Yhtyneet Medix

You were tested for 11 genes, which 4 may affect the efficacy or safety of your medication: **CYP2C19, CYP2C9, SLCO1B1, VKORC1**

Your genetic factors may affect the efficacy or safety of 51 drugs.

TEST SUMMARY

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DRUGS WITH GENETIC VARIATION OF SIGNIFICANT CLINICAL RELEVANCE

simvastatin

DRUGS WITH GENETIC VARIATION OF SOME CLINICAL RELEVANCE

citalopram, escitalopram, fosphenytoin, phenytoin, voriconazole, warfarin

DRUGS WITH GENETIC VARIATION OF MINOR CLINICAL RELEVANCE

acenocoumarol, amitriptyline, atorvastatin, brivaracetam, caffeine, carisoprodol, celecoxib, clobazam, clomipramine, clopidogrel, clozapine, diazepam, diclofenac, doxepin, dronabinol, eliglustat, esomeprazole, flibanserin, flurbiprofen, fluvastatin, glibenclamide, glimepiride, imipramine, lacosamide, lansoprazole, lesinurad, losartan, lovastatin, moclobemide, olanzapine, omeprazole, pantoprazole, paroxetine, phenprocoumon, pimozide, piroxicam, pravastatin, quinidine, rosuvastatin, sertraline, tamoxifen, tetrabenazine, trimipramine, vincristine

DRUGS WITH NO CLINICALLY RELEVANT GENETIC VARIATION

arformoterol, aripiprazole, atomoxetine, brexpiprazole, carvedilol, cevimeline, codeine, darifenacin, desipramine, desvenlafaxine, deutetrabenazine, dextromethorphan, donepezil, duloxetine, efavirenz, eltrombopag, estradiol, estriol, ethinylestradiol, fesoterodine, flecainide, fluoxetine, flupenthixol, fluvoxamine, galantamine, gefitinib, haloperidol, iloperidone, irbesartan, metoprolol, mirabegron, mirtazapine, modafinil, nebivolol, nefazodone, nevirapine, nortriptyline, ondansetron, oxycodone, palonosetron, perphenazine, prasugrel, primaquine, propafenone, propranolol, protriptyline, rabeprazole, ranolazine, risperidone, romiplostim, rucaparib, sertindole, tacrolimus, terbinafine, thioridazine, tibolone, ticagrelor, tolterodine, tramadol, tropisetron, umeclidinium, valbenazine, venlafaxine, vortioxetine, zuclopenthixol

Drug safety and efficacy (CYP1A2)

CYP1A2 is a liver enzyme which mediates metabolism of several drugs, caffeine and cancer-causing agents. Smoking, certain drugs and other exposures enhance the production of the enzyme. There is some genetic variation concerning CYP1A2 which may affect the efficacy of certain drugs. Environmental and drug exposures are likely more important factors altering the enzyme activity, though.

NORMAL | HIGH | LOW

Genotype of unknown clinical significance

*1D/*1J

13.05.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 5 of 5 single nucleotide polymorphisms (SNP).

Drug safety and efficacy (CYP2B6)

CYP2B6 is a liver enzyme. There is genetic variation concerning its activity, but there is no wide, coherent scientific evidence of how this affects drug metabolism. However, the genetic variation in CYP2B6 may affect for example the metabolism of HIV therapeutics.

NORMAL | DECREASED

Normal metabolism

*1/*1

13.05.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 3 of 3 single nucleotide polymorphisms (SNP).

Drug safety and efficacy (CYP2C19)

CYP2C19 is a liver enzyme that is responsible for the metabolism of many pharmaceuticals. These include several psychiatric and cardiovascular medications, for example. The activity of CYP2C19 can be exceptionally rapid or slow, depending on the genetic makeup of the individual. This either increases or lowers the efficacy of specific drugs. The CYP2C19 genetic test helps to determine the right medication with the right dose tailored to your personal genome.

PM | LPM | IM | LIM | NM | **RM** | UM

RM Rapid Metabolizer

*1/*17

13.05.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 10 of 10 single nucleotide polymorphisms (SNP).

Drug safety and efficacy (CYP2C9)

CYP2C9 is a liver enzyme that is responsible for the metabolism of many pharmaceuticals. The activity of CYP2C9 can be exceptionally rapid or slow, depending on the genetic makeup of the individual. This either increases or lowers the efficacy of specific drugs. The CYP2C9 genetic test helps to determine the right medication with the right dose tailored to your personal genome.

PM | LPM | **IM** | LIM | NM

IM Intermediate metabolizer

*1/*2

13.05.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 6 of 6 single nucleotide polymorphisms (SNP).

