ID: CLP3006

OMICS

Genetics for people

# Pharmacogenetics

## NEUROPSYCHIATRY

# MyPharma

# NEURO

# 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 |
|---|---|---|---|---|
| **Anticonvulsants** | Phenytoin<br>Phenobarbital<br>Lamotrigine | Topiramate | Valproic acid<br>Carbamazepine<br>Oxcarbazepine | Gabapentin<br>Mephenytoin<br>Methylpheno-barbital<br>Pregabalin |
| **Anxiolytics** | | Lorazepam<br>Midazolam<br>Oxazepam | | Alprazolam<br>Diazepam<br>Nitrous oxide |
| **Antipsychotics** | Aripiprazole<br>Haloperidol<br>Risperidone | Clozapine<br>Fluphenazine<br>Iloperidone<br>Lurasidone<br>Olanzapine<br>Perphenazine<br>Thioridazine | Amisulpride<br>Chlorpromazine<br>Lithium<br>Paliperidone<br>Quetiapine<br>Trifluoperazine | Ziprasidone |

| Category | High impact | Moderate impact | Limited impact | No associated impact |
|---|---|---|---|---|
| **Antidepressants** | Amitriptyline<br>Clomipramine<br>Desipramine<br>Fluvoxamine<br>Mirtazapine<br>Nortriptyline<br>Paroxetine<br>Trimipramine<br>Venlafaxine | Sketamine<br>Fluoxetine<br>Isoniazid | Citalopram<br>Escitalopram<br>Milnacipran<br>Morphine<br>Naltrexone<br>Sertraline | Duloxetine<br>Liothyronine |
| **Smoking cessation treatment** | | Bupropion<br>Varenicline | Nicotine | Clonidine |
| **ADHD** | | | Methylpheni-date | Dextroamphe-tamine |
| **Dementia** | | | | Memantine |

# DETAILED RESULTS

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

| | **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 |
| 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 |

| Risperidone | | | | N° AFFECTED VARIANTS 28/47 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| 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<br>rs10280101<br>rs11983225<br>rs12720067<br>rs2032583<br>rs2235015<br>rs2235040<br>rs2235067<br>rs4148739<br>rs4148740 | 3 | D **E** T O Pk | Lower likelihood of remission |

| Amitriptyline | | | | N° AFFECTED VARIANTS 11/13 |
|---|---|---|---|---|
| **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 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 |
| 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 |

| Paroxetine | | | | N° AFFECTED VARIANTS 26/34 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| 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 |
| 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.

| Phenobarbital | | | | N° AFFECTED VARIANTS 2/2 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| ABCB1 | rs1045642 | 3 | D **E** T O Pk | Increased risk of experiencing drug resistance |
| CYP1A1 | rs2606345 | 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.

| 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.

| 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.

| Clomipramine | | | | N° AFFECTED VARIANTS 2/5 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| FKBP5 | rs1360780 | 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 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.

| Fluvoxamine | | | | N° AFFECTED VARIANTS 5/8 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| ABCB1 | rs2032583 | 3 | D **E** T O Pk | Lower likelihood of remission |
| 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 |
| CYP2D6 | *4 | 1A | D E T O **Pk** | Lower metabolism |

**Therapeutic recommendation:** There are annotations for one or more affected variants where CPIC recommends a 25-50% reduction in the starting dose. In addition, it recommends an alternative drug that is not metabolised by CYP2D6 for slow metabolisers.

| 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.

| Lamotrigine | | | | N° AFFECTED VARIANTS 3/5 |
|---|---|---|---|---|
| **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 |
| 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 high risk impact, it is recommended to seek medical assessment.

## 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.

## Mirtazapine

N° AFFECTED VARIANTS 5/8

| Gene | Variant | Level of evidence | Affected parameter | Variant annotation |
|---|---|---|---|---|
| FKBP5 | rs4713916 | 3 | D **E** T O Pk | Reduced response to treatment |
| SH2B1 | rs3888190 | 3 | D E **T** O Pk | Increased risk of adverse effects |
| TPH2 | rs1487278 | 3 | D **E** T O Pk | Reduced response to treatment |

| Mirtazapine | | | | N° AFFECTED VARIANTS 5/8 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| CYP2B6 | *1 | 3 | D **E** T **O** Pk | Lower response to treatment and lower metabolism |
| CYP2D6 | *4 | 2A | 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 high risk impact, it is recommended to seek medical assessment.

| Trimipramine | | | | N° AFFECTED VARIANTS 1/4 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| CYP2D6 | *4 | 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.

