ID: CLP3006

OMICS

Genetics for people

Pharmacogenetics

CHRONIC PAIN

MyPharma

PAIN

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 in terms of ***"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
Non-steroidal anti-inflammatory drugs	Celecoxib Flurbiprofen Ibuprofen Meloxicam Piroxicam Tenoxicam Ketoprofen	Dextro-methorphan Nitroprusside	Aspirin Diclofenac Ketorolac	Lornoxicam Sulindacam Indomethacin
Antipyretics			Paracetamol	Dipyrone
Opioids	Codeine Hydrocodone Tramadol	Buprenorphine Fentanyl Oxycodone Sufentanil	Alfentanil Methadone Morphine Remifentanil	Butorphanol
Local anaesthetics	Rocuronium	Propofol	Sevoflurane	Desflurane Isoflurane Ketamine
Anxiolytics		Lorazepam Midazolam Oxazepam		Alprazolam Diazepam Nitrous oxide

Category	High impact	Moderate impact	Limited impact	No associated impact
Antidepressants	Amitriptyline Desipramine Nortriptyline Paroxetine Venlafaxine			Duloxetine
Antiepileptics	Phenytoin	Topiramate	Valproic acid Carbamazepine Oxcarbazepine	Gabapentin Pregabalin
Antipsychotics	Aripiprazole Haloperidol Risperidone	Olanzapine	Quetiapine	
Corticosteroids		Dexamethasone Methylprednisolone	Prednisone Triamcinolone	
Others	Metoprolol	Atenolol Dexmedetomidine Dobutamine Ephedrine/ Phenylephrine Isoproterenol Naloxone Propranolol		Bisoprolol Clonidine Memantine Mexiletine Succinylcholine

DETAILED RESULTS

All the drugs analysed that have been classified as High impact and Moderate impact by MyPharma Pain 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.

Metoprolol				N° AFFECTED VARIANTS 3/8
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ADRB2	rs1042713 rs1042714	3	D **E** T O Pk	Reduced response to treatment
CYP2D6	*4	1A	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where the DPWG recommends using smaller increments in dose titration and/or prescribing 25% (slow metabolisers) or 50% (intermediate metabolisers) of the standard dose if a gradual reduction in heart rate is desired or in case of symptomatic bradycardia. For ultrarapid metabolisers use the maximum dose for the relevant indication as the target dose, and if efficacy is still insufficient increase the dose up to 2.5 times the standard dose or use an alternative drug.

Risperidone				N° AFFECTED VARIANTS 28/47
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
-	rs1805054	3	D E **T** O Pk	Increased risk of adverse effects
ADRB2	rs1042713	3	D E **T** O Pk	Increased risk of adverse effects
AKT1	rs2494732 rs3803300	3	D **E** T O Pk	Reduced response to treatment
ANKK1	rs1800497	3	D **E** T O Pk	Reduced response to treatment
CCL2	rs2857657 rs4586 rs4795893	3	D **E** T O Pk	Reduced response to treatment

Risperidone				N° AFFECTED VARIANTS 28/47
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CNR1	rs1049353	3	D E **T** O Pk	Increased risk of adverse effects
COMT	rs165599 rs9606186	3	D **E** T O Pk	Reduced response to treatment
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
DRD3	rs6280	3	D **E** T O Pk	Reduced response to treatment
GRIN2B	rs1806201	3	D E **T** O Pk	Increased risk of adverse effects
GRM7	rs2069062	3	D **E** T O Pk	Reduced response to treatment
HRH3	rs3787430	3	D **E** T O Pk	Reduced response to treatment
HRH4	rs4483927	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	rs3813929 rs6318	3	D E **T** O Pk	Increased risk of adverse effects
NR1I2	rs1523130 rs2276707	3	D E T O **Pk**	Reduced drug elimination
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
CYP2D6	*4	1A	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where the DPWG recommends dose reduction for slow metabolisers. For ultrarapid metabolisers, it is recommended to use an alternative drug or titrate the dose according to the maximum dose.

Amitriptyline				N° AFFECTED VARIANTS 11/13
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs10248420 rs10280101 rs11983225 rs12720067 rs2032583 rs2235015 rs2235040 rs2235067 rs4148739 rs4148740	3	D **E** T O Pk	Lower likelihood of remission
CYP2D6	*4	1A	D E **T** O **Pk**	Increased risk of adverse effects and reduced 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.

Paroxetine				N° AFFECTED VARIANTS 26/34
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs10248420 rs10280101 rs11983225 rs12720067 rs2032583 rs2235015 rs2235040 rs2235067 rs4148739 rs4148740	3	D **E** T O Pk	Lower likelihood of remission
ADM	rs11042725	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
	rs2470890 rs2472304	3	D **E** T O Pk	Lower likelihood of remission
DRD3	rs6280	3	D **E** T O Pk	Reduced response to treatment

Paroxetine				N° AFFECTED VARIANTS 26/34
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
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
CYP2D6	*4	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 not metabolised by CYP2D6 for ultrarapid metabolisers. For slow metabolisers, a 50% reduction in starting dose, a slower titration and a 50% reduced maintenance dose is recommended. The DWPG recommends an alternative drug for ultrarapid metabolisers.