Drug safety and efficacy (CYP2D6)

CYP2D6 is a liver enzyme that is responsible for the metabolism of many pharmaceuticals. These include several antidepressants and pain medications, for example. The activity of CYP2D6 can be exceptionally rapid or slow, depending on the genetic makeup of the individual. These individuals should avoid certain drugs that are metabolized through the CYP2D6 enzyme. The CYP2D6 genetic test helps to determine the right medication with the right dose tailored to your personal genome.

NM Normal Metabolizer

*1/*6

13.05.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 14 of 14 single nucleotide polymorphisms (SNP).

Drug safety and efficacy (CYP3A4)

CYP3A4 is a liver enzyme which mediates metabolism of more drugs than any other human enzyme. Several drugs alter the activity of this enzyme and there is some genetic variation concerning CYP3A4. Due to the genetic variation the efficacy of certain drugs may be altered.

Normal metabolism

*1/*1

13.05.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 6 of 6 single nucleotide polymorphisms (SNP).

Drug safety and efficacy (CYP3A5)

CYP3A5 is a liver enzyme that is responsible for the metabolism of many pharmaceuticals. The most important of these is tacrolimus, an antirejection drug for organ transplantation. The activity of CYP3A5 might be exceptionally low, depending on the genetic composition of the individual. Majority of white people are poor CYP3A5 metabolizers. The variation alters the needed doses of certain drugs between individuals.

PM Poor metabolizer

*3/*3

13.05.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 7 of 7 single nucleotide polymorphisms (SNP).

Blood coagulation factor II (F2, prothrombin)

Blood coagulation factors assist in blood clotting when a blood vessel is damaged. These coagulation factors do not typically cause any harm to a person. However, some people possess a genetic variant, which leads to an increased risk of venous thrombosis. For these individuals, the risk of getting blood clots when taking hormonal contraceptives is significantly higher than normal. This genetic test shows whether or not you have an elevated risk of venous thrombosis.

No increased risk of venous thromboembolism

WT/WT

13.05.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

Blood coagulation factor V (F5 Leiden)

Blood coagulation factors assist in blood clotting when a blood vessel is damaged. These coagulation factors do not typically cause any harm to a person. However, some people possess a genetic variant, which leads to an increased risk of venous thrombosis. For these individuals, the risk of getting blood clots when taking hormonal contraceptives is significantly higher than normal. This genetic test shows whether or not you have an elevated risk of venous thrombosis.

No increased risk of venous thromboembolism

WT/WT

13.05.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

Drug safety and efficacy (SLCO1B1)

SLCO1B1 gene is associated with the efficacy of statins – a class of drugs that are commonly used to lower cholesterol levels. Some people possess a genetic variant that impedes the transportation of statins through the blood circulation to the liver. Individuals with an exceptionally poor activity of SLCO1B1 have an increased risk of myopathy when taking statins. This genetic test shows helps to determine whether or not you possess this genetic variant. This information can be used to select the right medical treatment for you.

Decreased function

*1/*5

13.05.2016 YHTYNEET MEDIX LABORATORIOT

Analyzed 1 of 1 single nucleotide polymorphisms (SNP).

Drug safety and efficacy (VKORC1)

VKORC1 (vitamin K epoxide reductase) is an enzyme that affects the starting dosage of warfarin. Warfarin is used to prevent and treat thrombotic disorders. This genetic test is a part of the diagnostics that helps to determine the proper warfarin dosage.

Reduced expression of the enzyme

*1/*2

13.05.2016 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 — With this genotype the metabolism of acenocoumarol is potentially decreased. 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 during dose titration and after initiating or discontinuing NSAIDs.

CYP2C9: IM Intermediate metabolizer

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.

VKORC1: Reduced expression of the enzyme

amitriptyline

B — With this genotype the exposure to amitriptyline is potentially decreased. Therefore its use should be avoided. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Consider alternative drug not metabolized by CYP2C19 (alternative TCAs: nortriptyline and desipramine). If use is warranted, 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).

CYP2C19: RM Rapid Metabolizer

A — Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

arformoterol

A — Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

aripiprazole

A — Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

atomoxetine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

atorvastatin

B Label-recommended dosage. With this genotype the risk for statin-induced myopathy may be increased but less for other statins than simvastatin.

SLCO1B1: Decreased function

A Label-recommended dosing and administration.

CYP3A4: Normal metabolism

brexpiprazole

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

brivaracetam

B Label-recommended dosing and administration.