| Fluoxetine | | | | N° AFFECTED VARIANTS 10/14 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| - | rs2433320 | 3 | D **E** T O Pk | Reduced response to treatment |
| ABCB1 | rs4148739 | 3 | D **E** T O Pk | Lower likelihood of remission |
| FKBP5 | rs4713916 | 3 | D **E** T O Pk | Reduced response to treatment |
| GSK3B | rs334558 | 3 | D **E** T O Pk | Reduced response to treatment |
| HTR1A | rs6295 | 3 | D **E** T O Pk | Reduced response to treatment |
| REEP5 | rs153549 rs153560 | 3 | D **E** T O Pk | Reduced response to treatment |
| SERPINE1 | rs1799889 rs2227631 | 3 | D **E** T O Pk | Reduced response to treatment |

| Fluoxetine | | | | N° AFFECTED VARIANTS 10/14 |
|---|---|---|---|---|
| **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.

| Clozapine | | | | N° AFFECTED VARIANTS 16/28 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| ABCB1 | rs10248420 rs7787082 | 3 | D **E** T O Pk | Reduced response to treatment |
| 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 |
| EPM2A | rs1415744 | 3 | D **E** T O Pk | Reduced response to treatment |
| HTR1A | rs6295 | 3 | D **E** T O Pk | Reduced response to treatment |
| HTR2C | rs3813929 | 3 | D E **T** O Pk | Increased risk of adverse effects |
| HTR3A | rs1062613 rs2276302 | 3 | D **E** T O Pk | Reduced response to treatment |
| ITIH3 | rs2535629 | 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 |

| Clozapine | | | | N° AFFECTED VARIANTS 16/28 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| CYP1A2 | *1 | 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. |
| 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 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.

| Isoniazid | | | | N° AFFECTED VARIANTS 11/18 |
|---|---|---|---|---|
| **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 *7B | 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 rs1799931 rs1801280 | 3 | D E **T** O Pk | Increased risk of toxicity in conjunction with phenytoin. |
| 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.

| Bupropion | | | | N° AFFECTED VARIANTS 11/15 |
|---|---|---|---|---|
| **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 |
| 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 |
| EPB41 | rs6702335 | 3 | D **E** T O Pk | Lower likelihood of abstinence in men |
| HTR2A | rs2770296 | 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.

| Sketamine | | | | N° AFFECTED VARIANTS 1/2 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| BDNF | rs6265 | 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.

| Varenicline | | | | N° AFFECTED VARIANTS 3/5 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| CHRNA5 | rs16969968 rs2036527 rs503464 | 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.

| Fluphenazine | | | | N° AFFECTED VARIANTS 1/1 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| CYP1A2 | rs762551 | 3 | D E **T** O Pk | Increased risk of having an increased QT interval |

**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.

| Thioridazine | | | | N° AFFECTED VARIANTS 1/2 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| CYP1A2 | rs762551 | 3 | D E **T** O Pk | Increased risk of having an increased QT interval |

**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.

| Iloperidone | | | | N° AFFECTED VARIANTS 1/1 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| CYP2D6 | rs1065852 | 3 | D E **T** O Pk | Increased risk of having an increased QT interval |

**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.

| Lurasidone | | | | N° AFFECTED VARIANTS 1/1 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| HTR1A | rs6295 | 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.

| Perphenazine | | | | N° AFFECTED VARIANTS 2/2 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| RGS4 | rs951439 | 3 | D **E** T O Pk | Lower response than olanzapine |
| | rs2842030 | 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.

| 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.

| Lithium | | | | N° AFFECTED VARIANTS 7/19 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| - | rs16973410 | 3 | D **E** T O Pk | Reduced response to treatment |
| ASIC2 | rs11869731 | 3 | D **E** T O Pk | Reduced response to treatment |
| CACNG2 | rs2284017 | 3 | D **E** T O Pk | Reduced response to treatment |
| FKBP5 | rs1360780 | 3 | D **E** T O Pk | Reduced response to treatment |
| OR52E2 | rs16909440 | 3 | D **E** T O Pk | Reduced response to treatment |
| OR52J2P;( | rs2499984 | 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.

