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Genetics for people

Pharmacogenetics

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BASIC

PHARMACOLOGICAL COMPATIBILITY

The pharmacological compatibility according to gene-drug interaction for each of the drugs analysed in the test is shown below. The drugs were chosen following pharmacogenetic annotations approved by the major expert consortia: US Food and Drug Administration (FDA), European Medicines Agency (EMA), Swiss Agency of Therapeutic Products (Swissmedic), Pharmaceuticals and Medical Devices Agency, Japan (PMDA) and Health Canada (Santé Canada) (HCSC).
Note: Drugs categories contain other drugs not listed due to the absence of pharmacogenetic annotations.

In the table, the drugs considered for each category are classified according to their potential impact into ***'No associated impact'***, ***'Limited impact'***, ***'Moderate impact'*** and ***'High impact'***. Drugs classified as ***'No associated impact'*** are those in which no analysed risk variants have been found in the patient. It is recommended to pay special attention to clinical notes and therapeutic recommendations for those drugs classified as ***'Moderate impact'*** and ***'High impact'***, which may include a drug change or dose modification, among others.

Category	High impact	Moderate impact	Limited impact	No associated impact
NSAIs		Aspirin Ketoprofen	Celecoxib Diclofenac Ibuprofen	
Antimigraine		Sumatriptan		
Opioids		Fentanyl Oxycodone	Buprenorphine Codeine Methadone Morphine Tramadol	
Local anaesthetics		Rocuronium Propofol	Sevoflurane	Enflurane Halothane Methoxyflurane Desflurane Isoflurane Ketamine
Corticosteroids		Dexamethasone		
Anti-infectives		Isoniazid	Atazanavir Efavirenz Nevirapine Ritonavir Voriconazole	

Category	High impact	Moderate impact	Limited impact	No associated impact
Anxiolytics		Nitrous oxide Lorazepam	Alprazolam	
Antidepressant	Amitriptyline Citalopram Clomipramine Escitalopram Imipramine Mirtazapine Sertraline Trimipramine	Duloxetine Fluoxetine	Desipramine Fluvoxamine Nortriptyline Paroxetine Venlafaxine	
Anti-epileptic		Lamotrigine Oxcarbazepine Topiramate	Valproic Acid Carbamazepine Phenytoin Gabapentin Mephenytoin	Pregabalin
Antipsychotic		Clozapine Olanzapine	Aripiprazole Haloperidol Quetiapine Risperidone	Thioridazine
ADHD			Methylphenid-ate	Dextroamphet-amine
Antiemetic			Ondansetron	
Tabaquism	Bupropion			
Antiarrhythmic		Digoxin		
Anticoagulant	Warfarin	Acenocoumarol Phenprocou-mon		
Antidiabetic			Metformin	Sitagliptin Vildagliptin
Antiplatelet	Clopidogrel			
Antihypertens-ives		Losartan	Enalapril	

Category	High impact	Moderate impact	Limited impact	No associated impact
Statins	Atorvastatin Fluvastatin Lovastatin Pitavastatin Pravastatin Rosuvastatin Simvastatin	Cerivastatin		
Beta blocking agents			Atenolol	Bisoprolol
Respiratory		Montelukast Salbutamol	Triamcinolone	
Oncology	Fluorouracil	Cyclophosph-amide Doxorubicin Imatinib	Cisplatin Thioguanine	
Immunosup-pressants	Tacrolimus	Mycophenolic Acid Methotrexate Sirolimus	Azathioprine Cyclosporine Mercaptopurine	
Proton pump	Omeprazole		Lansoprazole	Esomeprazole Rabeprazole
Diuretics		Allopurinol Spironolactone	Hydro-chlorothiazide Furosemide	
Urological	Sildenafil			
Ophthalmologic		Latanoprost		

DETAILED RESULTS

All the drugs analysed that have been classified as **High impact**, **Moderate impact** **and** **Limited impact** by MyPharma Basic pharmacogenetic algorithm are shown in detail below.

Each drug is reported in a table containing the genes (**Gene**) and details of the single nucleotide variants (**SNP**) or haplotypes interacting with it (**Variant/Haplotype**). In addition, the column **Level of evidence** indicates the level of evidence for the drug-gene variant combination (1A, 1B, 2A, 2B, 3) from the Pharmacogenomics Knowledge Base (PharmGKB), drug regulatory agencies (FDA, EMA) and international pharmacogenetics consortia (CPIC and DPWG), followed by the **Affected parameter**: [E]Efficacy, [D]Dose, [T]Toxicity, [O]Other and [Pk]Pharmacokinetics. Finally, the specific **clinical annotations** for each affected variant are included, based on the recommendations in the PharmGKB database.

The therapeutic recommendation associated with each medicine is shown after the table, in accordance to the results and information provided.

	Amitriptyline			N° AFFECTED VARIANTS 2/14
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs2032583	3	D E **T** O Pk	Increased risk of adverse effects
CYP2C19	*2	1A	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends using an alternative drug for slow, rapid or ultrarapid CYP2C19 metabolisers and for slow or ultrarapid CYP2D6 metabolisers. If it is to be administered, reduce the dose by 25% in intermediate metabolisers and 50% in slow metabolisers.

	Citalopram			N° AFFECTED VARIANTS 19/33
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
-	rs585719	3	D **E** T O Pk	Reduced response to treatment
	rs4675690	3	D E **T** O Pk	Increased risk of suicidal ideation
ABCB1	rs2032583 rs2235040	3	D E **T** O Pk	Increased risk of adverse effects
BDNF	rs6265	3	D **E** T O Pk	Reduced response to treatment
CRHR2	rs2270007	3	D **E** T O Pk	Reduced response to treatment
ERICH3	rs11580409	3	D **E** T O Pk	Reduced response to treatment

Citalopram				N° AFFECTED VARIANTS 19/33
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
FKBP5	rs1360780	3	D **E** T O Pk	Reduced response to treatment
GLDC	rs10975641	3	D **E** T O Pk	Reduced response to treatment
GRIA3	rs4825476	3	D E **T** O Pk	Increased risk of suicidal ideation
HTR1B	rs6296	3	D E **T** O Pk	Increased risk of adverse effects
HTR2A	rs7997012	3	D **E** T O Pk	Reduced response to treatment
	rs6313	3	D E **T** O Pk	Increased risk of adverse effects
REEP5	rs153549 rs153560	3	D **E** T O Pk	Reduced response to treatment
SRP19	rs495794	3	D **E** T O Pk	Reduced response to treatment
CYP2C19	*2	1A	D E **T** O **Pk**	Increased risk of adverse effects and reduced metabolism
CYP2D6	*1	3	**D** E T O Pk	Need for higher doses
	*2	3	**D** E T O Pk	There is no annotation for this drug-haplotype interaction. However, effects have been observed in standard activity haplotypes compared to reduced or increased activity haplotypes and consultation with your physician is recommended.

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends an alternative drug in ultrarapid and slow metabolisers that is not metabolised by CYP2C19. If administered, dose reduction by 50% is recommended. The DPWG recommends not to exceed the specific daily dose for slow and intermediate metabolisers.

Clomipramine				N° AFFECTED VARIANTS 2/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
FKBP5	rs1360780	3	D **E** T O Pk	Reduced response to treatment
CYP2C19	*2	1A	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends an alternative drug for CYP2D6 ultrarapid or slow metabolizers and CYP2C19 ultrarapid, rapid or slow metabolizers. If clomipramine is warranted, consider a 50% dose reduction in CYP2D6 or CYP2C19 slow metabolizers. For CYP2D6 intermediate metabolizers, a 25% dose reduction should be considered.

Escitalopram				N° AFFECTED VARIANTS 11/16
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
-	rs2069521	3	D E T O **Pk**	Reduced metabolism
BDNF	rs962369	3	D E **T** O Pk	Increased risk of suicidal ideation
CYP1A2	rs4646425 rs4646427	3	D E T O **Pk**	Reduced metabolism
	rs2069526	3	D E T O **Pk**	Reduced metabolism
ERICH3	rs11580409	3	D **E** T O Pk	Reduced response to treatment
GLDC	rs10975641	3	D **E** T O Pk	Reduced response to treatment
HTR1B	rs11568817	3	D E **T** O Pk	Increased risk of adverse effects
HTR2A	rs6311	3	D E **T** O Pk	Increased risk of adverse effects
HTR2C	rs6318	3	D **E** T O Pk	Reduced response to treatment
CYP2C19	*2	1A	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where the CPIC recommends using an alternative drug that is not metabolised by CYP2C19 for ultrarapid or slow metabolisers. The DPWG recommends not exceeding daily doses for slow and intermediate metabolisers and an alternative drug for ultrarapid metabolisers.

Imipramine				N° AFFECTED VARIANTS 1/3
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C19	*2	1A	D E T O **Pk**	Decreased metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends an alternative drug for CYP2D6 ultrarapid or slow metabolizers and CYP2C19 ultrarapid, rapid or slow metabolizers. If imipramine is warranted, consider a 50% dose reduction in CYP2D6 or CYP2C19 slow metabolizers. For CYP2D6 intermediate metabolizers, a 25% dose reduction should be considered.

Mirtazapine				N° AFFECTED VARIANTS 6/9
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
FKBP5	rs4713916	3	D **E** T O Pk	Reduced response to treatment
RABEP1	rs1000940	3	D E T **O** Pk	Increased risk of adverse effects
SH2B1	rs3888190	3	D E **T** O Pk	Increased risk of adverse effects
TPH2	rs10879346 rs1487278	3	D **E** T O Pk	Reduced response to treatment
CYP2B6	*1	3	D **E** T **O** Pk	Lower response to treatment and lower metabolism

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a high risk impact, it is recommended to seek medical assessment.

Sertraline				N° AFFECTED VARIANTS 6/9
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs2032583 rs2235040	3	D E **T** O Pk	Increased risk of adverse effects
REEP5	rs153549 rs153560	3	D **E** T O Pk	Reduced response to treatment
SRP19	rs495794	3	D **E** T O Pk	Reduced response to treatment
CYP2C19	*2	1A	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where the CPIC recommends reducing the dose to 50% and titrating the dose according to response or using an alternative drug that is not metabolised by CYPC219 for slow metabolisers. The DPWG recommends not exceeding 75 mg/day in slow metabolisers, and titrating the dose according to response, adverse effects and/or plasma concentration.

Trimipramine				N° AFFECTED VARIANTS 1/4
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C19	*2	1A	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends using an alternative drug for slow, rapid or ultrarapid CYP2C19 metabolisers and for slow or ultrarapid CYP2D6 metabolisers. If it is to be administered, reduce the dose by 25% in intermediate metabolisers and 50% in slow metabolisers.

Bupropion				N° AFFECTED VARIANTS 13/15
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ANKK1	rs1800497	3	D **E** T O Pk	Reduced response to treatment
CHRNA5	rs2036527	3	D **E** T O Pk	Lower response to treatment in women
	rs16969968 rs503464	3	D **E** T O Pk	Reduced response to treatment
COMT	rs165599	3	D **E** T O Pk	Reduced response to treatment
CYP2B6	rs2279343 rs3211371	3	D **E** T O Pk	Reduced response to treatment
DRD1	rs11746641 rs11749035 rs2168631	3	D **E** T O Pk	Reduced likelihood of abstinence
GALR1	rs2717162	3	D **E** T O Pk	Reduced response to treatment
HTR2A	rs2770296	3	D **E** T O Pk	Reduced response to treatment
CYP2C19	*2	3	D E T **O** Pk	Increased drug exposure

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a high risk impact, it is recommended to seek medical assessment.

Warfarin				N° AFFECTED VARIANTS 18/38
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
-	rs12777823	1A	**D** E T O Pk	Need for lower dose
APOB	rs1367117	3	D E **T** O Pk	Increased risk of bleeding
APOE	rs7412	3	D **E** T O Pk	Increased response time from the administration
CYP2C19	rs3814637	3	**D** E T O Pk	Need for higher dose
CYP2C9	rs4917639 rs10509680	3	**D** E T O Pk	Need for higher dose
CYP4F2	rs2108622	1A	**D** E T O Pk	Need for higher dose
DNMT3A	rs2304429	3	**D** E T O Pk	Need for higher dose
EPHX1	rs1877724	3	**D** E T O Pk	Need for higher dose
GGCX	rs11676382 rs2592551	3	**D** E T O Pk	Need for higher dose
NQO1	rs1800566	3	**D E** T O Pk	Lower response to treatment and need for higher doses
POR	rs41301394	3	**D** E T O Pk	Need for higher dose
VKORC1	rs8050894 rs2359612	1B	**D** E T O Pk	Need for higher dose
	rs9934438	1B	**D E** T O Pk	Increased dose, shorter prothrombin time AUC (R)-warfarin / (S)-warfarin and increased INR time in therapeutic range (TTR)
	rs2884737	2A	**D** E T O Pk	Need for higher dose
	rs11150606	3	**D** E T O Pk	Need for higher dose

Therapeutic recommendation: There are annotations for one or more affected variants where the DPWG and CPIC recommend dose modification. For more information, **please read the specific Annex related to warfarin in detail.**

Clopidogrel				N° AFFECTED VARIANTS 9/21
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
B4GALT2	rs1061781	3	D **E** T O Pk	Increased on-treatment platelet reactivity
CYP4F2	rs2108622	3	D E T **O** Pk	Increased risk of adverse cardiac events
ITGA2	rs1062535	3	D **E** T O Pk	Increased on-treatment platelet reactivity
NOS3	rs1799983	3	D E **T** O Pk	Increased risk of in-stent restenosis
P2RY12	rs6787801	3	D **E** T O Pk	Increased on-treatment platelet reactivity
	rs2046934	3	D **E** T O Pk	Increased risk of adverse cardiac events
PEAR1	rs57731889	3	D **E** T O Pk	Increased on-treatment platelet reactivity
PTGS1	rs1330344	3	D **E** T O Pk	Increased the risk of recurrent clinical events
CYP2C19	*2	1A	D **E T** O **Pk**	Higher risk of adverse cardiovascular and cerebrovascular events, lower metabolism and lower efficacy

Therapeutic recommendation: There are annotations for one or more affected variants where the CPIC recommends alternative antiplatelet therapy for slow or intermediate CYP2C19 metabolisers. The DPWG recommends to avoid clopidogrel use in patients who are CYP2C19 slow metabolizers and are undergoing percutaneous coronary intervention, stroke or TIA. For CYP2C19 intermediate metabolizers who are undergoing percutaneous coronary intervention, stroke, or TIA, choose an alternative drug or double the dose to 150 mg/day (600 mg loading dose).