Venlafaxine				N° AFFECTED VARIANTS 18/26
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs10248420 rs10280101 rs11983225 rs12720067 rs2032583 rs2235015 rs2235040 rs2235067 rs4148739 rs4148740	3	D **E** T O Pk	Lower likelihood of remission
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
GRIA3	rs3761554 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	rs1487278	3	D **E** T O Pk	Reduced response to treatment

Venlafaxine

N° AFFECTED VARIANTS 18/26

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
CYP2D6	*4	1A	D E **T** O **Pk**	Increased risk of adverse effects and reduced metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where the CPIC recommends an alternative drug not metabolised by CYP2D6 for slow metabolisers. The DPWG recommends an alternative drug or reduce the dose and monitor the plasma metabolite level for slow and intermediate metabolisers. For ultrarapid metabolisers, it is recommended to increase the dose to 150% or use an alternative drug.

Codeine

N° AFFECTED VARIANTS 3/5

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
ABCB1	rs1128503	3	D E **T** O Pk	Infants whose mother has this genotype are more likely to develop central nervous system depression.
OPRM1	rs1799971	3	**D** E T O Pk	Need for higher dose
CYP2D6	*4	1A	D **E** T O **Pk**	Lower response to treatment and lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends using an alternative drug other than tramadol for slow and ultrarapid metabolisers. For normal and intermediate metabolisers, an age- or weight-adapted dose of codeine is recommended.

Nortriptyline

N° AFFECTED VARIANTS 2/5

Gene	Variant	Level of evidence	Affected parameter	Variant annotation
GNB3	rs5443	3	D **E** T O Pk	Reduced response to treatment
CYP2D6	*4	1A	D E **T** O **Pk**	Increased risk of adverse effects and reduced metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends dose reduction to 25% in intermediate metabolisers. For slow or ultrarapid metabolisers, an alternative drug is recommended. If this is not possible, a dose reduction of 50% is recommended in slow metabolisers. The DPWG recommends reducing the dose for slow or intermediate metabolisers and for ultrarapid metabolisers it recommends an alternative drug or increasing the standard dose by 70%. In addition, it is recommended that plasma concentrations of nortriptyline and 10-hydroxynortriptyline be monitored.

Tramadol				N° AFFECTED VARIANTS 6/12
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
ARRB2	rs1045280	3	D E **T** O Pk	Increased risk of adverse effects
OPRD1	rs2234918	3	D E **T** O Pk	Increased risk of adverse effects
OPRM1	rs1799971	3	D **E** T O Pk	Lower response to treatment in combination with acetaminophen
CYP2D6	*4	1A	**D E T** O **Pk**	Lower metabolism, lower response to treatment, need for higher doses and higher risk of experiencing sedation

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends an alternative drug for slow or ultrarapid metabolisers. For normal and intermediate metabolisers, a dose adapted to age and weight is recommended. The DPWG recommends monitoring efficacy in slow and intermediate metabolisers. In case of inefficacy, it is recommended to increase the dose or use an alternative drug other than codeine, and to monitor for insufficient pain relief. For ultrarapid metabolisers, an alternative drug other than codeine or use 40% of the standard dose and watch for adverse effects.

Phenytoin				N° AFFECTED VARIANTS 15/19
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1128503	3	D E T O **Pk**	Increased plasma drug concentrations
CYP1A1	rs2606345	3	D **E** T O Pk	Lower response to treatment in women

Phenytoin				N° AFFECTED VARIANTS 15/19
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C9	*2	1A	D E **T** O **Pk**	Lower metabolism and higher risk of toxicity
	rs71486745	3	**D** E T O Pk	Need for higher dose
	rs12782374	3	**D** E T O **Pk**	Reduced metabolism and need for higher doses
	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
GABRA1	rs2279020	3	D **E** T O Pk	Increased risk of experiencing resistance to antiepileptic drugs
NAT2	rs1041983 rs1208 rs1799929 rs1799931 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: There are annotations for one or more affected variants where the CPIC recommends dose reduction. The DPWG recommends using the standard starting dose and reducing the maintenance dose, and monitoring response, serum concentrations and adverse effects.

Rocuronium				N° AFFECTED VARIANTS 2/2
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1128503	3	D **E** T O Pk	Reduced response to treatment
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 high risk impact, it is recommended to seek medical assessment.

Haloperidol				N° AFFECTED VARIANTS 2/7
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CNR1	rs1049353	3	D E **T** O Pk	Increased risk of adverse effects
CYP2D6	*4	1A	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where the DPWG recommends using 60% of the normal dose for slow metabolisers. For ultrarapid metabolisers it is recommended to increase the dose by 50% or use an alternative drug.

Celecoxib				N° AFFECTED VARIANTS 3/7
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C9	*2	1A	D E T O **Pk**	Lower metabolism
IL23R	rs7518660	3	D E **T** O Pk	Increased risk of developing adenoma
PTGER4	rs4133101	3	D E **T** O Pk	Increased risk of adverse effects

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends starting treatment with 25-50% of the minimum starting dose for slow metabolisers and the minimum starting dose for intermediate metabolisers.

Aripiprazole				N° AFFECTED VARIANTS 6/10
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
SH2B1	rs3888190	3	D E **T** O Pk	Increased risk of adverse effects
CYP2D6	*4	1A	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where the DPWG recommends reducing the maximum dose in slow metabolisers.

Desipramine				N° AFFECTED VARIANTS 3/4
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
MC1R	rs2228478 rs2228479	3	D **E** T O Pk	Lower likelihood of remission
CYP2D6	*4	1A	D E **T** O **Pk**	Increased risk of adverse effects and reduced metabolism

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

Hydrocodone				N° AFFECTED VARIANTS 2/2
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
OPRM1	rs1799971	3	D E **T** O Pk	Increased risk of adverse effects
CYP2D6	*4	1A	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends starting treatment at a weight- and age-appropriate dose in intermediate and slow metabolisers. If no response, consider an alternative drug.