| Nicotine | | | | N° AFFECTED VARIANTS 30/49 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| CHRM2 | rs324650 | 3 | D E T **O** Pk | Increased risk of nicotine dependence |

| Nicotine | | | | N° AFFECTED VARIANTS 30/49 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| CHRNA3 | rs1051730 | 3 | **D E** T O Pk | Lower response to treatment and need for higher doses |
| | rs578776 | 3 | D **E T** O Pk | Increased risk of nicotine dependence |
| | rs3743078 | 3 | D E **T** O Pk | Increased risk of tobacco addiction |
| | rs3743075 | 3 | D E **T** O Pk | Increased severity of nicotine dependence |
| CHRNA4 | rs2229959 | 3 | D E **T** O Pk | Lower likelihood of quitting smoking |
| 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 |
| | rs637137 rs684513 | 3 | D E **T** O Pk | Increased risk of tobacco addiction |
| CYP2A6 | rs28399468 | 3 | D E T **O** Pk | Reduced metabolism |
| | rs56113850 | 3 | D E T O **Pk** | Increased tendency to smoke due to increased nicotine elimination |
| | *1 | 3 | D E **T** O Pk | Increased risk of nicotine dependence |
| | rs28399433 | 3 | D E **T** O Pk | Increased severity of nicotine dependence |
| CYP2B6 | *1 | 3 | D E T O **Pk** | Lower metabolism |
| DRD1 | rs11746641 rs11749035 rs2168631 | 3 | D **E** T O Pk | Reduced likelihood of abstinence |
| | rs4532 rs686 | 3 | D E T **O** Pk | Increased risk of nicotine dependence |
| EPB41 | rs6702335 | 3 | D **E** T O Pk | Reduced likelihood of abstinence |
| FMO1 | rs10912675 rs7877 | 3 | D E T **O** Pk | Increased risk of nicotine dependence |

| Nicotine | | | | N° AFFECTED VARIANTS 30/49 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| GALR1 | rs2717162 | 3 | D **E** T O Pk | Reduced response to treatment |
| GRIN3A | rs11788456 | 3 | D E T **O** Pk | Increased risk of nicotine dependence |
| | rs10121600 | 3 | D E T **O** Pk | Increased risk of smoking |
| HTR3B | rs11606194 | 3 | D E **T** O Pk | Increased probability of relapse |
| OPRM1 | rs1799971 | 3 | D **E T** O Pk | Increased risk of nicotine dependence and reduced response to treatment |
| POR | rs1057868 | 3 | D E T O **Pk** | Reduced 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.

| Escitalopram | | | | N° AFFECTED VARIANTS 9/16 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| - | rs2069521 | 3 | D E T O **Pk** | Reduced metabolism |
| 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 |
| 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 |
| IL11 | rs1126757 | 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.

| 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.

| Citalopram | | | | N° AFFECTED VARIANTS 24/32 |
|---|---|---|---|---|
| **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 | rs10248420<br>rs10280101<br>rs11983225<br>rs12720067<br>rs2032583<br>rs2235015<br>rs2235040<br>rs2235067<br>rs4148739<br>rs4148740 | 3 | D **E** T O Pk | Lower likelihood of remission |
| BDNF | rs7124442 | 3 | D **E** T O Pk | Reduced response to treatment |
| CRHR2 | rs2270007 | 3 | D **E** T O Pk | Reduced response to treatment |

| Citalopram | | | | N° AFFECTED VARIANTS 24/32 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| ERICH3 | rs11580409 | 3 | D **E** T O Pk | Reduced response to treatment |
| FKBP5 | rs1360780 | 3 | D **E** T O Pk | Reduced response to treatment |
| GLDC | rs10975641 | 3 | D **E** T O Pk | Reduced response to treatment |
| GSK3B | rs334558 | 3 | D **E** T O Pk | Reduced response to treatment |
| HTR2A | rs7997012 | 3 | D **E** T O Pk | Reduced response to treatment |
| | rs6313 | 3 | D E **T** O Pk | Increased risk of adverse effects |
| NEDD4L | rs520210 | 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 | 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.

| 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.

| 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 |
| GABRA1 | rs2279020 | 3 | D **E** T O Pk | Increased risk of experiencing resistance to antiepileptic drugs |

| Carbamazepine | | | | N° AFFECTED VARIANTS 14/27 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| 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.

| Methylphenidate | | | | N° AFFECTED VARIANTS 2/10 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| DRD3 | rs6280 | 3 | D E **T** O Pk | Increased risk of adverse effects |
| 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.

| Sertraline | | | | N° AFFECTED VARIANTS 4/9 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| ABCB1 | rs2032583 rs4148739 | 3 | D **E** T O Pk | Lower likelihood of remission |
| REEP5 | rs153549 rs153560 | 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.

| Naltrexone | | | | N° AFFECTED VARIANTS 2/6 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| ANKK1 | rs1800497 | 3 | D **E** T O Pk | Reduced response to treatment |
| OPRD1 | rs4654327 | 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.