Atorvastatin				N° AFFECTED VARIANTS 22/40
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCA1	rs2230806	3	D **E** T O Pk	Decreased response to treatment
ABCB1	rs1045642 rs2032582	3	D **E** T O Pk	Decreased response to treatment
ABCC2	rs717620	3	**D** E T O Pk	Need for higher dose

Atorvastatin				N° AFFECTED VARIANTS 22/40
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCG8	rs11887534	3	D **E** T O Pk	Decreased response to treatment
AGTR1	rs5186	3	D E T O **Pk**	Reduced drug elimination
APOE	rs7412	2B	D **E** T O Pk	Decreased response to treatment
BDKRB2	rs1799722	3	D E T O **Pk**	Decreased response to treatment
COQ2	rs6535454	3	D E **T** O Pk	Increased risk of statin intolerance
	rs4693075	3	D E **T** O Pk	Increased risk of statin-related muscle symptoms
CYP3A4	rs2242480	3	D **E** T O Pk	Decreased response to treatment
CYP3A5	rs17161788	3	D **E** T O Pk	Decreased response to treatment
	*3	3	D **E** **T** O Pk	Decreased response to treatment and increased risk of myalgia and a greater degree of muscle damage
CYP7A1	rs3808607	3	D **E** T O Pk	Decreased response to treatment
MYLIP	rs9370867	3	D **E** T O Pk	Decreased ldl-c responses and less likely to achieve target ldl levels
POR	rs1057868	3	D **E** T O Pk	Smaller reduction in total cholesterol
SCARB1	rs5888	3	D **E** T O Pk	Decreased response to treatment
SLCO1B1	*5	1A	D E T O **Pk**	Increased atorvastatin concentrations
	rs4149056	1A	D E **T** O **Pk**	Increased risk of myopathy and increased exposure
	rs2306283	3	D **E** T O Pk	Smaller reduction in ldl cholesterol

Atorvastatin				N° AFFECTED VARIANTS 22/40
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
TNF	rs1800629	3	D E T **O** Pk	Decreased response to treatment
UGT1A3	*1	3	D **E** T O Pk	Decreased lactonization

Therapeutic recommendation: There are annotations for one or more affected variants where the Royal Dutch Pharmacists Association recommends choosing an alternative for patients with the SLCO1B1 521 CC or TC genotype (rs4149056) and with ADDITIONAL SIGNIFICANT RISK FACTORS for statin-induced myopathy. For patients without additional significant risk factors for statin-induced myopathy, they advise contacting their physician in case of muscle symptoms.

Fluvastatin				N° AFFECTED VARIANTS 7/13
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
APOE	rs7412	3	D **E** T O Pk	Decreased response to treatment
CETP	rs4783961	3	D **E** T O Pk	Decreased response to treatment
SLCO1B1	rs4149056	1A	D E **T** O **Pk**	Increased risk of myopathy and increased exposure
	*5	1A	D **E T** O **Pk**	Increased fluvastatin concentration and higher risk of myopathy
	rs11045819	3	D **E** T O Pk	Smaller reduction in ldl cholesterol
CYP2D6	*1	3	D **E** T O Pk	Decreased response to treatment
	*2	3	D **E** T O Pk	There is no annotation for this drug-haplotype interaction. However, effects have been observed in standard activity haplotypes compared to reduced or increased activity haplotypes and consultation with your physician is recommended.

Therapeutic recommendation: There are annotations for one or more affected variants where the Royal Dutch Pharmacists Association recommends choosing an alternative for

patients with the SLCO1B1 521 CC or TC genotype (rs4149056) and with ADDITIONAL SIGNIFICANT RISK FACTORS for statin-induced myopathy. For patients without additional significant risk factors for statin-induced myopathy, they advise contacting their physician in case of muscle symptoms.

	Lovastatin			N° AFFECTED VARIANTS 4/8
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CETP	rs708272	3	D **E** T O Pk	Decreased response to treatment
CYP3A5	rs776746	3	D **E** T O Pk	Decreased response to treatment
LDLR	rs5925	3	D **E** T O Pk	Smaller reduction in cholesterol
SLCO1B1	rs4149056	1A	D E **T** O **Pk**	Increased plasma drug concentration and increased likelihood of myopathy

Therapeutic recommendation: There are annotations for one or more affected variants where the Royal Dutch Pharmacists Association recommends choosing an alternative for patients with the SLCO1B1 521 CC or TC genotype (rs4149056) and with ADDITIONAL SIGNIFICANT RISK FACTORS for statin-induced myopathy. For patients without additional significant risk factors for statin-induced myopathy, they advise contacting their physician in case of muscle symptoms.

	Pitavastatin			N° AFFECTED VARIANTS 3/5
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCC2	rs717620	3	D E T O **Pk**	Reduced drug elimination
SLCO1B1	*5	1A	D E T O **Pk**	Increased atorvastatin concentrations
	rs4149056	1A	D E T O **Pk**	Increased plasma drug concentrations

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends prescribing ≤20mg for slow metabolisers and ≤40mg to intermediate metabolisers as a starting dose. Adjust atorvastatin doses based on disease-specific guidelines. The prescriber should be aware of the potential increased risk of myopathy, especially for the 40mg dose.

Pravastatin				N° AFFECTED VARIANTS 8/21
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCC2	rs113646094	3	D E T O **Pk**	Reduced drug elimination
ACE	rs4341	3	D **E** T O Pk	Decreased response to treatment
APOE	rs7412	3	D **E** T O Pk	Decreased response to treatment
IL1B	rs16944	3	D **E** T O Pk	Decreased response to treatment
LPL	rs328	3	D **E** T O Pk	Decreased response to treatment
MMP3	rs35068180	3	D **E** T O Pk	Decreased response to treatment
NPC1L1	rs17655652	3	D **E** T O Pk	Decreased response to treatment
SLCO1B1	rs4149056	1A	D E **T** O **Pk**	Increased risk of myopathy and increased exposure

Therapeutic recommendation: There are annotations for one or more affected variants where the Royal Dutch Pharmacists Association recommends choosing an alternative for patients with the SLCO1B1 521 CC or TC genotype (rs4149056) and with ADDITIONAL SIGNIFICANT RISK FACTORS for statin-induced myopathy. For patients without additional significant risk factors for statin-induced myopathy, they advise contacting their physician in case of muscle symptoms.

Rosuvastatin				N° AFFECTED VARIANTS 8/17
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
-	rs2808630	3	D **E** T O Pk	Decreased response to treatment
ABCA1	rs2230806	3	D **E** T O Pk	Decreased response to treatment
ABCG2	rs2231142	2A	D **E** T O Pk	Smaller reduction in ldl cholesterol
CETP	rs708272	3	D **E** T O Pk	Decreased response to treatment

Rosuvastatin				N° AFFECTED VARIANTS 8/17
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
COQ2	rs6535454	3	D E **T** O Pk	Increased risk of statin intolerance
	rs4693075	3	D E **T** O Pk	Increased risk of statin-related muscle symptoms
SLCO1B1	rs4149056	1A	D E **T** O **Pk**	Increased risk of myopathy and increased exposure
	*5	1A	D E **T** O **Pk**	Higher risk of myopathy and increased exposure to rosuvastatin

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends prescribing ≤20mg as a starting dose and adjusting rosuvastatin doses based on disease- and population-specific guidelines for slow metabolisers of SLCO1B1 or ABCG2. If a dose higher than 20mg is needed to achieve the desired efficacy, consider combination therapy (i.e. rosuvastatin plus non-statin medical therapy according to guidelines). Slow metabolisers of ABCG2 and SLOC1B1 should be prescribed ≤10mg as a starting dose.

Simvastatin				N° AFFECTED VARIANTS 10/33
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCA1	rs2230806	3	D **E** T O Pk	Decreased response to treatment
ABCB1	rs2032582	3	D **E** **T** O Pk	Increased risk of myalgia and decreased response to treatment
	rs1128503	3	D **E** **T** O Pk	Smaller reduction in ldl and total cholesterol and increased risk of myalgia
	rs1045642	3	D E **T** O Pk	Increased risk of myalgia
ABCC2	rs717620	3	**D** E T O Pk	Need for higher dose
CYP3A4	*37	3	D E T O **Pk**	There is no annotation for this drug-haplotype interaction. However, this haplotype does not have enzymatic activity, so it is recommended to consult your physician.

Simvastatin				N° AFFECTED VARIANTS 10/33
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
F3	rs3917643	3	D **E** T O Pk	Decreased response to treatment
SLCO1B1	rs4149056	1A	D E **T** O **Pk**	Increased risk of myopathy and increased exposure
	*5	1A	D E **T** O **Pk**	Increased simvastatin acid concentration and higher risk of myopathy
UGT1A9	rs2003569	3	D **E** T O Pk	Decreased response to treatment

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends prescribing an alternative statin based on the desired potency for slow SLCO1B1 metabolisers. If treatment with simvastatin is warranted in slow SLCO1B1 metabolisers, limit the dose to <20mg/day.

Fluorouracil				N° AFFECTED VARIANTS 31/77
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	3	D **E** **T** O Pk	Shorter disease-free survival time and increased risk of anaemia
ABCC2	rs3740066	3	D E **T** O Pk	Increased likelihood of nausea
	rs2273697	3	D E **T** O Pk	Increased risk of anaemia
	rs717620	3	D E **T** O Pk	Increased risk of thrombocytopenia
ABCC5	rs10937158 rs3749438	3	D E **T** O Pk	Increased risk for grade 3–4 severe diarrhea
ABCG1	rs225440	3	D E **T** O Pk	Increased risk of neutropenia
ALDH3A1	rs2228100	3	D E **T** O Pk	Increased risk of leukopenia and anemia
CBR1	rs20572	3	D E T O **Pk**	Increased drug exposure

Fluorouracil				N° AFFECTED VARIANTS 31/77
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C19	rs4244285	3	D **E** **T** O Pk	Decreased response to treatment and increased risk of neutropenia
	rs12248560	3	D E **T** O Pk	Increased risk of leukopenia
	rs4244285	3	D E **T** O Pk	Reduced metabolism
DPYD	rs17376848	1A	D E **T** O Pk	Increased risk of toxicity
	rs115632870	3	D E T **O** Pk	Decreased gene activity in response to fluorouracil exposure
EGFR	rs2293347	3	D **E** T O Pk	Decreased response to treatment
GALNT14	rs9679162	3	D **E** T O Pk	Decreased response to treatment
GSTP1	rs1695	3	D **E** T O Pk	Decreased response to treatment
HLA-G	rs17179108	3	D **E** T O Pk	Decreased response to treatment
LGR5	rs17109924	3	D **E** T O Pk	Shorter time to relapse
MTHFR	rs1801133	3	D **E** T O Pk	Decreased response to treatment
	rs1801131	3	D E **T** O Pk	Increased risk of toxicity
NOS3	rs2070744	3	D **E** T O Pk	Shorter disease-free survival time
PON1	rs662	3	D **E** T O Pk	Decreased response to treatment
SELE	rs3917412	3	D **E** T O Pk	Decreased response to treatment
SLC22A16	rs6907567	3	D **E** T O Pk	Need for higher doses
	rs714368	3	D **E** **T** **O** Pk	Increased likelihood of nausea

Fluorouracil

N° AFFECTED VARIANTS 31/77

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
TYMS	rs2847153	3	D **E** T O Pk	Lower probability of survival
	rs11280056	3	D **E T** O Pk	Increased risk of toxicity and decreased response to treatment
VEGFA	rs25648	3	D **E** T O Pk	Decreased response to treatment
XRCC1	rs1799782	3	D **E** T O Pk	Shorter survival time
XRCC3	rs861539	3	D **E** T O Pk	Lower probability of survival

Therapeutic recommendation: There are annotations for one or more affected variants where the CPIC and DPWG recommend using an alternative drug other than tegafur for slow metabolisers of DPYD. If administered, it should be at a very low dose with therapeutic monitoring. For intermediate metabolisers, a dose reduction to 50% is recommended. Patients with the AA genotype at rs67376798 may also require a 50% dose reduction. The DPWG considers DPYD genotyping as 'essential' and recommends DPYD testing before initiating treatment with fluoropyrimidines.

Tacrolimus

N° AFFECTED VARIANTS 23/41

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ABCB1	rs1128503 rs2032582	3	D **E** T O Pk	Decreased response to treatment
	rs1045642	3	D **E T** O **Pk**	Increased plasma concentrations, decreased absorption rate and increased estimated glomerular filtrarion rate (eGFR)
	rs9282564	3	D E T O **Pk**	Decreased response to treatment

Tacrolimus				N° AFFECTED VARIANTS 23/41
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP3A4	rs2242480	2A	D E T O **Pk**	Decreased metabolism
	rs4646437	2A	D E T O **Pk**	Need for higher dose
	*37	3	D E T O **Pk**	There is no annotation for this drug-haplotype interaction. However, this haplotype does not have enzymatic activity, so it is recommended to consult your physician.
	rs2740574	3	D E **T** O Pk	Greater likelihood of transplant rejection
CYP3A5	*3	1A	D E **T** O **Pk**	Decreased metabolism and increased risk of nephrotoxicity
	rs4646450	3	D E T O **Pk**	Decreased response to treatment
	rs15524	3	D E T O **Pk**	Need for higher dose
FOXP3	rs3761548	3	D E **T** O Pk	Increased risk of acute renal toxicity
HSD11B1	rs846908 rs4844880 rs846910	3	D E T O **Pk**	Increased plasma drug concentrations
IL10	rs1800896	3	**D** E T O Pk	Need for higher dose
IL18	rs1946518	3	D E T O **Pk**	Decreased metabolism
KCNJ11	rs5219	3	D E **T** O Pk	Increased risk of new-onset diabetes
NR1I2	rs3814055	3	D E T O **Pk**	Increased plasma drug concentrations
	rs2276707	3	D E T O **Pk**	Need for higher dose
PPARA	rs4253728	3	D E **T** O Pk	Decreased response to treatment
TCF7L2	rs290487	3	D E **T** O Pk	Increased risk of new-onset diabetes

Tacrolimus				N° AFFECTED VARIANTS 23/41
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C19	*2	3	**D E** T O Pk	Higher dose-normalized trough blood concentrations (C0/D) and longer post-transplantation hospital stay

Therapeutic recommendation: There are annotations for one or more affected variants where the CPIC and DPWG recommend increasing the starting dose by 1.5 to 2 times the recommended starting dose in patients who are normal or intermediate CYP3A5 metabolisers, although the total starting dose should not exceed 0.3 mg/kg/day.

Omeprazole				N° AFFECTED VARIANTS 2/3
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	3	D **E** T O **Pk**	Decreased absorption rate
CYP2C19	*2	1A	D E T O **Pk**	Decreased metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where the CPIC recommends increasing the starting daily dose and monitoring efficacy in CYP2C19 ultrarapid metabolisers. For fast and normal CYP2C19 metabolisers in the treatment of *H. Pylori* infection and erosive oesophagitis, increase the dose after initiation to the standard starting daily dose. Recommendations for intermediate and slow metabolisers for chronic treatment is to consider a 50% daily dose reduction.