CYP2C19: RM Rapid Metabolizer

caffeine

B Unknown metabolism of caffeine. This genotype is different from the most common genotype. However, there is no wide, coherent scientific evidence of its implication for the metabolism of caffeine.

CYP1A2: Genotype of unknown clinical significance

carisoprodol

B Label-recommended dosing and administration.

CYP2C19: RM Rapid Metabolizer

carvedilol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

celecoxib

B Label-recommeded dosage. Be alert for adverse drug effects since exposure to celecoxib is potentially increased with this genotype.

CYP2C9: IM Intermediate metabolizer

cevimeline

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

citalopram

C With this genotype the exposure to citalopram is potentially decreased which may lead to insufficient efficacy. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Consider an alternative drug not predominantly metabolized by CYP2C19.

CYP2C19: RM Rapid Metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

clobazam

B Label-recommended dosing and administration.

CYP2C19: RM Rapid Metabolizer

clomipramine

B 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 and CYP2C19 to other tricyclics including clomipramine: With this genotype the exposure to clomipramine is potentially decreased. Therefore its use should be avoided. Consider alternative drug not metabolized by CYP2C19 (alternative TCAs: nortriptyline and desipramine). If use is warranted, 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).

CYP2C19: RM Rapid Metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

clopidogrel

B Label-recommended dosing and administration. With this genotype the efficacy of clopidogrel to inhibit thrombocyte aggregation is potentially decreased but there is no consistent evidence of its clinical significance.

CYP2C9: IM Intermediate metabolizer

A Label-recommended dosing and administration.

CYP2C19: RM Rapid Metabolizer

clozapine

B Label-recommended dosage. This genotype is different from the most common genotype. However, there is no wide, consistent scientific evidence of its implication for the efficacy or the adverse effects of the drug.

CYP1A2: Genotype of unknown clinical significance

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

codeine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

darifenacin

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

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

dextromethorphan

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

diazepam

B Label-recommended dosing and administration.

CYP2C19: RM Rapid Metabolizer

diclofenac

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

CYP2C9: IM Intermediate metabolizer

donepezil

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

doxepin

B 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 and CYP2C19 to other tricyclics including doxepin: With this genotype the exposure to doxepin is potentially decreased. Therefore its use should be avoided. Consider alternative drug not metabolized by CYP2C19 (alternative TCAs: nortriptyline and desipramine). If use is warranted, 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).

CYP2C19: RM Rapid Metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

dronabinol

B Label-recommended dosing and administration. With this genotype the exposure to dronabinol is potentially increased (up to 2- to 3-fold higher exposure as compared to normal metabolizers). According to the drug label approved by U.S. Food and Drug Administration (FDA), monitoring for increased adverse reactions is recommended in patients known to carry genetic variants associated with diminished CYP2C9 function.

CYP2C9: IM Intermediate metabolizer

duloxetine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

efavirenz

A Label-recommended dosing and administration.

CYP2B6: Normal metabolism

eliglustat

B For normal CYP2D6 metabolizers the dose is 84 mg twice daily. If there is strong/moderate inhibitor drugs of CYP3A4 and CYP2D6 concomitantly in use, the drug is contraindicated.

CYP2D6: NM Normal 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

C With this genotype the exposure to escitalopram is potentially decreased which may lead to insufficient efficacy. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Consider an alternative drug not predominantly metabolized by CYP2C19.

CYP2C19: RM Rapid Metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

esomeprazole

B With this genotype, the efficacy of esomeprazole treatment is potentially reduced. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Helicobacter pylori eradication: increase dose by 50 - 100%. Be extra alert to insufficient response. Other indications: be extra alert to insufficient response. Consider dose increase by 50 - 100%.

CYP2C19: RM Rapid 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

flecainide

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

flibanserin

B Label-recommended dosing and administration.

CYP2C19: RM Rapid Metabolizer

B Label-recommended dosing and administration.

CYP2C9: IM Intermediate metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

flupenthixol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

fluvastatin

B Label-recommended dosage. With this genotype the risk for statin-induced myopathy may be increased but less for other statins than simvastatin.

SLCO1B1: Decreased function

fosphenytoin

C With this genotype the metabolism of phenytoin is reduced and thus the risk of toxicities is increased. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Consider 25% reduction of recommended starting maintenance dose. Subsequent doses should be adjusted according to therapeutic drug monitoring and response.

CYP2C9: IM Intermediate metabolizer

gefitinib

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

glimepiride

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

CYP2C9: IM Intermediate metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

fluoxetine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

flurbiprofen

B With this genotype the exposure to flurbiprofen is potentially increased. The drug should be used with caution.