Ibuprofen				N° AFFECTED VARIANTS 4/5
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
PTGS2	rs20417	3	D **E** T O Pk	Reduced response to treatment
CYP2C8	*1	3	**D** E T O Pk	Need for higher doses
	*3	3	D E T O **Pk**	Lower metabolism
CYP2C9	*2	1A	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends starting treatment with 25-50% of the minimum starting dose for slow metabolisers and the minimum starting dose for intermediate metabolisers.

Flurbiprofen				N° AFFECTED VARIANTS 1/2
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C9	*2	1A	D E T O **Pk**	Lower metabolism

Therapeutic recommendation: There are annotations for one or more affected variants where CPIC recommends starting treatment with 25-50% of the minimum starting dose for slow metabolisers and the minimum starting dose for intermediate metabolisers.

Tenoxicam				N° AFFECTED VARIANTS 1/2
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C9	*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 slow or intermediate metabolisers.

Ketoprofen				N° AFFECTED VARIANTS 3/3
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C9	*1	3	D **E** T O Pk	Reduced response to treatment
	*2	3	D E **T** O Pk	Increased severity of dyspepsia
CYP2D6	*4	3	D E **T** O Pk	Increased risk of experiencing sedation

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.

Piroxicam				N° AFFECTED VARIANTS 1/2
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C9	*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 not predominantly metabolised by CYP2C9 for slow and intermediate metabolisers.

Meloxicam				N° AFFECTED VARIANTS 1/2
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C9	*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 metabolisers. For intermediate metabolisers start treatment with 50% of the minimum starting dose or choose an alternative drug.

Atenolol				N° AFFECTED VARIANTS 19/27
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs3213619	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 rs1042714	3	D **E** T O Pk	Reduced response to treatment
AGT	rs5051 rs699	3	D **E** T O Pk	Reduced response to treatment
DPYS	rs2669429	3	D E **T** O Pk	Increased risk of adverse effects
EDN1	rs5370	3	D **E** T O Pk	Reduced response to treatment
FTO	rs9940629	3	D E **T** O Pk	Increased reduction of HDL-C
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
GNB3	rs2301339	3	D **E** T O Pk	Lower response to treatment in women
	rs5443	3	D **E** T O Pk	Reduced response to treatment
LDLR	rs688	3	D **E** T O Pk	Reduced response to treatment

Atenolol				N° AFFECTED VARIANTS 19/27
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
NR1H3	rs11039149	3	D E **T** O Pk	Increased risk of developing cardiovascular adverse effects
PLA2G4A	rs10157410	3	D E **T** O Pk	Increased risk of adverse effects
PROX1	rs340874	3	D E **T** O Pk	Increased risk of adverse effects
STN1	rs4387287	3	D **E** T O Pk	Reduced response to treatment
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, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Fentanyl				N° AFFECTED VARIANTS 12/23
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
CACNA1E	rs3845446	3	**D** E T O Pk	Need for higher dose
CYP3A4	rs2242480	2A	**D E** T O Pk	Lower response to treatment and need for higher doses
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
OPRD1	rs2234918	3	D E **T** O Pk	Increased risk of adverse effects
OPRM1	rs1799971 rs540825 rs9397685	3	D E **T** O Pk	Increased risk of adverse effects

Fentanyl				N° AFFECTED VARIANTS 12/23
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2D6	*4	3	**D** E T O Pk	There is no annotation for this drug-haplotype interaction. However, this haplotype has reduced enzyme activity, so it is recommended to consult your physician.
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.

Olanzapine				N° AFFECTED VARIANTS 29/57
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs10248420	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
BDNF	rs6265	3	D **E** T O Pk	Reduced response to treatment
CNR1	rs1049353	3	D E **T** O Pk	Increased risk of adverse effects
CYP3A43	rs472660	3	D E T O **Pk**	Reduced drug elimination

Olanzapine				N° AFFECTED VARIANTS 29/57
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
GNB3	rs5443	3	D E **T** O Pk	Increased risk of adverse effects
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 rs3813929 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
PMCH	rs7973796	3	D E **T** O Pk	Increased risk of adverse effects
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
SV2C	rs11960832	3	D **E** T O Pk	Reduced response to treatment

Olanzapine				N° AFFECTED VARIANTS 29/57
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
TBC1D1	rs9852	3	D E **T** O Pk	Increased risk of adverse effects
CYP2D6	*4	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.

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
CTNNB1	rs4135385	3	D **E T** O Pk	Reduced response to treatment in multiple myeloma

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.

Methylprednisolone				N° AFFECTED VARIANTS 1/1
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	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.

Oxycodone				N° AFFECTED VARIANTS 7/8
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	3	**D** E T O Pk	Need for higher dose
COMT	rs4680	3	D E **T** O Pk	Increased risk of vomiting in conjunction with naloxone
OPRD1	rs581111	3	D **E** T O Pk	Reduced response to treatment
OPRM1	rs1799971	3	D **E** T O Pk	Reduced response to treatment
UGT2B7	rs7439366	3	D **E** T O Pk	Reduced response to treatment
CYP2D6	*4	2A	D E T O **Pk**	Lower metabolism
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.

Propofol				N° AFFECTED VARIANTS 2/4
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1128503	3	D **E** T O Pk	Reduced response to treatment
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.