Sildenafil				N° AFFECTED VARIANTS 3/4
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ACE	rs4343	3	D **E** T O Pk	Decreased response to treatment
GNB3	rs5443	3	D **E** T O Pk	Decreased response to treatment
VEGFA	rs699947	3	D **E** T O Pk	Decreased response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a high risk impact, it is recommended to seek medical assessment.

Aspirin				N° AFFECTED VARIANTS 24/46
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
-	rs2768759	3	D **E** T O Pk	Reduced response to treatment
ACE	rs4291	3	D E **T** O Pk	Increased risk of adverse effects
ADORA1	rs2228079	3	D E **T** O Pk	Increased risk of adverse effects
CEP68	rs7572857	3	D E **T** O Pk	Increased risk of adverse effects
CHIA	rs3818822	3	D E **T** O Pk	Increased risk of adverse effects
CYP4F2	rs2108622	3	D **E** T **O** Pk	Increased platelet aggregation in conjunction with clopidogrel and epinephrine
FCER1G	rs11587213	3	D E **T** O Pk	Increased risk of adverse effects in the case of chronic urticaria.
GARS1-DT	rs1074373	3	D E **T** O Pk	Increased risk of adverse effects
GP1BA	rs6065	3	D **E** T O Pk	Reduced response to treatment and increased risk of aspirin resistance
IL1B	rs1143627	3	D E **T** O Pk	Increased risk of adverse effects
IL4	rs2243250	3	D E **T** O Pk	Increased risk of adverse effects
NOS3	rs1799983	3	D E **T** O Pk	Increased risk of adverse effects
PTGER2	rs2075797	3	D E **T** O Pk	Increased risk of adverse effects
PTGER3	rs7551789	3	D E **T** O Pk	Increased risk of adverse effects
PTGIR	rs1126510	3	D E **T** O Pk	Increased risk of adverse effects
TAPBP	rs1059288 rs2071888	3	D E **T** O Pk	Increased risk of adverse effects

Aspirin				N° AFFECTED VARIANTS 24/46
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
TBXA2R	rs4523	3	D **E** T O Pk	Reduced response to treatment
	rs1131882	3	D E **T** O Pk	Increased risk of mortality in patients with type 2 diabetes
TBXAS1	rs6962291	3	D E **T** O Pk	Increased risk of adverse effects
THRA	rs11819745	3	D E **T** O Pk	Increased risk of adverse effects
TLR3	rs3775291	3	D E **T** O Pk	Increased risk of adverse effects
TN-FRSF11A	rs1805034	3	D E **T** O Pk	Increased risk of adverse effects
ZBTB22	rs3130100	3	D E **T** O Pk	Increased risk of adverse effects

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Ketoprofen				N° AFFECTED VARIANTS 1/3
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C9	*1	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Sumatriptan				N° AFFECTED VARIANTS 4/7
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
BDNF	rs6265	3	D E T **O** Pk	Increased likelihood of headache
COMT	rs4680	3	D E T **O** Pk	Increased likelihood of headache

Sumatriptan				N° AFFECTED VARIANTS 4/7
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
DRD2	rs6275	3	D E T **O** Pk	Increased likelihood of headache
GNB3	rs5443	3	D **E** T O Pk	Less likely to have reduced pain or attack frequency

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Fentanyl				N° AFFECTED VARIANTS 13/24
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	3	**D** E T O Pk	Need for higher dose
ADRB2	rs1045280	3	D E **T** O Pk	Increased risk of adverse effects
	rs1042718	3	D E **T** O Pk	Increased risk of hypotension when combined with propofol, sevofluorane or remifentanil.
CACNA1E	rs3845446	3	**D** E T O Pk	Need for higher dose
COMT	rs4680	3	D E **T** O Pk	Increased risk of adverse effects
CYP3A4	rs2242480	2A	**D E** T O Pk	Lower response to treatment and need for higher doses
	*37	3	D E T O **Pk**	There is no annotation for this drug-haplotype interaction. However, this haplotype does not have enzymatic activity, so it is recommended to consult your physician.
KCNJ6	rs2835859	3	**D** E T O Pk	Need for higher dose
MYD88	rs6853	3	D E **T** O Pk	Increased risk of adverse effects

Fentanyl				N° AFFECTED VARIANTS 13/24
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
OPRM1	rs1799971	3	D **E** T O Pk	Reduced response to treatment
	rs540825 rs9397685	3	D E **T** O Pk	Increased risk of adverse effects
CYP3A5	*3	3	D E **T** O **Pk**	Increased risk of adverse effects and reduced metabolism

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Oxycodone				N° AFFECTED VARIANTS 7/10
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	3	**D** E T O Pk	Need for higher dose
OPRD1	rs581111	3	D **E** T O Pk	Reduced response to treatment
OPRM1	rs1799971	3	D E **T** O Pk	Increased risk of adverse effects in conjunction with naloxone
CYP2D6	*1	3	D E **T** O Pk	Increased risk of opioid dependence
	*2	3	D E **T** O Pk	There is no annotation for this drug-haplotype interaction. However, effects have been observed in standard activity haplotypes compared to reduced or increased activity haplotypes and consultation with your physician is recommended.
CYP3A4	*37	3	D E T O **Pk**	There is no annotation for this drug-haplotype interaction. However, this haplotype does not have enzymatic activity, so it is recommended to consult your physician.

Oxycodone				N° AFFECTED VARIANTS 7/10
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP3A5	*3	3	**D** E T O Pk	Need for higher doses

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Rocuronium				N° AFFECTED VARIANTS 1/2
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
SLCO1B1	rs2306283	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Propofol				N° AFFECTED VARIANTS 2/3
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ADRB2	rs1042718	3	D E **T** O Pk	Increased severity of hypotension in neurosurgery
CYP2B6	rs3745274	3	**D** E T O Pk	Need for higher dose

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Dexamethasone				N° AFFECTED VARIANTS 4/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs2229109	3	D **E** T O Pk	Decreased progression-free survival (PFS) in multiple myeloma
	rs1045642 rs2032582	3	D **E** T O Pk	Reduced survival in multiple myeloma

Dexamethasone				N° AFFECTED VARIANTS 4/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
GATA3	rs3824662	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Isoniazid				N° AFFECTED VARIANTS 13/18
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C19	rs4986893	3	D E **T** O Pk	Increased risk of adverse effects
CYP2C9	rs9332096	3	D E **T** O Pk	Increased risk of adverse effects
MAFK	rs4720833	3	D E **T** O Pk	Increased risk of hepatotoxicity
NAT2	*5B *6A	1B	D E **T** O **Pk**	Increased risk of hepatotoxicity and reduced metabolism
	rs1041983	3	D E **T** O Pk	Increased risk of toxicity and hepatotoxicity
	rs1208 rs1799929 rs1799930 rs1801280	3	D E **T** O Pk	Increased risk of toxicity in conjunction with phenytoin.
	rs4646244	3	D E **T** O **Pk**	Increased risk of hepatitis and reduced drug elimination
TNF	rs1800629	3	D E **T** O Pk	Increased risk of hepatotoxicity
CYP2B6	*1	3	D E **T** O Pk	Increased risk of hepatotoxicity

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Nitrous oxide				N° AFFECTED VARIANTS 1/2
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
MTHFR	rs1801131	3	D E **T** O Pk	Increased risk of increased homocysteine levels

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Lorazepam				N° AFFECTED VARIANTS 1/1
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
UGT2B15	rs1902023	3	D E T O **Pk**	Reduced drug elimination

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Duloxetine				N° AFFECTED VARIANTS 3/5
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
DRD3	rs167770 rs324023 rs324026	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Fluoxetine				N° AFFECTED VARIANTS 9/15
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
-	rs2433320	3	D **E** T O Pk	Reduced response to treatment
BDNF	rs61888800	3	D **E** T O Pk	Reduced response to treatment
FKBP5	rs4713916	3	D **E** T O Pk	Reduced response to treatment
HTR1A	rs6295	3	D **E** T O Pk	Reduced response to treatment

Fluoxetine				N° AFFECTED VARIANTS 9/15
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
HTR1B	rs9361233	3	D **E** T O Pk	Reduced response to treatment
REEP5	rs153560	3	D **E** T O Pk	Reduced response to treatment
SERPINE1	rs1799889 rs2227631	3	D **E** T O Pk	Reduced response to treatment
SRP19	rs495794	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Lamotrigine				N° AFFECTED VARIANTS 4/5
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCG2	rs3114020	3	D E T O **Pk**	Increased plasma drug concentrations
SCN2A	rs2304016	3	D **E** T O Pk	Increased risk of experiencing resistance to antiepileptic drugs
SLC22A1	rs628031	3	D E T O **Pk**	Increased plasma drug concentrations
UGT2B7	rs7668258	3	**D** E T O Pk	Need for higher dose

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Oxcarbazepine				N° AFFECTED VARIANTS 3/4
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
SCN2A	rs2304016	3	D **E** T O Pk	Increased risk of experiencing resistance to antiepileptic drugs
UGT1A	rs2741049	3	D **E** T O Pk	Reduced response to treatment

Oxcarbazepine				N° AFFECTED VARIANTS 3/4
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
UGT2B7	rs7439366	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Topiramate				N° AFFECTED VARIANTS 1/2
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
SCN2A	rs2304016	3	D **E** T O Pk	Increased risk of experiencing drug resistance

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Clozapine				N° AFFECTED VARIANTS 16/27
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CNR1	rs1049353	3	D E **T** O Pk	Increased risk of adverse effects
COMT	rs4680	3	D **E** T O Pk	Reduced response to treatment
DRD2	rs6277	3	D E **T** O Pk	Increased risk of adverse effects
DRD3	rs6280	3	D **E** T O Pk	Reduced response to treatment
EPM2A	rs1415744	3	D **E** T O Pk	Reduced response to treatment
GCG	rs13429709	3	D E T **O** Pk	Increased risk of adverse effects
HTR1A	rs6295	3	D **E** T O Pk	Reduced response to treatment
HTR3A	rs1062613 rs2276302	3	D **E** T O Pk	Reduced response to treatment

Clozapine				N° AFFECTED VARIANTS 16/27
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ITIH3	rs2535629	3	D **E** T O Pk	Reduced response to treatment
MTHFR	rs1801131	3	D E **T** O Pk	Increased risk of adverse effects
RABEP1	rs1000940	3	D E T **O** Pk	Increased risk of adverse effects
SH2B1	rs3888190	3	D E **T** O Pk	Increased risk of adverse effects
TBC1D1	rs9852	3	D E **T** O Pk	Increased risk of adverse effects
GSTM1	*I	3	D E **T** O Pk	Increased risk of neutropenia
GSTT1	*D	3	D E **T** O Pk	Increased risk of neutropenia

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Olanzapine				N° AFFECTED VARIANTS 31/57
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs10248420 rs4728709	3	D E **T** O Pk	Increased risk of adverse effects
AHR	rs4410790	3	D E T O **Pk**	Reduced metabolism
ANKK1	rs1800497	3	D E T O **Pk**	Reduced drug exposure
CNR1	rs1049353	3	D E **T** O Pk	Increased risk of adverse effects
CYP1A1	rs2472297	3	D E T O **Pk**	Reduced metabolism
CYP1A2	rs762551	3	D **E** T O Pk	Reduced response to treatment
CYP3A43	rs472660	3	D E T O **Pk**	Reduced drug elimination

Olanzapine				N° AFFECTED VARIANTS 31/57
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
DRD2	rs1799978	3	D **E** T O Pk	Increased response time from the administration
	rs1076560	3	D **E** T O Pk	Reduced response to treatment
	rs6275 rs6279	3	D E T **O** Pk	Increased prolactin in women
	rs1124493	3	D E T **O** Pk	Lower prolactin concentration in serum
	rs2734841 rs2734842	3	D E **T** O Pk	Increased prolactin in women
	rs6277	3	D E **T** O Pk	Increased risk of adverse effects
DRD3	rs6280	3	D **E** T O Pk	Reduced response to treatment
FMO1	rs7877	3	D E T O **Pk**	Increased serum drug concentration
GCG	rs13429709	3	D E T **O** Pk	Increased risk of adverse effects
GSTM3	rs36120609	3	D E T O **Pk**	Reduced drug elimination
HTR1A	rs10042486	3	D **E** T O Pk	Reduced response to treatment
HTR2A	rs6313	3	D **E** **T** O Pk	Increased risk of adverse effects and lower response to treatment
HTR2C	rs2497538 rs518147	3	D E **T** O Pk	Increased risk of adverse effects
	rs1414334	3	D E **T** O Pk	Increased risk of adverse effects in women
MTHFR	rs1801131	3	D E **T** O Pk	Increased risk of adverse effects
PMCH	rs7973796	3	D E **T** O Pk	Increased risk of adverse effects
RABEP1	rs1000940	3	D E T **O** Pk	Increased risk of adverse effects

Olanzapine				N° AFFECTED VARIANTS 31/57
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
RGS4	rs2842030	3	D **E** T O Pk	Reduced response to treatment
SH2B1	rs3888190	3	D E **T** O Pk	Increased risk of adverse effects
TBC1D1	rs9852	3	D E **T** O Pk	Increased risk of adverse effects

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Digoxin				N° AFFECTED VARIANTS 4/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ADRB1	rs1801253	3	D **E** T O Pk	Increased risk of emergency department visits
ADRB2	rs1042713	3	D **E** T O Pk	Decreased response to treatment
NOS1AP	rs10494366	3	D E **T** O Pk	Smaller qt-interval shortening effect
NOS3	rs1799983	3	D **E** T O Pk	Increased risk of emergency department visits

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Acenocoumarol				N° AFFECTED VARIANTS 2/8
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
VKORC1	rs9934438	2A	**D** E T O Pk	Need for higher dose
CYP2C9	*1	1B	**D** E T O Pk	Higher dose requirement

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Phenprocoumon				N° AFFECTED VARIANTS 5/8
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C9	rs4086116	3	**D** E T O Pk	Need for higher dose
CYP4F2	rs2108622	3	**D** E T O Pk	Need for higher dose
PPARA	rs4253728	3	**D** E T O Pk	Need for higher dose
STX4	rs10871454	3	**D** E T O Pk	Need for higher dose
VKORC1	rs9934438	2A	**D** E T O Pk	Need for higher dose

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Losartan				N° AFFECTED VARIANTS 5/7
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	3	D **E** T O Pk	Decreased response to treatment
AGTR1	rs5186	3	D **E** T O Pk	Decreased response to treatment
CAMK1D	rs10737062 rs10752271	3	D **E** T O Pk	Decreased response to treatment
CYP2C9	rs1934969	3	D E T **O** Pk	Decreased metabolism

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Cerivastatin				N° AFFECTED VARIANTS 1/1
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
SLCO1B1	rs4149056	3	D E **T** O Pk	Increased risk of cerivastatin-related rhabdomyolysis

