UM Ultrarapid Metabolizer

protriptyline

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

rabeprazole

A Label-recommended dosing. Exposure to and effect of rabeprazole are increased in intermediate metabolizers, which may even improve treatment efficacy.

CYP2C19: IM Intermediate Metabolizer

risperidone

C With this genotype the ratio of risperidone and its active metabolite is altered but their joint effect may not be changed compared to normal metabolizer. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Insufficient data to allow calculation of dose adjustment. Select alternative drug (e.g., quetiapine, olanzapine, clozapine) or be extra alert to ADEs and adjust dose to clinical response.

CYP2D6: UM Ultrarapid Metabolizer

rosuvastatin

A Label-recommended dosing and administration.

SLCO1B1: Normal function

sertindole

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

simvastatin

A Label-recommended dosing and administration.

CYP3A4: Normal metabolism

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid 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: UM Ultrarapid Metabolizer

ranolazine

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid 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

rucaparib

A Label-recommended dosing and administration.

CYP1A2: High inducibility

A Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

sertraline

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

CYP2C19: IM Intermediate Metabolizer

tacrolimus

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

SLCO1B1: Normal function

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

tamoxifen

A Initiate therapy with recommended standard of care dosing (tamoxifen 20 mg/day). Avoid moderate and strong CYP2D6 inhibitors.

CYP2D6: UM Ultrarapid 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

terbinafine

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

tetrabenazine

B Label-recommended dosing and administration. In ultrarapid metabolizers the titration time to appropriate dose may be longer than in normal metabolizers, and the needed dose is potentially increased.

CYP2D6: UM Ultrarapid Metabolizer

thioridazine

A Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid 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

tolterodine

B Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

tramadol

C With this genotype the speed of metabolism of tramadol to an active metabolite is increased, which may lead to symptoms of overdose. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Reduce dose by 30% and be alert to ADEs (e.g., nausea, vomiting, constipation, respiratory depression, confusion, urinary retention) or select alternative drug (e.g., acetaminophen, NSAID, morphine - not oxycodone or codeine).

CYP2D6: UM Ultrarapid Metabolizer

trimipramine

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

CYP2C19: IM Intermediate Metabolizer

tropisetron

C With this genotype the metabolism of tropisetron is potentially increased which may lead to reduced efficacy. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Select an alternative drug not predominantly metabolized by CYP2D6 (i.e. granisetron).

B Efficacy of trimipramine is potentially lower than normal with this genotype and therefore its use should be avoided. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Since tricyclic antidepressants have comparable pharmacokinetic properties, it may be reasonable to apply the dosing guideline for amitriptyline/nortriptyline and CYP2D6 to other tricyclics including trimipramine: Avoid tricyclic use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider titrating to a higher target dose (compared to normal metabolizers). Utilize therapeutic drug monitoring to guide dose adjustments. This recommendation applies to higher initial doses for treatment of conditions such as depression (and not for treatment of e.g. neuropathic pain; however, monitor the patients closely for response or consider alternative agents).

CYP2D6: UM Ultrarapid Metabolizer

umeclidinium

A Label-recommended dosing and administration.

CYP2D6: UM Ultrarapid Metabolizer

valbenazine

B 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: UM Ultrarapid Metabolizer

venlafaxine

B With this genotype the exposure to venlafaxine is potentially increased. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Be alert to decreased venlafaxine and increased, less active O-desmethylvenlafaxine plasma concentration. Titrate dose to a maximum of 150% of the normal dose or select alternative drug (e.g., citalopram, sertraline).

CYP2D6: UM Ultrarapid 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.

CYP2C19: IM Intermediate Metabolizer

vortioxetine

B Label-recommended dosing and administration. According to the summary of product characteristics provided by the manufacturer, in ultrarapid CYP2D6 metabolizers the plasma concentration of vortioxetine 10 mg/day were between those obtained in normal metabolisers at 5 mg/day and 10 mg/day. Depending on individual patient response, a dose adjustment may be considered.

CYP2D6: UM Ultrarapid 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*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.

CYP2C9: NM Normal Metabolizer

zuclopenthixol

B With this genotype the exposure to zuclopenthixol is potentially increased. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Insufficient data to allow calculation of dose adjustment. Be alert to low zuclopenthixol plasma concentrations or select alternative drug (flupenthixol, quetiapine, olanzapine, clozapine).

CYP2D6: UM Ultrarapid Metabolizer

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: Remarkably reduced expression of the enzyme

It should be noted that efficacy and safety of a drug may be influenced byother factors in addition to genotype. E.g. the phenotype of an enzyme could be markedly different than that predicted from the genotype due to increased expression or inhibition of the enzyme. On the other hand, drug response can be affected by several other proteins or the gene might have variants not examined by this test.

RAW DATA

Gene	RS	Genotype
CYP1A2	rs12720461	C/C
CYP1A2	rs2069514	G/G
CYP1A2	rs2069526	T/T
CYP1A2	rs35694136	T/T
CYP1A2	rs762551	A/A
CYP2B6	rs28399499	T/T
CYP2B6	rs3211371	C/C
CYP2B6	rs34223104	T/T
CYP2C19	rs12248560	C/C
CYP2C19	rs17884712	G/G
CYP2C19	rs28399504	A/A
CYP2C19	rs41291556	T/T
CYP2C19	rs4244285	G/A
CYP2C19	rs4986893	G/G
CYP2C19	rs56337013	C/C
CYP2C19	rs6413438	C/C
CYP2C19	rs72552267	G/G
CYP2C19	rs72558186	T/T
CYP2C9	rs1057910	A/A
CYP2C9	rs1799853	C/C
CYP2C9	rs28371685	C/C
CYP2C9	rs28371686	C/C
CYP2C9	rs56165452	T/T
CYP2C9	rs9332131	A/A
CYP2D6	CNV	3
CYP2D6	rs1065852	G/G
CYP2D6	rs1135840	C/G
CYP2D6	rs16947	G/A
CYP2D6	rs28371706	G/G
CYP2D6	rs28371725	C/C
CYP2D6	rs35742686	T/T

CYP2D6	rs3892097	C/C
CYP2D6	rs5030655	A/A
CYP2D6	rs5030656	TCT/TCT
CYP2D6	rs5030862	C/C
CYP2D6	rs5030865	C/C
CYP2D6	rs5030867	T/T
CYP2D6	rs59421388	C/C
CYP3A4	rs12721629	G/G
CYP3A4	rs2740574	T/T
CYP3A4	rs35599367	G/G
CYP3A4	rs4986910	A/A
CYP3A4	rs4987161	A/A
CYP3A4	rs55785340	A/A
CYP3A5	rs10264272	C/C
CYP3A5	rs28365083	G/G
CYP3A5	rs28383468	G/G
CYP3A5	rs28383479	C/C
CYP3A5	rs41303343	-/-
CYP3A5	rs55817950	G/G
CYP3A5	rs776746	C/C
F2	rs1799963	G/G
F5	rs6025	C/C
SLCO1B1	rs4149056	T/T
VKORC1	rs9923231	T/T