Sufentanil				N° AFFECTED VARIANTS 4/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1128503	3	**D** E T O Pk	Need for higher dose
CYP3A4	rs2242480	3	**D E** T O **Pk**	Lower response to treatment, need for higher dosage and lower metabolism

Sufentanil				N° AFFECTED VARIANTS 4/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
OPRM1	rs1799971	3	**D** E T O Pk	Need for higher dose
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.

Nitroprusside				N° AFFECTED VARIANTS 1/1
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ACE	rs4340	3	D **E** T O Pk	Reduced vasodilatation

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.

Dobutamine				N° AFFECTED VARIANTS 1/2
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
GNAS	rs62205366	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.

Ephedrine/ Phenylephrine				N° AFFECTED VARIANTS 1/1
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ADRB2	rs1042713	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.

Isoproterenol				N° AFFECTED VARIANTS 1/1
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ADRB2	rs1042713	3	D E T **O** Pk	Risk of desensitization

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.

Propranolol				N° AFFECTED VARIANTS 1/1
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ADRB2	rs1042713	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.

Buprenorphine				N° AFFECTED VARIANTS 4/8
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ARRB2	rs1045280	3	D E **T** O Pk	Increased risk of adverse effects
COMT	rs4680	3	D E **T** O Pk	Increased risk of adverse effects and prenatal abstinence syndrome.
OPRD1	rs529520	3	D **E** T O Pk	Reduced response to treatment
	rs2234918	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.

Naloxone				N° AFFECTED VARIANTS 1/3
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
COMT	rs4680	3	D E **T** O Pk	Increased risk of vomiting in conjunction with oxycodone

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.

Midazolam				N° AFFECTED VARIANTS 3/6
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
POR	rs1057868	3	D E T **O** Pk	Reduced metabolism
VDR	rs1544410	3	D E T O **Pk**	Reduced drug elimination
CYP3A5	*3	3	D E T O **Pk**	Reduced metabolism and elimination of the drug

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.

Dexmedetomidine				N° AFFECTED VARIANTS 1/1
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
PRKCB	rs9922316	3	D E T **O** Pk	Reduced vasoconstriction

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.

Oxazepam				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.

Dextromethorphan				N° AFFECTED VARIANTS 1/1
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2D6	*4	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, and given its classification as a drug with a moderate risk impact, it is recommended to seek medical assessment.

Ketorolac				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, it is recommended to seek medical assessment.

Aspirin				N° AFFECTED VARIANTS 21/46
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP4F2	rs2108622	3	D **E** T **O** Pk	Increased platelet aggregation in conjunction with clopidogrel and epinephrine
F13A1	rs5985	3	D **E** T O Pk	Reduced response to treatment
FCER1G	rs11587213	3	D E **T** O Pk	Increased risk of adverse effects if you have asthma
GP1BA	rs6065	3	D **E** T O Pk	Reduced response to treatment and increased risk of aspirin resistance
HNMT	rs1050891	3	D E **T** O Pk	Increased risk of adverse effects
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
ITGA2	rs1062535 rs1126643	3	D **E** T O Pk	Reduced response to treatment
NAT2	rs4271002	3	D E **T** O Pk	Increased risk of adverse effects
PEAR1	rs12041331	3	D **E** **T** O Pk	Increased risk of adverse effects and lower response to treatment
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
PTGS2	rs20417	3	D E **T** O Pk	Increased risk of coronary heart disease
SLC6A12	rs557881	3	D E **T** O Pk	Increased risk of adverse effects
TBXA2R	rs1131882	3	D E **T** O Pk	Increased risk of adverse effects
TGFB1	rs1800469	3	D E **T** O Pk	Increased risk of adverse effects

Aspirin				N° AFFECTED VARIANTS 21/46
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
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
TSC1	rs7862221	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.

Valproic acid				N° AFFECTED VARIANTS 7/19
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ANKK1	rs1800497	3	D E **T** O Pk	Increased risk of adverse effects
CYP1A1	rs2606345	3	D **E** T O Pk	Lower response to treatment in women
GABRA1	rs2279020	3	D **E** T O Pk	Increased risk of experiencing resistance to antiepileptic drugs
GRIN2B	rs1019385	3	**D** E T O Pk	Need for higher dose
SH2B1	rs3888190	3	D E **T** O Pk	Increased risk of adverse effects
UGT2B7	rs7668258	3	D E T O **Pk**	Increased plasma drug concentrations
CYP2C9	*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.

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
CCL11	rs1129844	3	D E **T** O Pk	Increased risk of adverse effects in 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
	rs4680	3	D E **T** O Pk	Increased severity of Neonatal Abstinence Syndrome.
CYP2B6	rs3745274	3	**D** E T O Pk	Need for higher doses for opioid addiction treatment
	rs2279343	3	**D** E **T** O Pk	Need for higher doses for the treatment of opioid addiction and risk of neonatal abstinence syndrome.
CYP3A4	rs3735451	3	D E **T** O Pk	Increased risk of adverse effects in opioid addiction treatment
DRD2	rs1799978 rs6275	3	**D** E T O Pk	Need for higher doses for opioid addiction treatment
GAD1	rs3749034	3	**D** E T O Pk	Need for higher doses for opioid addiction treatment
GNB3	rs5443	3	D E **T** O Pk	Increased risk of adverse effects in opioid addiction treatment

Methadone				N° AFFECTED VARIANTS 20/41
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
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
UGT2B7	rs7439366	3	D E T O **Pk**	Lower drug concentration in plasma
CYP2D6	*4	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, it is recommended to seek medical assessment.