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Montelukast

N° AFFECTED VARIANTS 7/11

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ABCC1	rs119774	3	D **E** T O Pk	Decreased response to treatment
ABCC9	rs704212	3	D E T O **Pk**	Decreased response to treatment
LTA4H	rs2660845	3	D **E** T O Pk	Increased risk of asthma exacerbations
LTC4S	rs730012	3	D **E** T O Pk	Decreased response to treatment
UGT1A3	rs7604115	3	D E T O **Pk**	Decreased response to treatment
	*1	3	D E T O **Pk**	Increased plasma drug concentration
CYP2C8	*1	3	D E T O **Pk**	Increased plasma drug concentration

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Salbutamol

N° AFFECTED VARIANTS 2/3

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
CRHR2	rs7793837 rs2267715	3	D **E** T O Pk	Decreased response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Cyclophosphamide

N° AFFECTED VARIANTS 33/59

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ABCB1	rs2032582	3	D **E** T **O** Pk	Shorter disease-free survival time
	rs1045642	3	D **E T** O Pk	Shorter disease-free survival time and increased risk of anaemia

Cyclophosphamide				N° AFFECTED VARIANTS 33/59
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCC2	rs3740066	3	D E **T** O Pk	Increased likelihood of nausea
	rs2273697	3	D E **T** O Pk	Increased risk of anaemia
	rs8187710 rs17222723	3	D E **T** O Pk	Increased risk of cardiotoxicity
AKR1C3	rs1937840	3	D **E** T O Pk	Decreased response to treatment
ALDH3A1	rs2228100	3	D E **T** O Pk	Increased risk of leukopenia and anemia
CBR1	rs9024	3	**D** E T O **Pk**	Increased drug exposure
	rs20572	3	D E T O **Pk**	Increased drug exposure
CTNNB1	rs4135385	3	D **E T** O Pk	Increased risk of neutropenia
CXCL12	rs1801157	3	D **E** T O Pk	Decreased response to treatment
CYP2B6	rs7254579	3	D E T O **Pk**	Reduced metabolism
CYP2C19	rs4244285	3	D **E T** O Pk	Decreased response to treatment and increased risk of neutropenia
	rs12248560	3	D E **T** O Pk	Increased risk of leukopenia
	rs4244285	3	D E **T** O Pk	Reduced metabolism
CYP3A4	rs2740574	3	D E **T** O Pk	Shorter period of time before chemotherapy-induced ovarian failure
EPHX1	rs1051740	3	D E **T** O Pk	Increased risk of nephrotoxicity
GATA3	rs3824662	3	D **E** T O Pk	Decreased response to treatment
GSTM3	rs36120609	3	D E **T** O Pk	Increased risk of adverse effects
GSTP1	rs1695	3	D **E** T O Pk	Decreased response to treatment

Cyclophosphamide				N° AFFECTED VARIANTS 33/59
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
LIG3	rs1052536	3	D E **T** O Pk	Increased risk of neutropenia
MUTYH	rs3219484	3	D E **T** O Pk	Increased risk of neutropenia
NOS3	rs1799983	3	D **E** T O Pk	Improved response to chemotherapy if cyclophosphamide is used as an adjuvant
	rs2070744	3	D **E** T O Pk	Shorter disease-free survival time
NQO2	rs1143684	3	D **E** T O Pk	Decreased response to treatment
PNPLA3	rs738409	3	D E **T** O Pk	Increased risk of hepatotoxicity
RAC2	rs13058338	3	D E **T** O Pk	Increased risk of toxicity
SLC22A16	rs723685	3	**D** E T O Pk	Need for higher doses
	rs6907567	3	D **E** T O Pk	Need for higher doses
	rs714368	3	D **E T O** Pk	Increased likelihood of nausea
	rs12210538	3	D E **T** O Pk	Increased risk of toxicity
SOD2	rs4880	3	D **E** T O Pk	Shorter survival time

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Doxorubicin				N° AFFECTED VARIANTS 23/38
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs2032582	3	D **E** T **O** Pk	Shorter disease-free survival time
	rs1045642	3	D **E T** O Pk	Shorter disease-free survival time and increased risk of anaemia

Doxorubicin				N° AFFECTED VARIANTS 23/38
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCC2	rs3740066	3	D E **T** O Pk	Increased likelihood of nausea
	rs2273697	3	D E **T** O Pk	Increased risk of anaemia
	rs8187710 rs17222723	3	D E **T** O Pk	Increased risk of cardiotoxicity
ABCC4	rs9561778	3	D E **T** O Pk	Increased risk of toxicity
AKR1C3	rs1937840	3	D **E** T O Pk	Decreased response to treatment
ALDH3A1	rs2228100	3	D E **T** O Pk	Increased risk of leukopenia and anemia
CBR1	rs9024	3	**D** E T O **Pk**	Increased drug exposure
	rs20572	3	D E T O **Pk**	Increased drug exposure
CYP2C19	rs4244285	3	D **E** **T** O Pk	Decreased response to treatment and increased risk of neutropenia
	rs12248560	3	D E **T** O Pk	Increased risk of leukopenia
GATA3	rs3824662	3	D **E** T O Pk	Decreased response to treatment
GSTP1	rs1695	3	D **E** T O Pk	Decreased response to treatment
NOS3	rs1799983	3	D **E** T O Pk	Improved response to chemotherapy if cyclophosphamide is used as an adjuvant
	rs2070744	3	D **E** T O Pk	Shorter disease-free survival time
NQO2	rs1143684	3	D **E** T O Pk	Decreased response to treatment
RAC2	rs13058338	3	D E **T** O Pk	Increased risk of toxicity

Doxorubicin				N° AFFECTED VARIANTS 23/38
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
SLC22A16	rs723685	3	**D** E T O Pk	Need for higher doses
	rs6907567	3	D **E** T O Pk	Need for higher doses
	rs714368	3	D **E T O** Pk	Increased likelihood of nausea
	rs12210538	3	D E **T** O Pk	Increased risk of toxicity

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Imatinib				N° AFFECTED VARIANTS 12/24
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB4	rs1202283	3	D **E** T O Pk	Shorter survival time
ABCC2	rs2273697	3	D **E** T O Pk	Shorter survival time
ABCG2	rs2231137	3	**D** E T O Pk	Need for higher doses
	rs12505410 rs13120400 rs2725252	3	D **E** T O Pk	Decreased response to treatment
CYP3A5	rs776746	3	D E T O **Pk**	Increased trough concentrations of imatinib
EGFR	rs10258429	3	D E **T** O Pk	Increased risk for conjunctival hemorrhage
NQO1	rs10517	3	D **E** T O Pk	Decreased survival time without disease progression
SLC22A1	rs628031	3	D **E** T O Pk	Decreased response to treatment
SLC22A5	rs2631372	3	D **E** T O Pk	Decreased response to treatment
SLCO1A2	rs3764043	3	D E T O **Pk**	Decreased clearance

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Mycophenolic Acid				N° AFFECTED VARIANTS 3/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCC2	rs2273697 rs717620	3	D E T O **Pk**	Reduced drug elimination
SLCO1B1	rs2306283	3	D E T O **Pk**	Reduced drug elimination

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Methotrexate				N° AFFECTED VARIANTS 39/72
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
-	rs4888024	3	D E **T** O Pk	Increased risk of end-of-induction minimal residual disease (mrd)
ABCB1	rs1045642	3	D **E T** O Pk	Increased risk of drug toxicity
ABCC1	rs3784864	3	D **E** T O Pk	Decreased response to treatment
	rs2238476	3	D **E T** O Pk	Decreased response to treatment and increased risk of toxicity
	rs246240	3	D E **T** O Pk	Increased risk of toxicity
ABCC2	rs3740065	3	D E **T** O Pk	Increased risk of toxicity
ABCC3	rs9895420	3	D **E** T O Pk	Shorter disease-free survival time
ABCC4	rs9516519	3	D E **T** O Pk	Increased risk for toxicity and increased plasma level
ABCG2	rs13120400	3	D **E** T O **Pk**	Decreased clearance
	rs12505410	3	D E T O **Pk**	Reduced drug elimination
	rs2231142	3	D E **T** O Pk	Increased risk of adverse events
AD-ORA2A	rs2298383	3	D E **T** O Pk	Increased risk of adverse events

Methotrexate				N° AFFECTED VARIANTS 39/72
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ARID5B	rs10821936	3	D E T **O** Pk	Lower methotrexate polyglutamate accumulation
	rs10994982	3	D E T O **Pk**	Reduced drug elimination
	rs4948496	3	D E **T** O **Pk**	Increased risk of leukopenia and increased plasma concentrations
ATIC	rs4673993	2B	D **E** T O Pk	Decreased response to treatment
	rs2372536	3	D **E** T O Pk	Decreased response to treatment
	rs16853826	3	D E **T** O Pk	More likely to discontinue treatment due to toxicity
ATP5F1E	rs1059150	3	D **E** T O Pk	Decreased response to treatment
CCND1	rs9344	3	D **E** **T** O Pk	Increased risk of drug toxicity
ENOSF1	rs11280056	3	D E **T** O Pk	Increased risk of adverse events
FOXP3	rs3761548	3	D **E** T O Pk	Decreased response to treatment
GATA3	rs3824662	3	D **E** T O Pk	Decreased response to treatment
GGH	rs3758149	3	D **E** T O **Pk**	Decreased response to treatment
	rs719235	3	D E **T** O Pk	Increased risk of bone marrow toxicity
GSTP1	rs1695	3	D **E** T O Pk	Decreased response to treatment and increased risk of cardiotoxicity
KLRD1	rs2302489	3	D **E** T O Pk	Decreased response to treatment
MTHFR	rs1801133	2A	D **E** **T** O **Pk**	Increased risk of graft vs host disease
	rs1801131	3	D **E** **T** O Pk	Increased risk of drug toxicity and decreased response to treatment

Methotrexate				N° AFFECTED VARIANTS 39/72
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
MTR	rs1805087	3	D **E** **T** O Pk	Decreased response to treatment
MTRR	rs1801394	3	D **E** **T** O Pk	Increased risk of drug toxicity and decrased response to treatment
NOS3	rs2070744	3	D **E** T O Pk	Shorter disease-free survival time
SLC16A7	rs3763980	3	D **E** T O Pk	Decreased response to treatment
SLC19A1	rs1051266	2A	D **E** **T** O Pk	Decreased response to treatment and increased risk of toxicity
	rs1051296	3	D E T O **Pk**	Increased plasma drug concentrations
SLCO1B1	rs4149056	3	D **E** T O **Pk**	Decreased response to treatment and decreased clearance
	rs2306283	3	D E T O **Pk**	Reduced drug elimination
TLR4	rs4986790	3	D E **T** O Pk	Increased risk of adverse events
TNFAIP3	rs6920220	3	D **E** T O Pk	Decreased response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Sirolimus				N° AFFECTED VARIANTS 3/9
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
NR1I2	rs3814055	3	D E **T** O Pk	Decreased metabolism
	rs6785049	3	D E **T** O Pk	Increased exposure
CYP3A5	*3	3	D E T O **Pk**	Decreased metabolism

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Allopurinol				N° AFFECTED VARIANTS 6/8
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
-	rs2734583	3	D E **T** O Pk	Increased risk of DRESS Syndrome or Stevens-Johnson Syndrome
AOX1	rs75995567 rs3731722	3	**D** E T O Pk	Need for higher dose
CYCSP5	rs3099844	3	D E **T** O Pk	Increased risk of severe cutaneous adverse reactions
PSORS1C1	rs3131003	3	D E **T** O Pk	Increased risk of severe cutaneous adverse reactions
UGT1A	rs34650714	3	**D** E T O Pk	Need for higher dose

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Spironolactone				N° AFFECTED VARIANTS 3/4
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ADD1	rs4961	3	D **E** T O Pk	Decreased response to treatment
ADRB1	rs1801253	3	D **E** T O Pk	Increased risk of emergency room visits
NOS3	rs1799983	3	D **E** T O Pk	Increased risk of emergency room visits

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Latanoprost				N° AFFECTED VARIANTS 2/3
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCC4	rs11568658	3	D **E** T O Pk	Decreased response to treatment

Latanoprost				N° AFFECTED VARIANTS 2/3
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
PTGFR	rs3753380	3	D **E** T O Pk	Decreased response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Celecoxib				N° AFFECTED VARIANTS 1/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
IL23R	rs7518660	3	D E **T** O Pk	Increased risk of developing adenoma

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Diclofenac				N° AFFECTED VARIANTS 1/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
TN-FRSF11A	rs1805034	3	D E **T** O Pk	Increased risk of adverse effects

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Ibuprofen				N° AFFECTED VARIANTS 1/3
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C8	*1	3	**D** E T O Pk	Need for higher doses

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Buprenorphine				N° AFFECTED VARIANTS 3/8
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ARRB2	rs1045280	3	D E **T** O Pk	Increased risk of adverse effects
OPRD1	rs529520	3	D **E** T O Pk	Reduced response to treatment
OPRM1	rs1799971	3	D E **T** O Pk	Increased risk of adverse effects

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Codeine				N° AFFECTED VARIANTS 1/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2D6	*1	3	D E **T** O Pk	Increased risk of opioid dependence

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Methadone				N° AFFECTED VARIANTS 20/41
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	3	**D** E T O **Pk**	Recommendation subject to other parameters, susceptible to dose increase.
	rs9282564	3	D E T O **Pk**	Increased plasma drug concentrations
ALDH5A1	rs2760118	3	D **E** T O Pk	Reduced response to opioid addiction treatment
CNR1	rs806368	3	**D** E T O Pk	Need for higher doses for opioid addiction treatment
COMT	rs933271	3	D **E** T O Pk	Reduced response to opioid addiction treatment

Methadone				N° AFFECTED VARIANTS 20/41
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2B6	rs2279343	3	**D** E **T** O Pk	Need for higher doses for the treatment of opioid addiction and risk of neonatal abstinence syndrome.
	rs3745274	3	**D** E **T** O Pk	Need for higher doses for the treatment of opioid addiction and risk of neonatal abstinence syndrome.
CYP3A4	rs2246709	3	D E **T** O Pk	Increased severity of adverse effects in opioid addiction treatment
DRD2	rs1799978 rs6275	3	**D** E T O Pk	Need for higher doses for opioid addiction treatment
KCNJ6	rs2070995	3	D E T **O** Pk	Increased withdrawal symptoms in heroin addicts on methadone treatment
NGF	rs2239622	3	**D** E T O Pk	Need for higher doses for opioid addiction treatment
OPRD1	rs678849	3	D **E** T O Pk	Reduced response to opioid addiction treatment
	rs797397	3	D E T O **Pk**	Lower drug concentration in plasma
OPRK1	rs3802281	3	**D** E T O Pk	Need for higher doses for opioid addiction treatment
OPRL1	rs2229205	3	**D** E T O Pk	Need for higher doses for opioid addiction treatment
OPRM1	rs10485058	3	D **E** T O Pk	Reduced response to opioid addiction treatment
	rs1799971	3	D E **T** O Pk	Increased risk of Neonatal Abstinence Syndrome.