CYP2C9: IM Intermediate metabolizer

fluvoxamine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

galantamine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

glibenclamide

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

CYP2C9: IM Intermediate metabolizer

haloperidol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

iloperidone

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

imipramine

B 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 and CYP2C19 to other tricyclics including imipramine: With this genotype the exposure to imipramine is potentially decreased. Therefore its use should be avoided. Consider alternative drug not metabolized by CYP2C19 (alternative TCAs: nortriptyline and desipramine). If use is warranted, 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).

CYP2C19: RM Rapid Metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

irbesartan

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

CYP2C9: IM Intermediate metabolizer

lacosamide

B Label-recommended dosing and administration.

CYP2C19: RM Rapid Metabolizer

lansoprazole

B With this genotype, the efficacy of lansoprazole treatment is potentially reduced. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Helicobacter pylori eradication: increase dose by 200%. Be extra alert to insufficient response. Other incications: be extra alert to insufficient response. Consider dose increase by 200%.

CYP2C19: RM Rapid Metabolizer

lesinurad

B With this genotype the exposure to lesinurad is potentially increased. The drug should be used with caution.

CYP2C9: IM Intermediate metabolizer

losartan

B Label-recommended dosing and administration. With this genotype the metabolism of losartan to its active metabolite is potentially decreased which may reduce the treatment efficacy. Scientific evidence for this is scarce though.

CYP2C9: IM Intermediate metabolizer

lovastatin

B Label-recommended dosage. With this genotype the risk for statin-induced myopathy may be increased but less for other statins than simvastatin.

SLCO1B1: Decreased function

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

moclobemide

B Label-recommended dosing and administration.

CYP2C19: RM Rapid Metabolizer

modafinil

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

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: Normal metabolism

nortriptyline

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

olanzapine

B Label-recommended dosage. This genotype is different from the most common genotype. However, there is no wide, consistent scientific evidence of its implication for the efficacy or the adverse effects of the drug.

CYP1A2: Genotype of unknown clinical significance

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

omeprazole

B With this genotype, the efficacy of omeprazole treatment is potentially reduced. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Helicobacter pylori eradication: increase dose by 100 - 200%. Be extra alert to insufficient response. Other indications: be extra alert to insufficient response. Consider dose increase by 100 - 200%.

CYP2C19: RM Rapid Metabolizer

ondansetron

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

oxycodone

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

palonosetron

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

pantoprazole

B With this genotype, the efficacy of pantoprazole treatment is potentially reduced, though the scientific evidence of this is inconsistent. Recommendation by a Dutch board of experts (Dutch Pharmacogenetics Working Group): Helicobacter pylori eradication: increase dose by 400%. Be extra alert to insufficient response. Other indications: be extra alert to insufficient response. Consider dose increase by 400%.

CYP2C19: RM Rapid Metabolizer

paroxetine

B Label-recommended dosage. This genotype is different from the most common genotype. However, there is no wide, coherent scientific evidence of its implication for the efficacy or the adverse effects of the drug.

CYP1A2: Genotype of unknown clinical significance

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

perphenazine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

phenprocoumon

B With this genotype the metabolism of phenprocoumon is potentially decreased. 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.

CYP2C9: IM Intermediate metabolizer

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.

VKORC1: Reduced expression of the enzyme

phenytoin

C With this genotype the metabolism of phenytoin is reduced and thus the risk of toxicities is increased. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Consider 25% reduction of recommended starting maintenance dose. Subsequent doses should be adjusted according to therapeutic drug monitoring and response.

CYP2C9: IM Intermediate metabolizer

pimozide

B Label-recommended dosing and administration. According to the drug label approved by the U.S. Food and Drug Administration (FDA) the titration interval is two days for adults and three days for children. The recommended maximum dose is 10 mg/day for adults and 0.5 mg/kg/day for children.

CYP2D6: NM Normal Metabolizer

piroxicam

B Label-recommended dosing and administration. With this genotype the exposure to piroxicam and the risk for gastrointestinal bleeding are potentially increased.

CYP2C9: IM Intermediate metabolizer

prasugrel

A Label-recommended dosing and administration.

CYP2B6: Normal metabolism

A Label-recommended dosing and administration.

CYP2C19: RM Rapid Metabolizer

A Label-recommended dosing and administration.

CYP2C9: IM Intermediate metabolizer

A Label-recommended dosing and administration.

CYP3A5: PM Poor metabolizer

pravastatin

B Label-recommended dosage. With this genotype the risk for statin-induced myopathy may be increased but less for other statins than simvastatin.

SLCO1B1: Decreased function

primaquine

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

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

rabeprazole

A Label-recommended dosing and administration.