Morphine				N° AFFECTED VARIANTS 7/14
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	3	D **E** T O Pk	Reduced response to treatment
COMT	rs6269	3	D **E** T O Pk	Reduced response to treatment
OPRK1	rs1051660	3	**D** E T O Pk	Need for higher dose
OPRM1	rs1799971	3	**D E T** O Pk	Increased risk of adverse effects, lower response to treatment and need for higher doses
SLC6A4	rs1042173	3	**D** E T O Pk	Need for higher dose

Morphine				N° AFFECTED VARIANTS 7/14
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
UGT2B7	rs7439366	3	D **E** T O **Pk**	Lower response to treatment and lower plasma drug concentration
	rs7438135	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.

Oxcarbazepine				N° AFFECTED VARIANTS 2/4
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

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.

Prednisone				N° AFFECTED VARIANTS 3/7
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	3	D E T **O** Pk	Risk of needing steroids up to one year after heart transplantation in pediatric patients
CTLA4	rs4553808	3	D E **T** O Pk	Increased risk of early onset of peripheral neuropathy in conjunction with bortezomib
CXCL12	rs1801157	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.

Remifentanil				N° AFFECTED VARIANTS 2/5
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1045642	3	**D E** T O Pk	Lower response to treatment and need for higher doses
	rs1128503	3	D **E T** O Pk	Increased risk of adverse effects and 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.

Sevoflurane				N° AFFECTED VARIANTS 2/45
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs1128503	3	D **E T** O Pk	Increased risk of adverse effects and lower response to treatment
FASTKD3;I	rs1801394	3	D **E** T **O** Pk	Lower response to treatment and higher risk of lowering mean arterial 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.

Carbamazepine				N° AFFECTED VARIANTS 14/27
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
ABCB1	rs4148739 rs4148740	3	D E T O **Pk**	Reduced metabolism
ABCC2	rs3740066	3	D E T O **Pk**	Reduced metabolism
CYP1A1	rs2606345	3	D **E** T O Pk	Reduced response to treatment
CYP1A2	rs762551	3	D E T O **Pk**	Reduced drug elimination
EPHX1	rs1051740	3	D E T O **Pk**	Reduced metabolism

Carbamazepine				N° AFFECTED VARIANTS 14/27
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
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	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
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.

Quetiapine				N° AFFECTED VARIANTS 7/16
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
HTR1A	rs10042486	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.

Diclofenac				N° AFFECTED VARIANTS 3/8
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
CYP2C9	*2	3	D E T O **Pk**	Lower metabolism
TN-FRSF11A	rs1805034	3	D E **T** O Pk	Increased risk of adverse effects
CYP2C8	*3	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.

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.

Alfentanil				N° AFFECTED VARIANTS 1/1
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
OPRM1	rs1799971	3	**D E T** O **Pk**	Lower response to treatment, need for higher doses, greater severity of adverse effects and higher drug concentration in plasma.

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.

Paracetamol				N° AFFECTED VARIANTS 3/10
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
OPRM1	rs1799971	3	D **E** T O Pk	Reduced response to treatment

Paracetamol				N° AFFECTED VARIANTS 3/10
Gene	**Variant**	**Level of evidence**	**Affected parameter**	**Variant annotation**
TN-FRSF11A	rs1805034	3	D E **T** O Pk	Increased risk of adverse effects
UGT2B15	rs1902023	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.

GENETIC RESULTS

HAPLOTYPES

Gene	Reference haplotype	Haplotype	Type of Metaboliser
CYP2B6	*1/*1	*1/*1	NORMAL
CYP2C19	*38/*38	*1/*1	NORMAL
CYP2C8	*1/*1	*1/*3	INTERMEDIATE
CYP2C9	*1/*1	*1/*2	INTERMEDIATE
CYP2D6	*1/*1	*4/*4	SLOW
CYP3A4	*1/*1	*1/*1	NORMAL
CYP3A5	*1/*1	*3/*3	SLOW
NAT2	*4/*4	*5B/*7B	SLOW
TPMT	*1/*1	*1/*1	NORMAL
UGT1A1	*1/*1	*1/*1	NORMAL

VARIANTS

Gene	Marker	Genotype	Gene	Marker	Genotype
-	rs10739150	GG	-	rs1104514	AG
-	rs11959113	GG	-	rs12346562	CA
-	rs1446468	TC	-	rs16973410	CT
-	rs1805054	CC	-	rs2056527	CC
-	rs2069521	GG	-	rs2433320	GA
-	rs2562456	CT	-	rs2768759	AA
-	rs2769605	CT	-	rs2952768	TC
-	rs2965667	TT	-	rs352428	GG
-	rs4675690	CT	-	rs585719	CC
-	rs74795342	GG	-	rs75222709	TT
-	rs78015114	TT	-	rs79663003	TT
ABCB1	rs10248420	AG	ABCB1	rs10267099	AA
ABCB1	rs10280101	AA	ABCB1	rs1045642	GG
ABCB1	rs1128503	AG	ABCB1	rs11983225	TT
ABCB1	rs12720067	CC	ABCB1	rs2032582	CC
ABCB1	rs2032583	AA	ABCB1	rs2229109	CC
ABCB1	rs2235015	CC	ABCB1	rs2235040	CC
ABCB1	rs2235067	CC	ABCB1	rs3213619	AG