Methadone

N° AFFECTED VARIANTS 20/41

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
CYP2D6	*1	3	**D E** T O Pk	Lower response to treatment and need for higher doses
	*2	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Morphine

N° AFFECTED VARIANTS 5/14

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ABCB1	rs1045642	3	D **E** T O Pk	Reduced response to treatment
COMT	rs4680	3	**D** E T O Pk	Need for higher dose
OPRK1	rs1051660	3	**D** E T O Pk	Need for higher dose
OPRM1	rs1799971	3	D E **T** O Pk	Increased risk and severity of adverse effects
UGT2B7	rs7439366	3	D **E** T O **Pk**	Lower response to treatment and lower plasma drug concentration

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Tramadol

N° AFFECTED VARIANTS 5/12

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ABCB1	rs2032582	3	D **E** T O Pk	Reduced response to treatment
	rs1045642	3	D **E** **T** O **Pk**	Increased drug elimination, risk of reduced efficacy and increased risk of developing dependence
	rs1128503	3	D E T O **Pk**	Increased drug elimination
ARRB2	rs1045280	3	D E **T** O Pk	Increased risk of adverse effects
OPRM1	rs1799971	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Sevoflurane

N° AFFECTED VARIANTS 4/45

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ADRB2	rs1042718	3	D E **T** O Pk	Increased severity of hypotension in neurosurgery
FASTKD3	rs1801394	3	D **E** T **O** Pk	Lower response to treatment and higher risk of lowering mean arterial blood pressure
GRIN2B	rs1806201	3	D E T **O** Pk	Increased risk of increased mean arterial pressure
KCNK3	rs1275988	3	D E T **O** Pk	Increased risk of increased mean arterial pressure

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Atazanavir				N° AFFECTED VARIANTS 1/9
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP3A5	*3	3	D E T O **Pk**	Decreased metabolism

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Efavirenz				N° AFFECTED VARIANTS 5/15
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	3	D E T **O** Pk	Decreased clearance
	rs3842	3	D E T **O** Pk	Increased plasma concentrations
CYP2B6	rs8192709	3	D E T O **Pk**	Decreased metabolism
HNF4A	rs1884613	3	D E T O **Pk**	Increased plasma drug concentrations
NR1I3	rs2307424	3	D E T O **Pk**	Increased plasma drug concentrations

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Nevirapine				N° AFFECTED VARIANTS 6/14
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
-	rs6545803	3	D E **T** O Pk	Increased risk of drug-induced rash
ABCB1	rs1045642	3	D E **T** O Pk	Increased risk of hepatotoxicity
ABCC10	rs2125739	3	D E T O **Pk**	Increased plasma drug concentrations
CCHCR1	rs746647 rs1265112	3	D E **T** O Pk	Increased risk of drug-induced rash
CYCSP5	rs3099844	3	D E **T** O Pk	Increased risk of Stevens-Johnson Syndrome

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Ritonavir				N° AFFECTED VARIANTS 3/9
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs2032582	3	D E T O **Pk**	Increased plasma drug concentration
ABCC1	rs212091	3	D **E** T O Pk	Increased risk for virological failure when treated with highly active antiretroviral therapy (HAART)
APOC3	rs5128	3	D E **T** O Pk	Increased severity of triglyceride elevation

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Voriconazole				N° AFFECTED VARIANTS 1/3
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
SLCO2B1	rs3781727	3	D E T O **Pk**	Reduced drug elimination

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Alprazolam				N° AFFECTED VARIANTS 2/3
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP3A4	*37	3	D **E T** O Pk	There is no annotation for this drug-haplotype interaction. However, this haplotype does not have enzymatic activity, so it is recommended to consult your physician.
	rs35599367	3	D E T O **Pk**	Increased plasma drug concentrations

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Desipramine				N° AFFECTED VARIANTS 1/5
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
BDNF	rs61888800	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Fluvoxamine				N° AFFECTED VARIANTS 5/9
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs2032583 rs2235040	3	D E **T** O Pk	Increased risk of adverse effects
FGF2	rs1449683	3	D **E** T O Pk	Reduced response to treatment
HTR1A	rs10042486 rs1364043	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Nortriptyline				N° AFFECTED VARIANTS 2/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
BDNF	rs962369	3	D E **T** O Pk	Increased risk of suicidal ideation
GNB3	rs5443	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Paroxetine

N° AFFECTED VARIANTS 15/35

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ABCB1	rs2032583 rs2235040	3	D E **T** O Pk	Increased risk of adverse effects
COMT	rs4680	3	D **E** T O Pk	Reduced response to treatment
CYP1A2	rs762551	3	**D** E **T** O Pk	Increased risk of adverse effects and need for higher doses
	rs4646425 rs4646427	3	D **E** T O Pk	Increased response time from the administration
FKBP5	rs1360780	3	D **E** T O Pk	Reduced response to treatment
GDNF	rs2216711 rs2973049	3	D **E** T O Pk	Reduced response to treatment
HTR1A	rs10042486 rs1364043 rs6295	3	D **E** T O Pk	Reduced response to treatment
REEP5	rs153549 rs153560	3	D **E** T O Pk	Reduced response to treatment
SRP19	rs495794	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Venlafaxine

N° AFFECTED VARIANTS 11/27

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ABCB1	rs2032583 rs2235040	3	D E **T** O Pk	Increased risk of adverse effects
COMT	rs4680	3	D **E** T O Pk	Lower response in depressive disorders
FKBP5	rs1360780	3	D **E** T O Pk	Reduced response to treatment
GABRQ	rs3810651	3	D **E** T O Pk	Reduced response to treatment

Venlafaxine				N° AFFECTED VARIANTS 11/27
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
GRIA3	rs3761555 rs502434	3	D **E** T O Pk	Reduced response to treatment
SLC6A2	rs2242446	3	D **E** T O Pk	Reduced response to treatment
TPH2	rs10879346 rs1487278	3	D **E** T O Pk	Reduced response to treatment
CYP2C19	*2	3	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Valproic Acid				N° AFFECTED VARIANTS 9/20
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ANKK1	rs1800497	3	D E **T** O Pk	Increased risk of developing adverse effects
GABRA1	rs2279020	3	D **E** T O Pk	Increased risk of experiencing drug resistance
GRIN2B	rs1019385	3	**D** E T O Pk	Need for higher dose
LEPR	rs1137101	3	D E **T** O Pk	Increased risk of developing adverse effects
POLG	rs3087374	3	D E **T** O Pk	Increased risk of hepatotoxicity
RABEP1	rs1000940	3	D E T **O** Pk	Increased risk of developing adverse effects
SH2B1	rs3888190	3	D E **T** O Pk	Increased risk of developing adverse effects
UGT2B7	rs7668258	3	D E T O **Pk**	Increased plasma drug concentrations
CYP2C9	*1	3	**D** E T O **Pk**	Higher dose requirement

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Carbamazepine				N° AFFECTED VARIANTS 13/27
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCC2	rs4148386	3	D E T O **Pk**	Reduced drug elimination
EPHX1	rs1051740	3	D E T O **Pk**	Reduced metabolism
GABRA1	rs2279020	3	D **E** T O Pk	Increased risk of experiencing resistance to antiepileptic drugs
HSPA1A	rs1043620	3	D E **T** O Pk	Increased risk of developing severe hypersensitivity
HSPA1L	rs2227956	3	D E **T** O Pk	Increased risk of developing severe hypersensitivity
NR1I2	rs3814055	3	D E T O **Pk**	Reduced drug elimination
	rs2461817 rs4688040 rs7643645	3	D E T O **Pk**	Reduced metabolism
SCN1A	rs3812718	2B	**D** E T O Pk	Need for higher dose
SCN2A	rs2304016	3	D **E** T O Pk	Increased risk of experiencing resistance to antiepileptic drugs
TNF	rs1800629	3	D E **T** O Pk	Increased risk of developing severe hypersensitivity
UGT2B7	rs28365063	3	D E T O **Pk**	Reduced drug elimination

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Phenytoin				N° AFFECTED VARIANTS 10/18
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C9	rs1934969	3	D E T O **Pk**	Increased plasma drug concentrations
EPHX1	rs1051740	3	D E **T** O Pk	Increased risk of having a child with a craniofacial anomaly

Phenytoin				N° AFFECTED VARIANTS 10/18
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
GABRA1	rs2279020	3	D **E** T O Pk	Increased risk of experiencing resistance to antiepileptic drugs
NAT2	rs1041983 rs1208 rs1799929 rs1799930 rs1801280	3	D E **T** O Pk	Increased risk of toxicity in conjunction with isoniazid
SCN1A	rs3812718	3	**D** E T O Pk	Need for higher dose
SCN2A	rs2304016	3	D **E** T O Pk	Increased risk of experiencing resistance to antiepileptic drugs

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Gabapentin				N° AFFECTED VARIANTS 1/1
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
SLC7A5	rs4240803	3	D **E** T O Pk	Lower response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Mephenytoin				N° AFFECTED VARIANTS 1/5
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C19	*2	3	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Aripiprazole				N° AFFECTED VARIANTS 6/11
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ANKK1	rs1800497	3	D **E** T O Pk	Reduced response to treatment
CNR1	rs1049353	3	D E **T** O Pk	Increased risk of adverse effects
DRD2	rs2514218 rs6277	3	D **E** T O Pk	Reduced response to treatment
RABEP1	rs1000940	3	D E T **O** Pk	Increased risk of adverse effects
SH2B1	rs3888190	3	D E **T** O Pk	Increased risk of adverse effects

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Haloperidol				N° AFFECTED VARIANTS 2/8
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CNR1	rs1049353	3	D E **T** O Pk	Increased risk of adverse effects
COMT	rs4680	3	D E **T** O Pk	Increased risk of developing extrapyramidal symptoms

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Quetiapine				N° AFFECTED VARIANTS 10/17
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CNR1	rs1049353	3	D E **T** O Pk	Increased risk of adverse effects
COMT	rs4818 rs5993883 rs6269	3	D **E** T O Pk	Reduced response to treatment
CYP3A5	rs776746	3	D E T O **Pk**	Reduced metabolism

Quetiapine				N° AFFECTED VARIANTS 10/17
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
DRD3	rs6280	3	D E T O **Pk**	Reduced drug elimination
HTR1A	rs10042486	3	D **E** T O Pk	Reduced response to treatment
RABEP1	rs1000940	3	D E T **O** Pk	Increased risk of adverse effects
SH2B1	rs3888190	3	D E **T** O Pk	Increased risk of adverse effects
CYP3A4	*37	3	D E T O **Pk**	There is no annotation for this drug-haplotype interaction. However, this haplotype does not have enzymatic activity, so it is recommended to consult your physician.

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Risperidone				N° AFFECTED VARIANTS 23/48
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
-	rs1805054	3	D E **T** O Pk	Increased risk of adverse effects
ABCB1	rs1128503	3	D **E** T O Pk	Reduced response to treatment
ADRB2	rs1042713	3	D E **T** O Pk	Increased risk of adverse effects
AKT1	rs2494732	3	D **E** T O Pk	Reduced response to treatment
ANKK1	rs1800497	3	D **E** T O Pk	Reduced response to treatment
CCL2	rs2857657	3	D **E** T O Pk	Reduced response to treatment
CNR1	rs1049353	3	D E **T** O Pk	Increased risk of adverse effects
COMT	rs9606186	3	D **E** T O Pk	Reduced response to treatment

Risperidone				N° AFFECTED VARIANTS 23/48
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP3A4	rs35599367	3	D E T O **Pk**	Reduced drug elimination
DRD2	rs1799978	3	D **E** T O Pk	Increased response time from the administration
	rs2514218	3	D **E** T O Pk	Reduced response to treatment
GRM7	rs2069062	3	D **E** T O Pk	Reduced response to treatment
HRH3	rs3787430	3	D **E** T O Pk	Reduced response to treatment
HTR1A	rs10042486	3	D **E** T O Pk	Reduced response to treatment
HTR2A	rs6313	3	D E **T** O Pk	Increased risk of developing cardiovascular adverse effects
HTR2C	rs3813928	3	D **E** T O Pk	Reduced response to treatment
	rs6318	3	D E **T** O Pk	Increased risk of adverse effects
LEP	rs7799039	3	D E **T** O Pk	Increased risk of adverse effects
NR1I2	rs2276707	3	D E T O **Pk**	Reduced drug elimination
RABEP1	rs1000940	3	D E T **O** Pk	Increased risk of adverse effects
RGS4	rs2661319 rs951439	3	D **E** T O Pk	Reduced response to treatment
SH2B1	rs3888190	3	D E **T** O Pk	Increased risk of adverse effects

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Methylphenidate

N° AFFECTED VARIANTS 2/11

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ADGRL3	rs6551665	3	D **E** T O Pk	Reduced response to treatment
DRD3	rs6280	3	D E **T** O Pk	Increased risk of adverse effects

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Ondansetron

N° AFFECTED VARIANTS 4/6

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ABCB1	rs1045642 rs2032582	3	D **E** T O Pk	Increased likelihood of nausea and vomiting
CYP3A5	rs776746	3	D E T **O** Pk	Decreased metabolism
SLC6A4	rs1042173	3	D **E** T O Pk	Decreased response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Metformin

N° AFFECTED VARIANTS 8/17

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
-	rs578427	3	D E T O **Pk**	Reduced drug elimination
CAPN10	rs3792269	3	D **E** T O Pk	Decreased response to treatment
SLC22A1	rs628031	3	D **E T** O Pk	Decreased response to treatment and increased risk of gastrointestinal toxicity
	rs202220802	3	D E T O **Pk**	Increased trough metformin steady-state concentration
SLC22A3	rs2076828	3	D **E** T O Pk	Decreased response to treatment

Metformin				N° AFFECTED VARIANTS 8/17
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
SLC47A1	rs2289669	3	D **E** T O Pk	Decreased response to treatment
SLC47A2	rs12943590	3	D E T O **Pk**	Decreased clearance
SP1	rs784888	3	D **E** T O **Pk**	Decreased clearance

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Enalapril				N° AFFECTED VARIANTS 2/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
BDKRB2	rs1799722	3	D E **T** O Pk	Increased likelihood of cough
SLCO1B1	rs4149056	3	D E **T** O Pk	Increased likelihood of cough

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Atenolol				N° AFFECTED VARIANTS 11/27
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs10267099	3	D E **T** O Pk	Increased risk of adverse effects
ADRA2A	rs1800545	3	D **E** T O Pk	Reduced response to treatment
ADRB2	rs1042713	3	D **E** T O Pk	Reduced response to treatment
AGT	rs5051 rs699	3	D **E** T O Pk	Reduced response to treatment
EDN1	rs5370	3	D **E** T O Pk	Reduced response to treatment