CYP2C19: RM Rapid Metabolizer

ranolazine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

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

rosuvastatin

B Label-recommended dosage. With this genotype the risk for statin-induced myopathy may be increased but less for other statins than simvastatin.

SLCO1B1: Decreased function

rucaparib

A Label-recommended dosing and administration.

CYP1A2: Genotype of unknown clinical significance

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

sertindole

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

sertraline

B With this genotype the exposure to sertraline is potentially decreased which may lead to insufficient efficacy. The evidence is scarce though, and therefore this recommendation is classified as optional. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Initiate therapy with recommended starting dose. If patient does not respond to recommended maintenance dosing, consider alternative drug not predominantly metabolized by CYP2C19.

CYP2C19: RM Rapid Metabolizer

simvastatin

D With this genotype the risk for simvastatin-induced myopathy is increased. Prescribe a lower dose or consider an alternative statin (e.g. pravastatin or rosuvastatin); consider routine creatine kinase surveillance.

SLCO1B1: Decreased function

A Label-recommended dosing and administration.

CYP3A4: Normal metabolism

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

tamoxifen

B Metabolism of tamoxifen is variable on different allelic combinations which fall under the phenotype of normal metabolizer. Check the exact CYP2D6 star allele genotype from the pharmacogenetic report and choose the dosing guideline by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC) according to the activity

terbinafine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

score (AS) of the CYP2D6 enzyme. AS 1.5 to 2.0 (a pair of two normal function alleles (e.g. *1, *2, *34, *35, *39) OR a pair of a normal function allele and a reduced function allele (e.g. *9, *10, *17, *29, *41): Initiate therapy with recommended standard of care dosing (tamoxifen 20 mg/day). Avoid moderate and strong CYP2D6 inhibitors. AS 1.0 (a pair of a normal function allele (e.g. *1, *2, *34, *35, *39) and a no function allele (e.g. *3, *5, *6, *7, *8, *11, *12, *14A, *15, *19, *20, *69) OR a pair of two reduced function alleles (e.g. *9, *10, *17, *29, *41)): Lower endoxifen (an active tamoxifen metabolite) concentrations compared to normal metabolizers; higher risk of breast cancer recurrence, event-free and recurrence-free survival compared to normal metabolizers. Consider hormonal therapy such as an aromatase inhibitor for postmenopausal women or aromatase inhibitor along with ovarian function suppression in premenopausal women, given that these approaches are superior to tamoxifen regardless of CYP2D6 genotype. If aromatase inhibitor use is contraindicated, consideration should be given to use a higher but FDA (or other drug administration authority) approved tamoxifen dose (40 mg/day). Avoid CYP2D6 strong to weak inhibitors. This recommendation is graded by CPIC as 'strong' for AS 1.5-2.0, 'moderate' for AS 1.0 with allele combinations including *10 allele and 'optional' for AS 1.0 with allele combinations without *10 allele (data extrapolated from evidence considering *10 allele).

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

tetrabenazine

B Label-recommended dosage. According to the U.S. Food and Drug Administration (FDA) the recommended maximum daily dose is 100 mg with a maximum single dose of 37.5 mg.

CYP2D6: 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: RM Rapid Metabolizer

tolterodine

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

tramadol

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

trimipramine

B 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 and CYP2C19 to other tricyclics including trimipramine: With this genotype the exposure to trimipramine is potentially decreased. Therefore its use should be avoided. Consider alternative drug not metabolized by CYP2C19 (alternative TCAs: nortriptyline and desipramine). If use is warranted, utilize therapeutic drug monitoring to guide dose adjustments. This recommendation applies to higher

tropisetron

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

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).

CYP2C19: RM Rapid Metabolizer

A Label-recommended dosing and administration.

CYP2D6: NM Normal Metabolizer

umeclidinium

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

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 decreased and probality of achieving therapeutic concentrations with standard dosing is modest. Recommendation by an international board of experts, Clinical Pharmacogenetics Implementation Consortium (CPIC): Choose an alternative agent that is not dependent on CYP2C19 metabolism as primary therapy in lieu of voriconazole. Such agents include isavuconazole, liposomal amphotericin B, and posaconazole. Recommendation for pediatric patients: Initiate therapy with recommended standard case dosing. Use therapeutic dose monitoring to titrate dose to therapeutic trough concentrations.

CYP2C19: RM Rapid 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*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: IM Intermediate metabolizer

zuclopenthixol

A Label-recommended dosing and administration.

CYP2D6: NM Normal 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: Reduced expression of the enzyme

Do not make changes in drug dosage without consulting a licenced physician. 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.