Gene	Marker	Genotype	Gene	Marker	Genotype
ABCB1	rs3842	TT	ABCB1	rs4148739	TT
ABCB1	rs4148740	AA	ABCB1	rs4728709	GA
ABCB1	rs7787082	GA	ABCB1	rs9282564	TT
ABCB5	rs17143212	CC	ABCC2	rs2273697	GG
ABCC2	rs3740066	CT	ABCC2	rs4148386	GA
ABCG2	rs2231142	GG	ABCG2	rs3114020	CC
ACE	rs4291	TT	ACE	rs4340	ID
ADGRL3	rs1355368	GG	ADGRL3	rs6551665	GA
ADGRL3	rs6813183	CC	ADGRL3	rs734644	CC
ADH1B	rs2066702	GG	ADH1C	rs698	TC
ADM	rs11042725	CC	ADORA1	rs16851030	CC
ADORA1	rs2228079	TG	ADRA2A	rs1800545	GA
ADRB1	rs1801253	CC	ADRB2	rs1042713	GA
ADRB2	rs1042714	GC	ADRB2	rs1042718	CC
ADRB2	rs1045280	TT	ADRB3	rs4994	AA
AGT	rs5050	TT	AGT	rs5051	CC
AGT	rs699	AA	AHR	rs4410790	TC
AKT1	rs2494732	TC	AKT1	rs3803300	CC
ALDH2	rs671	GG	ALDH5A1	rs2760118	CT
ALOX12	rs11078659	GG	ANKK1	rs1800497	GG
ANKS1B	rs7968606	CC	ARRB2	rs1045280	TT
ASIC2	rs11869731	GC	ASTN2	rs958804	TC
BACH1	rs2070401	AA	BAG6	rs750332	TT
BCHE	rs118204423	GG	BCHE	rs1799807	TT
BCHE	rs1803274	CC	BCHE	rs28933390	CC
BDNF	rs61888800	GG	BDNF	rs6265	CT
BDNF	rs7124442	TT	BDNF	rs962369	TT
BMP5	rs41271330	GG	CACNA1C	rs1051375	GA
CACNA1E	rs3845446	TT	CACNA1S	rs1800559	CC
CACNA1S	rs772226819	GG	CACNG2	rs2284017	TT
CCL11	rs1129844	GA	CCL2	rs2857657	GC
CCL2	rs4586	TT	CCL2	rs4795893	GG
CEP68	rs7572857	GG	CHIA	rs3818822	GG
CHRM2	rs324650	TA	CHRNA3	rs1051730	GG
CHRNA3	rs3743075	TT	CHRNA3	rs3743078	GG

Gene	Marker	Genotype	Gene	Marker	Genotype
CHRNA3	rs578776	GG	CHRNA4	rs1044396	AA
CHRNA4	rs2229959	AA	CHRNA5	rs16969968	GG
CHRNA5	rs2036527	GG	CHRNA5	rs503464	TT
CHRNA5	rs55781567	CC	CHRNA5	rs588765	TT
CHRNA5	rs637137	TT	CHRNA5	rs660652	AA
CHRNA5	rs684513	CC	CHRNB2	rs2072658	GG
CHRNB2	rs2072660	CC	CHRNB2	rs2072661	GG
CHRNB4	rs3813567	AA	CNR1	rs1049353	CT
CNR1	rs806368	TT	CNR1	rs806378	CC
COL1A1	rs1800012	CC	COMT	rs165599	AA
COMT	rs4633	TT	COMT	rs4680	AA
COMT	rs4818	CC	COMT	rs5993883	TT
COMT	rs6269	AA	COMT	rs933271	TT
COMT	rs9606186	CC	CRHR1	rs242941	CC
CRHR2	rs2270007	CC	CTLA4	rs4553808	GG
CTNNB1	rs4135385	AG	CXCL12	rs1801157	CC
CYP1A1	rs2472297	CT	CYP1A1	rs2606345	AA
CYP1A2	rs2069526	TT	CYP1A2	rs2470890	CT
CYP1A2	rs2472304	GA	CYP1A2	rs4646425	CC
CYP1A2	rs4646427	TT	CYP1A2	rs762551	CA
CYP2A6	rs140471703	CC	CYP2A6	rs28399433	AA
CYP2A6	rs28399468	CC	CYP2A6	rs376817657	CC
CYP2A6	rs5031016	AA	CYP2A6	rs56113850	TC
CYP2B6	rs2279343	AG	CYP2B6	rs3211371	CC
CYP2B6	rs3745274	GG	CYP2B6	rs8192709	CC
CYP2C19	rs11188072	CC	CYP2C19	rs12248560	CC
CYP2C19	rs145119820	GG	CYP2C19	rs28399504	AA
CYP2C19	rs4986893	GG	CYP2C9	rs1057910	AA
CYP2C9	rs12782374	GG	CYP2C9	rs1934969	AT
CYP2C9	rs71486745	II	CYP2C9	rs9332096	CC
CYP2D6	rs1065852	GG	CYP2D6	rs1080985	GG
CYP2D6	rs3892097	CT	CYP2D6	rs5030655	II
CYP2E1	rs3813867	GG	CYP2E1	rs2031920	CC
CYP3A4	rs2242480	CC	CYP3A4	rs2246709	AA
CYP3A4	rs2740574	TT	CYP3A4	rs35599367	GG