Atenolol

N° AFFECTED VARIANTS 11/27

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
GALNT2	rs2144300	3	D E T **O** Pk	Increased reduction of HDL-C
	rs2144297	3	D E **T** O Pk	Increased reduction of HDL-C
NR1H3	rs11039149	3	D E **T** O Pk	Increased risk of developing cardiovascular adverse effects
PROX1	rs340874	3	D E **T** O Pk	Increased risk of adverse effects
TBX2	rs8068318	3	D **E** T O Pk	Reduced response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Triamcinolone

N° AFFECTED VARIANTS 1/2

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
HCG22	rs2523864	3	D E **T** O Pk	Increased risk of increased intraocular pressure

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Cisplatin

N° AFFECTED VARIANTS 29/64

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ABCB1	rs1045642	3	D **E** **T** O Pk	Shorter disease-free survival time and increased risk of anaemia
COMT	rs4646316 rs9332377	3	D E **T** O Pk	Increased risk of hearing loss
EPHX1	rs1051740	3	D E **T** O Pk	Increased risk of nephrotoxicity

Cisplatin				N° AFFECTED VARIANTS 29/64
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ERCC1	rs11615	3	D **E** **T** O Pk	Decreased response to treatment and increased risk of toxicity
ERCC2	rs238406	3	D E **T** O Pk	Increased risk of leukopenia
GALNT14	rs9679162	3	D **E** T O Pk	Decreased response to treatment
GALNT18	rs7937567	3	D **E** T O Pk	Decreased response to treatment
GPX5	rs451774	3	D **E** T O Pk	Shorter survival time
GSTM3	rs36120609	3	D E **T** O Pk	Increased risk of developing adverse effects
GSTP1	rs1695	3	D **E** T O Pk	Decreased response to treatment
LIG3	rs1052536	3	D E **T** O Pk	Increased risk of neutropenia
MLLT3	rs10964552	3	D **E** T O Pk	Decreased response to treatment
MTR	rs1805087	3	D **E** T O Pk	Decreased response to treatment
MUTYH	rs3219484	3	D E **T** O Pk	Increased risk of neutropenia
RARS	rs244898	3	D **E** T O Pk	Decreased response to treatment
REV1	rs3087403	3	D **E** T O Pk	Decreased response to treatment
REV3L	rs462779	3	D **E** T O Pk	Decreased response to treatment
RRM1	rs232043 rs720106 rs2284449	3	D **E** T O Pk	Decreased response to treatment
SLC16A5	rs4788863	3	D E **T** O Pk	Increased risk of ototoxicity
SLC22A2	rs316019	3	D E **T** O Pk	Increased risk of ototoxicity

Cisplatin

N° AFFECTED VARIANTS 29/64

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
SLC31A1	rs7851395	3	D **E** T O Pk	Shorter survival time
	rs10981694	3	D E **T** O Pk	Increased risk of ototoxicity
UBE2I	rs9597	3	D **E** T O Pk	Decreased response to treatment
VEGFA	rs25648	3	D **E** T O Pk	Decreased response to treatment
XPC	rs2228001	3	D E **T** O Pk	Increased risk of neutropenia
XRCC1	rs1799782	3	D **E** T O Pk	Shorter survival time

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Thioguanine

N° AFFECTED VARIANTS 1/2

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
GATA3	rs3824662	3	D **E** T O Pk	Decreased response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Azathioprine

N° AFFECTED VARIANTS 3/9

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
-	rs2647087	3	D E **T** O Pk	Increased risk of pancreatitis
FTO	rs16952570	3	D E **T** O Pk	Increased risk of leukopenia and neutropenia
PACSIN2	rs2413739	3	D **E** T O Pk	Decreased response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Cyclosporine

N° AFFECTED VARIANTS 9/15

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ABCB1	rs1128503	3	**D** E **T** O Pk	Need for higher dose and risk of neurotoxicity
ABCC2	rs2273697	3	D E T O **Pk**	Increased drug exposure
CTLA4	rs231775	3	D E **T** O Pk	Increased risk of adverse events
CYP3A4	rs4646437	3	D **E** T O **Pk**	Increased risk for biopsy-proven acute rejection (BPAR) at 12 month post-transplant
	rs28371759	3	D E T **O** Pk	Increased drug metabolism
	rs35599367	3	D E T **O** Pk	Lower metabolism and increased risk of adverse events
	rs2740574	3	D E **T** O Pk	Increased likelihood of kidney transplant rejection
POR	rs1057868	3	D E T O **Pk**	Increased trough concentrations of cyclosporine
TNF	rs1800629	3	D **E** T O Pk	Increased risk for biopsy-proven acute rejection (BPAR) at 12 month post-transplant

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Mercaptopurine

N° AFFECTED VARIANTS 5/17

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
-	rs2647087	3	D E **T** O Pk	Increased risk of pancreatitis
FTO	rs16952570	3	D E **T** O Pk	Increased risk of leukopenia and neutropenia
GATA3	rs3824662	3	D **E** T O Pk	Decreased response to treatment

Mercaptopurine				N° AFFECTED VARIANTS 5/17
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
GSTP1	rs1695	3	D E **T** O Pk	Increased risk of drug toxicity
SLCO1B1	rs11045879	3	D E **T** O Pk	Decreased response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Lansoprazole				N° AFFECTED VARIANTS 1/2
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	3	D E T O **Pk**	Increased plasma drug concentrations

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Hydrochlorothiazide				N° AFFECTED VARIANTS 10/19
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
-	rs12346562	3	D **E** T O Pk	Decreased response to treatment
	rs10792367	3	D **E** T O Pk	Smaller reduction in blood pressure
C5orf56	rs12521868	3	D **E** T O Pk	Decreased response to treatment
DOT1L	rs2269879	3	D **E** T O Pk	Decreased response to treatment
HMGCS2	rs9943291	3	D E **T** O Pk	Increased risk of diabetes
PLCE1	rs932764	3	D **E** T O Pk	Decreased response to treatment
TCF7L2	rs4132670 rs4506565 rs7917983	3	D E **T** O Pk	Increased risk of diabetes

Hydrochlorothiazide				N° AFFECTED VARIANTS 10/19
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
WNK1	rs880054	3	D **E** T O Pk	Smaller reduction in blood pressure

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

Furosemide				N° AFFECTED VARIANTS 1/5
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
SLC12A3	rs1529927	3	D **E** T O Pk	Decreased response to treatment

Therapeutic recommendation: The expert consortia does not contain genotype-based clinical guidance for the affected variants. Despite this, it is recommended to seek medical assessment.

GENETIC RESULTS

HAPLOTYPES

Gene	Reference haplotype	Haplotype	Type of Metaboliser
CYP1A2	*1/*1	*1M/*1M	ULTRARAPID
CYP2B6	*1/*1	*1/*1	NORMAL
CYP2C19	*38/*38	*2/*2	SLOW
CYP2C8	*1/*1	*1/*1	NORMAL
CYP2C9	*1/*1	*1/*1	NORMAL
CYP2D6	*1/*1	*1/*2	NORMAL
CYP3A4	*1/*1	*1/*37	SLOW
CYP3A5	*1/*1	*3/*3	SLOW
CYP3A7	*1A/*1A	*1A/*1A	NORMAL
GSTM1	*I/*I	*I/*I	NORMAL
GSTT1	*I/*I	*I/*D	SLOW
NAT2	*4/*4	*5B/*6A	SLOW
NUDT15	*1/*1	*1/*1	NORMAL
SLCO1B1	*1/*1	*1/*5	SLOW
TPMT	*1/*1	*1/*1	NORMAL
UGT1A1	*1/*1	*1/*1	NORMAL
UGT1A3	*1/*1	*1/*1	NORMAL
UGT1A6	*1A/*1A	*1A/*1B	INTERMEDIATE

VARIANTS

Gene	Marker	Genotype	Gene	Marker	Genotype
-	rs2734583	AG	-	rs2768759	CC
-	rs2965667	TT	-	rs10739150	GG
-	rs1104514	AA	-	rs12346562	AA
-	rs2647087	AC	-	rs2498804	CA
-	rs12118636	GG	-	rs17661089	AA
-	rs352428	GG	-	rs585719	CC
-	rs4675690	TT	-	rs11636687	TT
-	rs2069521	GG	-	rs11959113	GG
-	rs2952768	TT	-	rs2960436	AA
-	rs2292997	GG	-	rs2433320	GA
-	rs11065987	AA	-	rs10792367	CG

Gene	Marker	Genotype	Gene	Marker	Genotype
-	rs578427	CC	-	rs9345389	AA
-	rs4888024	AG	-	rs1786929	AG
-	rs6545803	GT	-	rs1805054	CC
-	rs2808630	TT	-	rs1346268	TC
-	rs11265572	GG	-	rs2769605	CT
-	rs12777823	AA	ABCA1	rs12003906	GG
ABCA1	rs2230806	TT	ABCB1	rs10248420	GG
ABCB1	rs10280101	CC	ABCB1	rs11983225	CC
ABCB1	rs12720067	TT	ABCB1	rs2235015	AA
ABCB1	rs2235040	TT	ABCB1	rs2235067	TT
ABCB1	rs4148739	CC	ABCB1	rs4148740	GG
ABCB1	rs7787082	AA	ABCB1	rs2032583	GG
ABCB1	rs2032582	CC	ABCB1	rs10267099	GA
ABCB1	rs3213619	AA	ABCB1	rs1045642	GG
ABCB1	rs1128503	GG	ABCB1	rs2229109	CC
ABCB1	rs3842	TC	ABCB1	rs9282564	TT
ABCB1	rs4728709	GG	ABCB4	rs1202283	GG
ABCB5	rs17143212	CC	ABCC1	rs45511401	GG
ABCC1	rs28364006	AA	ABCC1	rs35592	TT
ABCC1	rs3784864	GA	ABCC1	rs2238476	GG
ABCC1	rs246240	AA	ABCC1	rs119774	CC
ABCC1	rs212091	TC	ABCC10	rs2125739	TT
ABCC11	rs7194667	TT	ABCC2	rs717620	CC
ABCC2	rs3740066	CC	ABCC2	rs4148386	GG
ABCC2	rs2273697	GG	ABCC2	rs8187710	AA
ABCC2	rs17222723	AA	ABCC2	rs3740065	GG
ABCC2	rs113646094	CC	ABCC3	rs4148416	CC
ABCC3	rs1051640	AA	ABCC3	rs9895420	TA
ABCC4	rs3765534	CC	ABCC4	rs9561778	GG
ABCC4	rs17268282	GG	ABCC4	rs9561765	GG
ABCC4	rs11568658	CC	ABCC4	rs7317112	AG
ABCC4	rs9516519	TT	ABCC5	rs10937158	CC
ABCC5	rs3749438	AA	ABCC9	rs704212	CC
ABCG1	rs225440	CT	ABCG2	rs2231142	GG
ABCG2	rs2231137	CC	ABCG2	rs12505410	TT

Gene	Marker	Genotype	Gene	Marker	Genotype
ABCG2	rs13120400	TT	ABCG2	rs2725252	AA
ABCG2	rs3114020	CC	ABCG2	rs17731538	GG
ABCG2	rs2231135	AA	ABCG8	rs11887534	GG
ACE	rs4291	AA	ACE	rs4341	CC
ACE	rs4343	AA	ACSS2	rs17309872	AA
ACYP2	rs1872328	GG	ADAMTS1	rs428785	GG
ADD1	rs4961	GT	ADGRL3	rs1355368	GG
ADGRL3	rs6551665	AA	ADGRL3	rs6813183	CC
ADGRL3	rs734644	CC	ADH1C	rs698	CC
ADM	rs11042725	CA	ADORA1	rs16851030	CC
ADORA1	rs2228079	TT	ADORA2A	rs2298383	TT
ADORA2A	rs3761422	CC	ADORA2A	rs2267076	CC
ADORA2A	rs2236624	CC	ADORA2A	rs5760410	AA
ADRA2A	rs1800545	GA	ADRB1	rs1801253	CC
ADRB2	rs1042713	GG	ADRB2	rs1042714	CC
ADRB2	rs1042718	AA	ADRB2	rs1045280	TT
ADRB3	rs4994	AA	AGT	rs5050	TT
AGT	rs5051	CC	AGT	rs699	AA
AGTR1	rs5186	AC	AHR	rs4410790	TC
AKR1C3	rs1937840	CG	AKT1	rs2494752	GG
AKT1	rs1130214	CA	AKT1	rs2494732	TC
AKT1	rs3803300	TC	ALDH3A1	rs2228100	GG
ALDH5A1	rs2760118	CT	ALOX12	rs11078659	GG
ALOX5	rs2115819	AG	AMHR2	rs784892	GG
ANKK1	rs1800497	GG	AOX1	rs75995567	TT
AOX1	rs3731722	AA	AOX1	rs55754655	AA
APOA5	rs662799	AA	APOB	rs679899	AA
APOB	rs1367117	GG	APOC3	rs2854116	CT
APOC3	rs5128	CC	APOE	rs7412	CC
AQP1	rs28362731	GG	ARID5B	rs10821936	TT
ARID5B	rs10994982	AG	ARID5B	rs4948496	CC
ARRB2	rs1045280	TT	ASTN2	rs958804	TC
ATIC	rs4673993	TC	ATIC	rs2372536	CG
ATIC	rs16853826	GG	ATM	rs1801516	GG
ATP5F1E	rs1059150	TT	B4GALT2	rs1061781	CC

Gene	Marker	Genotype	Gene	Marker	Genotype
BACH1	rs2070401	AA	BAG6	rs750332	TT
BCL2L11	rs724710	CC	BDKRB2	rs1799722	CT
BDNF	rs6265	CC	BDNF	rs7124442	CT
BDNF	rs61888800	GT	BDNF	rs962369	TC
BLMH	rs1050565	TC	BMP5	rs41271330	GG
C5orf56	rs12521868	GT	CA10	rs967676	TC
CACNA1C	rs1051375	GG	CACNA1E	rs3845446	TT
CACNA1S	rs1800559	CC	CACNA1S	rs772226819	GG
CALU	rs1043550	AA	CALU	rs339097	AA
CAMK1D	rs10737062	AA	CAMK1D	rs10752271	AA
CAPN10	rs3792269	AG	CAPN10	rs5030952	CC
CBR1	rs9024	GG	CBR1	rs20572	CC
CCHCR1	rs130072	CT	CCHCR1	rs746647	GG
CCHCR1	rs1265112	CC	CCL11	rs1129844	GG
CCL2	rs2857657	GC	CCL2	rs4586	TC
CCL2	rs4795893	GA	CCND1	rs9344	GA
CEP68	rs7572857	GA	CES1P1	rs3785161	AA
CETP	rs4783961	GA	CETP	rs708272	GA
CETP	rs5882	GA	CHIA	rs3818822	GA
CHRNA5	rs16969968	GG	CHRNA5	rs2036527	GG
CHRNA5	rs503464	TT	CHST1	rs9787901	GG
CMPK1	rs4492666	AA	CNR1	rs1049353	CC
CNR1	rs806378	CC	CNR1	rs806368	TC
COL1A1	rs1800012	CC	COMT	rs4680	GA
COMT	rs165599	GG	COMT	rs4646316	CT
COMT	rs9332377	CT	COMT	rs933271	TT
COMT	rs6269	AG	COMT	rs4818	CG
COMT	rs5993883	TT	COMT	rs9606186	CC
COQ2	rs4693075	GG	COQ2	rs6535454	AA
CRHR1	rs242941	CC	CRHR2	rs2270007	CC
CRHR2	rs7793837	TT	CRHR2	rs2267715	GG
CRP	rs1205	CT	CRTC2	rs8450	GG
CSK	rs1378942	AA	CTH	rs1021737	GT
CTLA4	rs231775	AA	CTLA4	rs4553808	AG
CTNNB1	rs4135385	AA	CXCL12	rs1801157	CC