| Amisulpride | | | | N° AFFECTED VARIANTS 2/7 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| 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.

| 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.

| Chlorpromazine | | | | N° AFFECTED VARIANTS 1/2 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| CYP1A2 | rs762551 | 3 | D E **T** O Pk | Increased risk of having an increased QT interval |

**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.

| Trifluoperazine | | | | N° AFFECTED VARIANTS 1/2 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| CYP1A2 | rs762551 | 3 | D E **T** O Pk | Increased risk of having an increased QT interval |

**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.

| Milnacipran | | | | N° AFFECTED VARIANTS 2/3 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| HTR1A | rs10042486<br>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.

| Paliperidone | | | | N° AFFECTED VARIANTS 1/4 |
|---|---|---|---|---|
| **Gene** | **Variant** | **Level of evidence** | **Affected parameter** | **Variant annotation** |
| 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.

# GENETIC RESULTS

## HAPLOTYPES

| Gene | Reference haplotype | Haplotype | Type of Metaboliser |
|---|---|---|---|
| CYP1A2 | *1A/*1A | *1/*1M | RAPID |
| CYP2A6 | *1/*1 | *1/*1 | NORMAL |
| CYP2B6 | *1/*1 | *1/*1 | NORMAL |
| CYP2C19 | *38/*38 | *1/*1 | NORMAL |
| CYP2C9 | *1/*1 | *1/*2 | INTERMEDIATE |
| CYP2D6 | *1/*1 | *4/*4 | SLOW |
| CYP3A4 | *1/*1 | *1/*1 | NORMAL |
| CYP3A5 | *1/*1 | *3/*3 | SLOW |
| GSTM1 | *II/*II | *I/*D | INTERMEDIATE |
| GSTT1 | *I/*I | *D/*D | 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 |

| Gene | Marker | Genotype | Gene | Marker | Genotype |
|---|---|---|---|---|---|
| ABCB1 | rs2032583 | AA | ABCB1 | rs2229109 | CC |
| ABCB1 | rs2235015 | CC | ABCB1 | rs2235040 | CC |
| ABCB1 | rs2235067 | CC | ABCB1 | rs3213619 | AG |
| 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 |

| Gene | Marker | Genotype | Gene | Marker | Genotype |
|---|---|---|---|---|---|
| CEP68 | rs7572857 | GG | CHIA | rs3818822 | GG |
| CHRM2 | rs324650 | TA | CHRNA3 | rs1051730 | GG |
| CHRNA3 | rs3743075 | TT | CHRNA3 | rs3743078 | GG |
| 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 |

| Gene | Marker | Genotype | Gene | Marker | Genotype |
|---|---|---|---|---|---|
| CYP2E1 | rs3813867 | GG | CYP2E1 | rs2031920 | CC |
| CYP3A4 | rs2242480 | CC | CYP3A4 | rs2246709 | AA |
| CYP3A4 | rs2740574 | TT | CYP3A4 | rs35599367 | GG |
| 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 |

| Gene | Marker | Genotype | Gene | Marker | Genotype |
|---|---|---|---|---|---|
| GABRQ | rs3810651 | TA | GAD1 | rs3749034 | GG |
| GAL | rs948854 | TT | GALNT2 | rs2144297 | TC |
| GALNT2 | rs2144300 | CT | GALR1 | rs2717162 | TT |
| 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 |

| Gene | Marker | Genotype | Gene | Marker | Genotype |
|---|---|---|---|---|---|
| ITGA2 | rs1126643 | CT | ITIH3 | rs2535629 | GA |
| KCNJ6 | rs2070995 | CC | KCNJ6 | rs2835859 | TT |
| KCNK3 | rs1275988 | CC | KMT2E | rs117986340 | GG |
| 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 |

| Gene | Marker | Genotype | Gene | Marker | Genotype |
|---|---|---|---|---|---|
| PROX1 | rs340874 | CC | PTGER2 | rs2075797 | CC |
| PTGER3 | rs7551789 | AT | PTGER4 | rs4133101 | TC |
| PTGES | rs2302821 | AA | PTGIR | rs1126510 | GG |
| 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 |

| Gene | Marker | Genotype | Gene | Marker | Genotype |
|---|---|---|---|---|---|
| STN1 | rs4387287 | AC | SULT1A1 | rs1042028 | CC |
| SV2C | rs11960832 | TT | TAAR6 | rs4305746 | GA |
| TAPBP | rs1059288 | AA | TAPBP | rs2071888 | GG |
| 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 Neuro 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 Neuro 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 Neuro 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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