Gene	Marker	Genotype	Gene	Marker	Genotype
CYP3A4	rs3735451	TC	CYP3A4	rs4646437	GG
CYP3A4	rs4646440	GG	CYP3A43	rs472660	GG
CYP3A5	rs15524	AA	CYP3A5	rs776746	CC
CYP4F2	rs2108622	CT	DBH	rs1611115	TC
DDC	rs12718541	GG	DPYS	rs2669429	AG
DRD1	rs11746641	TT	DRD1	rs11749035	CC
DRD1	rs2168631	GG	DRD1	rs265976	GG
DRD1	rs4532	CT	DRD1	rs5326	CC
DRD1	rs686	GA	DRD2	rs1076560	CC
DRD2	rs1079597	CC	DRD2	rs1124493	TG
DRD2	rs1799978	TT	DRD2	rs2283265	CC
DRD2	rs2440390	CC	DRD2	rs2514218	CT
DRD2	rs2734841	AC	DRD2	rs2734842	GC
DRD2	rs4436578	CT	DRD2	rs6275	AG
DRD2	rs6277	GA	DRD2	rs6279	GC
DRD3	rs167770	AA	DRD3	rs167771	AA
DRD3	rs324023	CC	DRD3	rs324026	TT
DRD3	rs6280	TT	DRD3	rs963468	AA
DROSHA	rs639174	CC	EDN1	rs5370	GG
EPB41	rs6702335	GG	EPHX1	rs1051740	TC
EPHX1	rs2234922	AA	EPM2A	rs1415744	TC
ERICH3	rs11580409	AC	F13A1	rs5985	CC
FAAH	rs2295632	GG	FAAH	rs324420	CC
FAAH	rs3766246	GG	FAAH	rs4141964	CC
FASTKD3	rs1801394	GG	FCER1G	rs11587213	AA
FGF2	rs1449683	CC	FKBP5	rs1360780	CC
FKBP5	rs4713916	GG	FMO1	rs10912675	TC
FMO1	rs12720462	CC	FMO1	rs7877	CT
FMO3	rs2266780	AA	FMO3	rs2266782	GG
FSIP1	rs7179742	AA	FTO	rs12595985	CC
FTO	rs9940629	AG	GABRA1	rs2279020	GG
GABRA1	rs2290732	AA	GABRA2	rs279858	TT
GABRQ	rs3810651	TA	GAD1	rs3749034	GG
GAL	rs948854	TT	GALNT2	rs2144297	TC
GALNT2	rs2144300	CT	GALR1	rs2717162	TT

Gene	Marker	Genotype	Gene	Marker	Genotype
GARS1-DT	rs1074373	CC	GATA3	rs3824662	CC
GCG	rs13429709	TT	GDNF	rs2216711	GA
GDNF	rs2973049	TC	GIPR	rs10423928	TT
GLDC	rs10975641	CG	GNAS	rs62205366	TT
GNB3	rs2301339	GA	GNB3	rs5443	CT
GP1BA	rs6065	CC	GRIA3	rs3761554	TT
GRIA3	rs3761555	TT	GRIA3	rs4825476	AA
GRIA3	rs502434	TC	GRIK1	rs2832407	CC
GRIN2B	rs1019385	CA	GRIN2B	rs1806201	GG
GRIN3A	rs10121600	CC	GRIN3A	rs11788456	GA
GRK4	rs1801058	CC	GRK4	rs1801253	CC
GRM3	rs724226	AG	GRM7	rs2069062	GG
GSK3B	rs334558	AG	GSK3B	rs6438552	GG
GSTA1	rs3957357	AG	GSTM3	rs36120609	II
HCG22	rs2523864	CT	HCG22	rs3873352	CC
HLA-DPB1	rs1042136	AA	HNMT	rs1050891	AA
HRH3	rs3787430	CC	HRH4	rs4483927	TT
HSPA1A	rs1043620	CC	HSPA1L	rs2227956	AA
HTR1A	rs10042486	CT	HTR1A	rs1364043	TG
HTR1A	rs6295	CG	HTR1B	rs11568817	AA
HTR1B	rs130058	TT	HTR1B	rs6296	CG
HTR1B	rs9361233	TT	HTR2A	rs2770296	TT
HTR2A	rs6311	TT	HTR2A	rs6313	AA
HTR2A	rs6314	GG	HTR2A	rs7997012	GG
HTR2A	rs9316233	CC	HTR2C	rs1414334	GG
HTR2C	rs2497538	CC	HTR2C	rs3813928	GG
HTR2C	rs3813929	CC	HTR2C	rs518147	GG
HTR2C	rs6318	GG	HTR3A	rs1062613	TC
HTR3A	rs2276302	GA	HTR3B	rs11606194	TT
HTR3B	rs3758987	TC	IL11	rs1126757	CC
IL1B	rs1143627	AA	IL23R	rs7518660	GA
IL4	rs2243250	CC	ITGA2	rs1062535	GA
ITGA2	rs1126643	CT	ITIH3	rs2535629	GA
KCNJ6	rs2070995	CC	KCNJ6	rs2835859	TT
KCNK3	rs1275988	CC	KMT2E	rs117986340	GG