Gene	Marker	Genotype	Gene	Marker	Genotype
CYBA	rs4673	AG	CYCSP5	rs3099844	CA
CYP1A1	rs2606345	CA	CYP1A1	rs2472297	CC
CYP1A2	rs762551	AA	CYP1A2	rs2069526	TT
CYP1A2	rs4646425	CC	CYP1A2	rs4646427	TT
CYP1A2	rs2470890	TT	CYP1A2	rs2472304	AA
CYP1B1	rs1056836	GC	CYP2A6	rs28399433	AA
CYP2B6	rs2279343	AG	CYP2B6	rs3211371	CC
CYP2B6	rs12721655	AA	CYP2B6	rs7254579	TC
CYP2B6	rs8192709	CC	CYP2B6	rs2279345	CC
CYP2B6	rs35303484	AA	CYP2B6	rs8192719	CC
CYP2B6	rs3745274	GG	CYP2B6	rs28399499	TT
CYP2C19	rs4244285	AA	CYP2C19	rs12248560	CC
CYP2C19	rs4986893	GG	CYP2C19	rs11188072	CC
CYP2C19	rs145119820	GG	CYP2C19	rs28399504	AA
CYP2C19	rs3814637	CC	CYP2C9	rs1057910	AA
CYP2C9	rs9332096	CC	CYP2C9	rs1934969	TT
CYP2C9	rs4086116	CC	CYP2C9	rs71486745	DD
CYP2C9	rs12782374	AA	CYP2C9	rs4917639	AA
CYP2C9	rs10509680	GG	CYP2C9	rs4918758	CC
CYP2D6	rs1065852	GG	CYP2D6	rs28371706	GG
CYP2D6	rs1080985	CG	CYP2E1	rs2070676	CC
CYP2E1	rs3813867	GG	CYP2E1	rs2031920	CC
CYP3A4	rs35599367	GA	CYP3A4	rs2740574	TT
CYP3A4	rs2242480	CC	CYP3A4	rs4646437	GG
CYP3A4	rs28371759	AA	CYP3A4	rs4986910	AG
CYP3A4	rs2246709	GG	CYP3A4	rs3735451	TT
CYP3A4	rs4646440	GG	CYP3A43	rs472660	GG
CYP3A5	rs776746	CC	CYP3A5	rs17161788	TT
CYP3A5	rs15524	AA	CYP3A5	rs4646450	GG
CYP4F2	rs2108622	CT	CYP4F2	rs2189784	GA
CYP7A1	rs3808607	GT	DBH	rs1611115	TC
DHFR	rs442767	GG	DHFR	rs1650723	CT
DNMT3A	rs2304429	TT	DOT1L	rs2269879	CC
DPYD	rs72549306	CC	DPYD	rs72549303	II
DPYD	rs72549309	II	DPYD	rs1801266	GG

Gene	Marker	Genotype	Gene	Marker	Genotype
DPYD	rs1801268	CC	DPYD	rs148994843	CC
DPYD	rs59086055	GG	DPYD	rs67376798	TT
DPYD	rs78060119	CC	DPYD	rs3918290	CC
DPYD	rs115232898	TT	DPYD	rs75017182	GG
DPYD	rs55886062	AA	DPYD	rs1801160	CC
DPYD	rs56038477	CC	DPYD	rs17376848	AG
DPYD	rs2297595	TT	DPYD	rs1801265	AG
DPYD	rs1801159	TT	DPYD	rs115632870	CC
DPYD	rs72728438	TT	DPYS	rs2669429	AA
DRD1	rs11746641	TT	DRD1	rs11749035	CC
DRD1	rs2168631	GG	DRD1	rs265976	GG
DRD1	rs4532	CT	DRD1	rs5326	CC
DRD2	rs2514218	CT	DRD2	rs6277	GA
DRD2	rs4436578	CT	DRD2	rs1799978	TT
DRD2	rs6275	AG	DRD2	rs2283265	CC
DRD2	rs1076560	CC	DRD2	rs1124493	TG
DRD2	rs6279	GC	DRD2	rs2440390	CC
DRD2	rs2734841	AC	DRD2	rs2734842	GC
DRD3	rs6280	CT	DRD3	rs167770	GA
DRD3	rs324023	TC	DRD3	rs324026	CT
DRD3	rs963468	GA	DRD3	rs167771	AA
DROSHA	rs639174	CT	DUSP1	rs881152	GG
EDN1	rs5370	GG	EGFR	rs2293347	CC
EGFR	rs10258429	CT	ENOSF1	rs11280056	ID
EPB41	rs6702335	AG	EPHX1	rs2234922	AA
EPHX1	rs1051740	TC	EPHX1	rs1877724	CC
EPM2A	rs1415744	TC	ERCC1	rs11615	AA
ERCC1	rs3212986	CC	ERCC2	rs13181	TT
ERCC2	rs1799793	CC	ERCC2	rs238406	TG
ERICH3	rs11580409	AC	ESR1	rs2207396	GG
F13A1	rs5985	AA	F3	rs3917643	TT
FAAH	rs324420	CC	FAAH	rs2295632	GG
FAAH	rs3766246	GG	FAAH	rs4141964	CC
FASTKD3	rs1801394	GG	FCER1G	rs11587213	AG
FDPS	rs11264359	AG	FDPS	rs2297480	TT

Gene	Marker	Genotype	Gene	Marker	Genotype
FGF2	rs1449683	CC	FKBP5	rs1360780	CC
FKBP5	rs4713916	GG	FMO1	rs12720462	CC
FMO1	rs7877	CT	FMO3	rs2266780	AG
FMO3	rs1736557	GG	FMO5	rs7541245	CC
FOXP3	rs3761548	GT	FPGS	rs1544105	CC
FSIP1	rs7179742	AA	FTO	rs12595985	CC
FTO	rs9940629	AA	FTO	rs16952570	TT
FTO	rs79206939	GG	GABRA1	rs2279020	GA
GABRA1	rs2290732	AG	GABRA2	rs279858	TT
GABRQ	rs3810651	TT	GAD1	rs3749034	AA
GAL	rs948854	TT	GALNT14	rs9679162	GT
GALNT14	rs12613732	TG	GALNT18	rs7937567	GA
GALNT2	rs2144300	CC	GALNT2	rs2144297	TT
GALR1	rs2717162	TC	GARS1-DT	rs1074373	AC
GATA3	rs3824662	CA	GCG	rs13429709	TC
GDNF	rs2216711	GA	GDNF	rs2973049	TC
GGCX	rs11676382	CC	GGCX	rs2592551	AA
GGH	rs11545077	CT	GGH	rs3758149	GA
GGH	rs11545078	GG	GGH	rs719235	CC
GIPR	rs10423928	TT	GLDC	rs10975641	CC
GLP1R	rs6923761	GG	GNB3	rs2301339	GG
GNB3	rs5443	CC	GNMT	rs10948059	TT
GP1BA	rs6065	CC	GPX5	rs451774	AA
GRIA3	rs4825476	GG	GRIA3	rs3761554	TC
GRIA3	rs3761555	TT	GRIA3	rs502434	TC
GRIK1	rs2832407	CC	GRIN2B	rs1806201	GA
GRIN2B	rs1019385	CA	GRM3	rs724226	GG
GRM7	rs2069062	GG	GSK3B	rs334558	GG
GSTM3	rs36120609	ID	GSTP1	rs1695	GG
GSTP1	rs1138272	CC	HCG22	rs2523864	CT
HCG22	rs3873352	CC	HLA-C	rs9461684	CT
HLA-DPB1	rs1042136	AA	HLA-G	rs9380142	AA
HLA-G	rs17179108	CC	HMGCR	rs17238540	TT
HMGCR	rs17671591	CT	HMGCR	rs17244841	AA
HMGCS2	rs9943291	TT	HNF4A	rs1884613	CC

Gene	Marker	Genotype	Gene	Marker	Genotype
HNMT	rs1050891	AG	HRH3	rs3787430	CT
HRH4	rs4483927	GT	HSD11B1	rs846908	GG
HSD11B1	rs4844880	TT	HSD11B1	rs846910	GG
HSPA1A	rs1043620	CC	HSPA1L	rs2227956	AA
HTR1A	rs6295	CG	HTR1A	rs10042486	CT
HTR1A	rs1364043	TG	HTR1B	rs6296	CC
HTR1B	rs130058	TT	HTR1B	rs11568817	AC
HTR1B	rs9361233	TC	HTR2A	rs2770296	TT
HTR2A	rs7997012	GG	HTR2A	rs6311	TT
HTR2A	rs6313	AA	HTR2A	rs9316233	CC
HTR2A	rs6314	GG	HTR2A	rs6305	GG
HTR2C	rs1414334	GG	HTR2C	rs3813929	CT
HTR2C	rs6318	GG	HTR2C	rs2497538	CC
HTR2C	rs518147	GC	HTR2C	rs3813928	GA
HTR3A	rs1062613	CC	HTR3A	rs2276302	GA
HTR3B	rs2276307	AA	HTR7	rs1935349	CC
IL10	rs1800872	GG	IL10	rs1800896	TC
IL10	rs1800871	GG	IL11	rs1126757	CT
IL18	rs5744247	GG	IL18	rs1946518	TG
IL1B	rs1143627	GA	IL1B	rs16944	AG
IL23R	rs7518660	AA	IL3	rs181781	GG
IL4	rs2243250	CC	IRS1	rs13431554	AA
ITGA2	rs1062535	GG	ITGA2	rs1126643	CC
ITGB3	rs5918	TT	ITIH3	rs2535629	GA
ITPA	rs1127354	CC	ITPA	rs7270101	AA
KCNJ1	rs11600347	CC	KCNJ1	rs12795437	GG
KCNJ11	rs5219	TC	KCNJ6	rs2835859	TT
KCNJ6	rs2070995	TC	KCNK3	rs1275988	TT
KCNQ1	rs2237895	AC	KLRC1	rs7301582	CT
KLRD1	rs2302489	TT	KMT2E	rs117986340	GG
LDLR	rs688	CC	LDLR	rs5925	TT
LEP	rs4731426	GC	LEP	rs7799039	GA
LEPR	rs1805094	GG	LEPR	rs1137101	AG
LGR5	rs17109924	TT	LIG3	rs1052536	CC
LIPC	rs1800588	CT	LPL	rs328	CC

Gene	Marker	Genotype	Gene	Marker	Genotype
LTA4H	rs2660845	GA	LTC4S	rs730012	AA
MAFK	rs4720833	AA	MAP3K1	rs726501	GG
MAP3K1	rs16886403	TT	MC1R	rs2228478	AG
MC1R	rs2228479	GA	MC4R	rs489693	CC
MC4R	rs17782313	TT	MIR27A	rs895819	TT
MLLT3	rs10964552	CC	MMP3	rs35068180	DD
MTHFR	rs1801131	GG	MTHFR	rs1801133	GG
MTHFR	rs4846051	AA	MTR	rs1805087	AG
MTR	rs3768142	TT	MTRR	rs1801394	GG
MUTYH	rs3219484	CC	MYD88	rs6853	AA
MYLIP	rs9370867	AG	NAT2	rs4271002	GG
NAT2	rs1041983	CT	NAT2	rs1208	GA
NAT2	rs1799929	CT	NAT2	rs1799930	GA
NAT2	rs1799931	GG	NAT2	rs1801280	TC
NAT2	rs4646244	TA	NCF4	rs1883112	GA
NEDD4L	rs520210	AA	NEDD4L	rs4149601	GA
NEDD4L	rs292449	CC	NGF	rs2239622	GG
NOD2	rs2066844	CT	NOS1AP	rs10494366	GT
NOS2	rs11080344	TC	NOS3	rs1799983	TG
NOS3	rs2070744	CT	NPC1L1	rs17655652	TC
NPPA-AS1	rs5063	CC	NQO1	rs1800566	GA
NQO1	rs10517	GG	NQO2	rs1143684	CT
NR1H3	rs11039149	AG	NR1I2	rs2461817	AC
NR1I2	rs3814055	TT	NR1I2	rs4688040	GG
NR1I2	rs7643645	AA	NR1I2	rs1523130	TT
NR1I2	rs2276707	CC	NR1I2	rs6785049	GG
NR1I3	rs2307424	GA	NR1I3	rs3003596	GG
NR3C2	rs5522	TT	NRAS	rs1065634	TT
NTRK2	rs10465180	TT	NUDT15	rs116855232	CC
OPRD1	rs529520	AC	OPRD1	rs678849	CT
OPRD1	rs2234918	CT	OPRD1	rs797397	GA
OPRD1	rs581111	AG	OPRK1	rs3802281	TC
OPRK1	rs1051660	CA	OPRL1	rs2229205	CT
OPRM1	rs1799971	AA	OPRM1	rs79910351	CC
OPRM1	rs540825	TT	OPRM1	rs9397685	AA

Gene	Marker	Genotype	Gene	Marker	Genotype
OPRM1	rs10485058	AG	OSGEP	rs1760944	TT
P2RY1	rs1065776	CC	P2RY12	rs6809699	CC
P2RY12	rs6787801	GG	P2RY12	rs2046934	AA
P2RY12	rs3732759	AG	PACSIN2	rs2413739	CT
PEAR1	rs12041331	GG	PEAR1	rs57731889	CC
PEAR1	rs41273215	CC	PIK3CA	rs2699887	CT
PLA2G4A	rs12746200	AA	PLA2G4A	rs10157410	GG
PLCE1	rs932764	AA	PLCG1	rs2228246	AA
PMCH	rs7973796	GA	PNPLA3	rs738409	CC
POLG	rs3087374	CA	POLR3G	rs2562519	CT
PON1	rs662	TC	POR	rs1057868	CT
POR	rs41301394	CT	PPARA	rs4253728	GA
PPARA	rs4823613	AG	PPARG	rs3856806	CC
PPARG	rs1801282	CC	PRKAG2	rs10224002	AG
PRKCB	rs11649514	GG	PROC	rs1799808	TT
PROX1	rs340874	TC	PSORS1C1	rs3131003	GG
PSORS1C1	rs9263726	GG	PTEN	rs2299939	CC
PTGER2	rs2075797	CC	PTGER3	rs7551789	AA
PTGER4	rs4133101	CC	PTGES	rs2302821	AA
PTGFR	rs3766355	CC	PTGFR	rs3753380	TC
PTGIR	rs1126510	AA	PTGS1	rs10306114	AA
PTGS1	rs1330344	TT	PTGS2	rs20417	CG
PTGS2	rs4648287	AA	RABEP1	rs1000940	AA
RAC2	rs13058338	TA	RAF1	rs11710163	AG
RARS	rs244898	CC	REEP5	rs153549	AG
REEP5	rs153560	GA	REV1	rs3087403	CC
REV3L	rs462779	AA	RGS4	rs2842030	GT
RGS4	rs951439	CT	RGS4	rs2661319	TC
RGS5	rs1056515	TT	RHOA	rs11716445	GG
RRM1	rs232043	AA	RRM1	rs720106	TT
RRM1	rs2284449	TT	RYR1	rs112563513	GG
RYR1	rs118192116	CC	RYR1	rs118192122	GG
RYR1	rs118192124	CC	RYR1	rs118192161	CC
RYR1	rs118192162	AA	RYR1	rs118192163	GG
RYR1	rs118192167	AA	RYR1	rs118192168	GG

Gene	Marker	Genotype	Gene	Marker	Genotype
RYR1	rs118192170	TT	RYR1	rs118192175	CC
RYR1	rs118192177	CC	RYR1	rs118192178	CC
RYR1	rs121918592	GG	RYR1	rs121918594	GG
RYR1	rs121918595	CC	RYR1	rs1801086	GG
RYR1	rs193922747	TT	RYR1	rs193922753	GG
RYR1	rs193922768	CC	RYR1	rs193922770	CC
RYR1	rs193922772	GG	RYR1	rs193922802	GG
RYR1	rs193922803	CC	RYR1	rs193922807	GG
RYR1	rs193922809	GG	RYR1	rs193922816	CC
RYR1	rs193922818	GG	RYR1	rs193922832	GG
RYR1	rs193922843	GG	RYR1	rs193922876	CC
RYR1	rs193922878	CC	RYR1	rs28933396	GG
RYR1	rs28933397	CC	RYR1	rs63749869	GG
RYR2	rs2819742	GG	SCAP	rs12487736	CC
SCARB1	rs5888	AG	SCN1A	rs3812718	CT
SCN2A	rs2304016	AA	SELE	rs3917412	CC
SERPINE1	rs6092	GG	SERPINE1	rs1799889	AG
SERPINE1	rs2227631	AA	SH2B1	rs3888190	CC
SLC12A3	rs1529927	GG	SLC16A5	rs4788863	TC
SLC16A7	rs3763980	AA	SLC19A1	rs12659	GG
SLC19A1	rs1051266	CC	SLC19A1	rs1051296	AA
SLC22A1	rs628031	AG	SLC22A1	rs683369	CC
SLC22A1	rs622342	AA	SLC22A1	rs594709	GA
SLC22A1	rs202220802	II	SLC22A1	rs2282143	CC
SLC22A1	rs34130495	GG	SLC22A1	rs35167514	II
SLC22A1	rs12208357	CC	SLC22A16	rs723685	AG
SLC22A16	rs6907567	AG	SLC22A16	rs714368	TC
SLC22A16	rs12210538	AA	SLC22A2	rs316019	CC
SLC22A3	rs2076828	GG	SLC22A3	rs8187725	CC
SLC22A4	rs1050152	CT	SLC22A5	rs2631372	GG
SLC30A9	rs1047626	AG	SLC31A1	rs7851395	GG
SLC31A1	rs10981694	TT	SLC39A14	rs17060812	CC
SLC47A1	rs2289669	GA	SLC47A2	rs12943590	GG
SLC47A2	rs34834489	AA	SLC6A12	rs557881	AA
SLC6A2	rs2242446	CT	SLC6A4	rs1042173	CC

Gene	Marker	Genotype	Gene	Marker	Genotype
SLC7A5	rs4240803	GG	SLCO1A2	rs3764043	CC
SLCO1A2	rs4149009	TT	SLCO1B1	rs4149056	TC
SLCO1B1	rs4149036	CC	SLCO1B1	rs2306283	AA
SLCO1B1	rs11045819	CC	SLCO1B1	rs2291073	TT
SLCO1B1	rs11045879	TC	SLCO1B1	rs11045821	GG
SLCO1B1	rs4149081	GA	SLCO1B3	rs4149117	GG
SLCO1B3	rs7311358	AA	SLCO2B1	rs12422149	GG
SLCO2B1	rs3781727	TT	SOD2	rs4880	AG
SP1	rs784888	GG	SRP19	rs495794	AG
STAT6	rs1059513	TC	STK39	rs6749447	TT
STN1	rs4387287	CC	STX1B	rs72800847	AA
STX1B	rs4889606	AA	STX4	rs10871454	CC
SV2C	rs11960832	CT	TAAR6	rs4305746	AA
TAPBP	rs1059288	AG	TAPBP	rs2071888	GC
TBC1D1	rs9852	CC	TBX2	rs8068318	CT
TBXA2R	rs4523	AA	TBXA2R	rs1131882	AA
TBXAS1	rs6962291	TT	TCF19	rs2073724	CT
TCF7L2	rs4132670	GA	TCF7L2	rs4506565	AT
TCF7L2	rs7917983	TC	TCF7L2	rs290487	CC
TGFB1	rs1800469	GG	TH	rs2070762	AA
THBD	rs1042580	TC	THRA	rs11819745	GG
TLR3	rs3775291	CT	TLR4	rs4986790	AG
TLR4	rs1927907	CT	TNF	rs1800629	GA
TNFAIP3	rs6920220	GA	TNFRSF11A	rs1805034	CT
TPH2	rs10879346	TT	TPH2	rs1487278	TT
TPMT	rs1142345	TT	TPMT	rs12201199	AA
TPMT	rs1800460	CC	TRAF3IP2	rs76228616	GG
TSC1	rs7862221	TT	TYMP	rs11479	GG
TYMS	rs2847153	GA	TYMS	rs11280056	ID
TYMS	rs183205964	GG	UBE2I	rs9597	CC
UGT1A	rs34650714	CC	UGT1A	rs2741049	TC
UGT1A	rs2070959	AA	UGT1A	rs6759892	TT
UGT1A	rs28898617	AA	UGT1A1	rs887829	CC
UGT1A1	rs1042640	CC	UGT1A1	rs8330	CC
UGT1A1	rs10929303	CC	UGT1A1	rs10929302	GG

Gene	Marker	Genotype	Gene	Marker	Genotype
UGT1A3	rs7604115	CC	UGT1A6	rs1105879	AA
UGT1A7	rs7586110	TT	UGT1A9	rs2003569	GG
UGT2B15	rs1902023	AC	UGT2B7	rs7662029	AG
UGT2B7	rs28365063	AA	UGT2B7	rs7439366	TC
UGT2B7	rs10028494	AA	UGT2B7	rs7668258	TC
UGT2B7	rs11940316	TC	UGT2B7	rs4554144	CT
UGT2B7	rs6600879	CG	UGT2B7	rs6600880	TA
UGT2B7	rs6600893	TC	UGT2B7	rs7438135	GA
UGT2B7	rs7668282	TT	UGT2B7	rs12233719	GG
VDR	rs11168293	GG	VEGFA	rs25648	CT
VEGFA	rs2010963	GG	VEGFA	rs699947	AA
VKORC1	rs9923231	CC	VKORC1	rs9934438	GG
VKORC1	rs61742245	CC	VKORC1	rs55894764	CC
VKORC1	rs17878544	TT	VKORC1	rs8050894	CC
VKORC1	rs2359612	GG	VKORC1	rs2884737	AA
VKORC1	rs72547529	CC	VKORC1	rs104894542	AA
VKORC1	rs17886199	AA	VKORC1	rs104894539	CC
VKORC1	rs104894541	TT	VKORC1	rs11150606	TT
VKORC1	rs104894540	AA	VKORC1L1	rs4072879	AA
WNK1	rs880054	TT	WNT5B	rs2010851	AA
XPC	rs2228001	GT	XPO1	rs11125883	CC
XRCC1	rs1799782	GG	XRCC1	rs25487	CC
XRCC3	rs861539	GG	XRCC4	rs2075685	GT
YEATS4	rs7297610	CC	ZBTB22	rs3130100	TC

ANNEX: DETAILED INFORMATION ON WARFARIN

This annex details more precisely the needs related to the recommendations for warfarin, prescribed for people with cardiovascular problems. For the correct calculation of the recommended dose, the algorithm proposed by IWPC has been used (***I**nternational **W**arfarin **P**harmacogenetics **C**onsortium*), which takes into account anthropometric factors such as age, weight, height or ancestry, and genetic information from impact variants in the VKORC1 and CYP2C9 genes.

Therefore, based on ancestry, genetics and anthropometric characteristics, the warfarin dose recommendation for the patient is as follows:

RECOMMENDED DAILY DOSE: 7.59 mg

Additionally, CPIC recommends a dose adjustment considering additional genetic information, such as the CYP4F2 gene, among others. Based on this information, it is recommended to modify the dose as follows:

INCREASE DOSE BY 5 %

CALCULATION LIMITS

This dose is indicative, as for greater precision it should be taken into account if the patient is taking enzyme inducers (carbamazepine, rifampicin, phenytoin...), in which case the dose should be increased, or enzyme inhibitors (amioradone, statins, antifungals...), in which case the dose should be reduced. It is therefore recommended to follow the patient's clinical history in order to adjust the dose with a higher level of precision.

These calculations are made on the basis of demonstrated and published scientific evidence. For dose calculation, the IWPC algorithm takes into account the following haplotype combinations for CYP2C9: *1/*1, *1/*2, *2/*2, *2/*3, *1/*3 and *3/*3, together with the rs9923231 variant of VKORC1. This algorithm also leads to a dose reduction in African, African-American or Asian ancestry.

For the calculation of the modification, the following CYP2C9 haplotypes are taken into account: *5, *6 and *11. In addition, the CPIC adjustment takes into account other genetic information such as the CYP4F2 gene and the rs12777823 marker. An association between rs12777823 and warfarin dose has been found only in people of African-American ancestry, so although the variant is listed as a risk, it is not taken into account in the dose calculation. Conversely, if the patient has an ancestry other than African-American, the haplotype present in the CYP4F2 gene is studied, where the haplotype combinations are taken into account: *1/*1, *1/*3 and *3/*3. If the patient presents other alleles or combinations that imply reduced or slow metabolism, it is recommended to see a medical professional for a more precise assessment.

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CONSIDERATIONS

Pharmacogenetics studies the influence of human genetics on the activity of a drug, its transport and metabolism. This knowledge allows specific drugs to be targeted to different groups of people classified according to their genetics, known as **Personalised Medicine**.

MyPharma Basic is a pharmacogenetic test which evaluates the pharmacological compatibility of 113 drugs with the genotype of each person. The genetic variants included in this study are single nucleotide polymorphisms (SNPs) and complete haplotypes of a gene. The main objective is to provide a tool with high clinical value and interpretability for healthcare specialists. To this end, the design of variants and drugs included in this test has been based on their usefulness and clinical validity. Therefore, the test includes those variants with the highest level of scientific evidence available to date for each of the target genes.

Pharmacogenomics Knowledge Database (PharmGKB) is the largest public database, formed by a consortium of pharmacogenomics and pharmacogenetics experts responsible of the collection, selection, incorporation and dissemination of all knowledge related to the impact of human genetic variation on drug response. PharmGKB is funded by the National Institute of Health (NIH) and the National Institute of General Medical Sciences (NIGMS) in the United States, and is a member of the NIH Pharmacogenomics Research Partnership (PGRN). PharmGKB was founded by Stanford University in year 2000.

The results of the MyPharma Basic test should serve as a tool to be taken into consideration when making personalised therapeutic decisions. The response to drugs is also affected by other factors such as concomitant treatments with other drugs, diseases, toxic habits, age, gender, etc. The final decision on treatment for each patient should always be made by the medical specialist or prescriber based on a thorough assessment of the patient.

TECHNOLOGY

DNA Microarray technology consists of a solid surface with microscopic reactions (microreactions) or DNA chip, on which molecular probes are attached to detect the presence of target DNA molecules. Probe-target hybridization is usually detected and quantified by measuring the intensity of a given fluorescence provided by the molecular probe in samples. This type of technology allows the detection of thousands of specific DNA fragments present in a DNA sample. On the other hand, the specificity in terms of DNA sequence recognition is very high since single nucleotide exchange (single-base resolution) can be detected using short oligonucleotide probes (20-25 nucleotides). As a result, DNA Microarray technology has also evolved to be applied as a DNA sequencing technique to genotype several hundred thousand single nucleotide variants (SNVs) in target genes located throughout the genome (Whole Genome DNA Microarray).

Bead Chip Infinium Global Screening Array Orion (GSA Orion) is a line of DNA chips developed by Illumina for its DNA Microarray iScan platform, widely used in population genetic studies and precision medicine, providing optimized content with 100% reliable and reproducible high-quality genotyping results. The construction of the GSA Chip was carried out in collaboration with a consortium of experts, and for the selection of SNVs, information from prestigious scientific databases such as gnomAD, NHGRI-EBI-GWAS Catalog, ClinVAr, MHC-HLA-KIR and PharmGKB has been used. The GSA allows the analysis of approximately 700,000 SNVs that cover variants of interest (hot spots) throughout the entire genome, impacting a wide range of genetic traits with physiological and pathophysiological implications. In addition, it allows the customization by users to incorporate Ad Hoc 50,000-100,000 variants of interest.

QUALITY

Laboratory has standard and effective procedures to protect against technical and operational problems. However, results can be altered due to problems with sample collection (contamination) and labelling (identification), delay in receiving the sample in the laboratory (integrity), among other problems. This could lead to invalidation of the test results. In such cases, you would be asked to repeat the entire testing process.

As with all genetic tests, there is a small chance that laboratory may report inaccurate information. If there is a suspicion of an error in the detected genotype, a verification test may be requested.

RISKS AND LIMITATIONS

The results presented in this report are limited to the scientific knowledge existing at the date of test processing.

This test only detects the specified genetic variants, it does not detect other minority variants, even if they are related to other pathologies. The metaboliser types provided refer to general phenotypes. Enzyme activity may be substrate dependent. The recommendations described throughout this report of results are indicative, OVERGENES is not responsible for any possible misinterpretation of the results provided. MyPharma Basic is not a medical report.

These results should **NOT** be interpreted as a diagnostic tool, it only informs about the genetic predisposition of each individual to respond to possible treatment with any of these drugs.

Genetics for people

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