Gene	Marker	Genotype	Gene	Marker	Genotype
LDLR	rs688	TT	LEP	rs4731426	CC
LEP	rs7799039	AA	LEPR	rs1137101	GG
LTC4S	rs730012	AA	MAFK	rs4720833	AG
MC1R	rs2228478	AA	MC1R	rs2228479	GG
MC4R	rs17782313	TT	MC4R	rs489693	CC
MTHFR	rs1801131	TG	MTHFR	rs1801133	GG
MYD88	rs6853	AA	NAT2	rs1041983	CT
NAT2	rs1208	GA	NAT2	rs1799929	CT
NAT2	rs1799930	GG	NAT2	rs1799931	GA
NAT2	rs1801280	TC	NAT2	rs4271002	GC
NAT2	rs4646244	TT	NEDD4L	rs520210	GG
NFKBIA	rs696	CT	NGF	rs2239622	GG
NOS2	rs11080344	TT	NOS3	rs1799983	GG
NR1D1	rs2071427	CT	NR1D1	rs2314339	CC
NR1H3	rs11039149	AG	NR1I2	rs1523130	CC
NR1I2	rs2276707	CC	NR1I2	rs2461817	CC
NR1I2	rs3814055	CC	NR1I2	rs4688040	GG
NR1I2	rs7643645	AA	NTRK2	rs10465180	CT
OPRD1	rs2234918	TT	OPRD1	rs4654327	AA
OPRD1	rs529520	AC	OPRD1	rs581111	AG
OPRD1	rs678849	CT	OPRD1	rs797397	GA
OPRK1	rs1051660	CA	OPRK1	rs3802281	TT
OPRL1	rs2229205	CC	OPRM1	rs10485058	AA
OPRM1	rs1799971	AG	OPRM1	rs540825	TT
OPRM1	rs79910351	CC	OPRM1	rs9397685	AA
OR52E2	rs16909440	CC	OR52J2P	rs2499984	AA
P2RY1	rs1065776	CC	PEAR1	rs12041331	AA
PLA2G4A	rs10157410	GC	PLA2G4A	rs12746200	AA
PLCG1	rs2228246	AA	PMCH	rs7973796	GA
POLG	rs3087374	CC	POR	rs1057868	CC
PPARG	rs1801282	CC	PPARG	rs3856806	CC
PRKCB	rs11649514	GG	PRKCB	rs9922316	TG
PROX1	rs340874	CC	PTGER2	rs2075797	CC
PTGER3	rs7551789	AT	PTGER4	rs4133101	TC
PTGES	rs2302821	AA	PTGIR	rs1126510	GG

Gene	Marker	Genotype	Gene	Marker	Genotype
PTGS1	rs10306114	AA	PTGS2	rs20417	CC
PTGS2	rs4648287	AA	RABEP1	rs1000940	AG
REEP5	rs153549	GG	REEP5	rs153560	AA
RGS4	rs2661319	TC	RGS4	rs2842030	GT
RGS4	rs951439	CT	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
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
SCN1A	rs3812718	CT	SCN2A	rs2304016	AA
SCN4A	rs80338792	CC	SERPINE1	rs1799889	AG
SERPINE1	rs2227631	AG	SERPINE1	rs6092	GG
SH2B1	rs3888190	CC	SLC22A1	rs12208357	CC
SLC22A1	rs34130495	GG	SLC22A1	rs35167514	II
SLC22A1	rs628031	GG	SLC30A9	rs1047626	AG
SLC39A14	rs17060812	CC	SLC6A12	rs557881	AG
SLC6A2	rs2242446	CT	SLC6A4	rs1042173	AA
SLC7A5	rs4240803	GG	SLCO1B1	rs2306283	AA
SOD2	rs4880	AG	SRP19	rs495794	GG
STN1	rs4387287	AC	SULT1A1	rs1042028	CC
SV2C	rs11960832	TT	TAAR6	rs4305746	GA
TAPBP	rs1059288	AA	TAPBP	rs2071888	GG

Gene	Marker	Genotype	Gene	Marker	Genotype
TBC1D1	rs9852	CC	TBX2	rs8068318	CT
TBXA2R	rs1131882	GG	TBXA2R	rs4523	GG
TBXAS1	rs6962291	AA	TGFB1	rs1800469	AG
TH	rs2070762	AG	THRA	rs11819745	GA
TLR3	rs3775291	CT	TNF	rs1800629	GG
TNFRSF11A	rs1805034	CC	TPH2	rs10879346	CT
TPH2	rs1487278	TT	TRPV1	rs224534	GA
TSC1	rs7862221	TC	UGT1A	rs1042640	GC
UGT1A	rs10929303	TC	UGT1A	rs2070959	AA
UGT1A	rs2741049	TC	UGT1A	rs28898617	AA
UGT1A	rs6759892	TT	UGT1A	rs8330	GC
UGT1A1	rs10929302	GG	UGT1A1	rs887829	CC
UGT1A6	rs1105879	AA	UGT2B10	rs112561475	GG
UGT2B15	rs1902023	AC	UGT2B7	rs10028494	AC
UGT2B7	rs11940316	TT	UGT2B7	rs12233719	GG
UGT2B7	rs28365063	AA	UGT2B7	rs4554144	CC
UGT2B7	rs6600879	CC	UGT2B7	rs6600880	TT
UGT2B7	rs6600893	TT	UGT2B7	rs7438135	GG
UGT2B7	rs7439366	TT	UGT2B7	rs7662029	AA
UGT2B7	rs7668258	TT	UGT2B7	rs7668282	TT
VDR	rs11568820	CT	VDR	rs1544410	CT
VDR	rs4516035	TT	XPO1	rs11125883	AC
ZBTB22	rs3130100	TT			

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 Pain is a pharmacogenetic test which evaluates the pharmacological compatibility of 73 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 Pain 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 Pain 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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