Psychiatric Pharmacogenetics Report



DISCLAIMER: Do not alter your medication dose or stop your medication without first consulting your healthcare provider.

Name: Jane Doe Date of Report: April 16, 2021 Data Source: 23andMe

About this report

This report contains pharmacogenetic alleles and implications for drug response for the genetic data submitted. Both the genotypes presented and implicated medications are predictions based on the submitted data and published pharmacogenetics literature. This is not a clinical report and the data contained here in no way should be used as clinical guidance.

The information presented in this report is based on allele mappings and therapeutic implications developed by the <u>Clinical</u> <u>Pharmacogenomics Implementation Consortium</u> (CPIC®) and the <u>US Food and Drug administration</u> (FDA). Gene2Rx is not affiliated with CPIC or the FDA in any way. The contents of this page have not been endorsed by CPIC or the FDA and are the sole responsibility of Gene2Rx.

This report includes information about how your pharmacogenetics may influence your response to drugs used for psychiatric purposes. This report does not contain information about all drugs used for psychiatric purposes, only those that have known pharmacogenetic interactions. If you do not see your medication listed here, there are currently no prescription guidelines published by either the FDA or CPIC.

The implications of taking medication for which you may have an atypical response are based on probabilities. You may or may not experience and of side effects or altered efficaciousness. Consult your healthcare provider before making any changes to your healthcare.

The quality of uploaded data is not verified and may contain errors that result alter your pharmacogenetic report. Genotyping panels (such as those used by direct to consumer genetics services) offer an incomplete representation of an individuals genetics. You may harbor additional genetic variation that can affect drug response.

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Pharmacogenetics Summary

This table contains the specific variants identified in each of the genes assessed for your Gene2Rx report. These genes are important for modulating response to medications and have been determined to be clinically actionable for some medications.

The "Genotype" column indicates the specific alleles identified in your DNA. These correspond to patterns of genetic variants within each gene. There are two alleles for each gene, one for each copy.

The "Phenotype" column indicates the predicted effect that your genotype will have on the function of the proteins encoded by each gene. These phenotypes will determine how you will respond to different medications. See the legend below for descriptions of the symbols associated with each phenotype.

	Gene	Genotype	Phenotype
¥	CYP2C19	*1/*2	Intermediate Metabolizer
×	CYP2D6	*4/*4	Poor Metabolizer

Legend

Symbols in the Gene Summary table represent the predicted function of the gene. A non-normal allele does not necessarily lead to a change in drug response.

- Normal function
- Decreased function
- Increased function
- × Severely decreased or no function
- 2 Unknown function. The effect of this particular genotype on function is not known.

Drugs with Potential Atypical Response

Based on your genetics, you may have an atypical response to medications listed in this section. Listed below are drug classes followed by tables containing drugs within those classes and how your pharmacogenetics may influence how you respond to the drug. Each table contains generic names for the drug, brand names, the associated gene, your gene phenotype, and a description of how your genotype may affect your drug response. Each row also contains a link to the CPIC guideline or FDA drug label from which the information was derived, which also contains therapeutic recommendations for your healthcare provider.

Some drugs have guidance based on multiple genes. Results are assessed for each gene individually and grouped together in the report.

Drugs are often used for multiple indications and can belong to multiple drug classes. We have grouped the drugs in this report based on their most common use, but you may find that some drugs are used for purposes other than indicated by the drug classes in this report.

Therapeutic Guidance Legend

- Normal therapeutic guidance
- Alternate dosing recommended
- Alternate drug recommended

Note: Phenotypes with an unknown effect on drug response will have normal therapeutic guidance, despite the effect being unknown.

Antidepressants - SNRI

Generic name	Brand names	Gene	Your gene phenotype	Implication	Source
Venlafaxine	Effexor XR	CYP2D6	Poor Metabolizer	Alters systemic parent drug and metabolite concentrations. Consider dosage reductions.	<u>FDA</u>

Antidepressants - SSRI

	Generic name	Brand names	Gene	Your gene phenotype	Implication	Source
A	Fluvoxamine	Luvox	CYP2D6	Poor Metabolizer	Greatly reduced metabolism when compared to extensive metabolizers. Higher plasma concentrations may increase the probability of side effects.	<u>CPIC</u>
A	Paroxetine	Paxil, Seroxat	CYP2D6	Poor Metabolizer	Greatly reduced metabolism when compared to extensive metabolizers. Higher plasma concentrations may increase the probability of side effects.	<u>CPIC</u>
▲	Vortioxetine	Trintellix, Brintellix	CYP2D6	Poor Metabolizer	Results in higher systemic concentrations. The maximum recommended dose is 10 mg.	<u>FDA</u>

	Generic name	Brand names	Gene	Your gene phenotype	Implication	Source
			CYP2C19	Intermediate Metabolizer	Reduced metabolism of tertiary amines compared to normal metabolizers.	<u>CPIC</u>
	Amitriptyline	Elavil	CYP2D6	Poor Metabolizer	Greatly reduced metabolism of TCAs to less active compounds compared to normal metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.	<u>CPIC</u>
			CYP2C19	Intermediate Metabolizer	Reduced metabolism of tertiary amines compared to normal metabolizers.	<u>CPIC</u>
A	Clomipramine	Anafranil	CYP2D6	Poor Metabolizer	Greatly reduced metabolism of TCAs to less active compounds compared to normal metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.	<u>CPIC</u>
	Desipramine	Norpramin	CYP2D6	Poor Metabolizer	Greatly reduced metabolism of TCAs to less active compounds compared to normal metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.	<u>CPIC</u>
			CYP2C19	Intermediate Metabolizer	Reduced metabolism of tertiary amines compared to normal metabolizers.	<u>CPIC</u>
A	Doxepin	Sinequan, Quitaxon, Aponal	CYP2D6	Poor Metabolizer	Greatly reduced metabolism of TCAs to less active compounds compared to normal metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.	<u>CPIC</u>
			CYP2C19	Intermediate Metabolizer	Reduced metabolism of tertiary amines compared to normal metabolizers.	<u>CPIC</u>
A	Imipramine	Tofranil	CYP2D6	Poor Metabolizer	Greatly reduced metabolism of TCAs to less active compounds compared to normal metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.	<u>CPIC</u>
Δ	Nortriptyline	Pamelor	CYP2D6	Poor Metabolizer	Greatly reduced metabolism of TCAs to less active compounds compared to normal metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.	<u>CPIC</u>
			CYP2C19	Intermediate Metabolizer	Reduced metabolism of tertiary amines compared to normal metabolizers.	<u>CPIC</u>
A	Trimipramine	Surmontil	CYP2D6	Poor Metabolizer	Greatly reduced metabolism of TCAs to less active compounds compared to normal metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.	<u>CPIC</u>

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Antip	sychotics					
	Generic name	Brand names	Gene	Your gene phenotype	Implication	Source
A	Aripiprazole Lauroxil	Aristada	CYP2D6	Poor Metabolizer	Results in higher systemic concentrations. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations.	<u>FDA</u>
A	Aripiprazole	Abilify	CYP2D6	Poor Metabolizer	Results in higher systemic concentrations and higher adverse reaction risk. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations.	<u>FDA</u>
A	Brexpiprazole	Rexulti	CYP2D6	Poor Metabolizer	Results in higher systemic concentrations. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations.	<u>FDA</u>
A	lloperidone	Fanapt	CYP2D6	Poor Metabolizer	Results in higher systemic concentrations and higher adverse reaction risk (QT prolongation). Reduce dosage by 50%.	<u>FDA</u>
	Perphenazine	Trilafon	CYP2D6	Poor Metabolizer	Results in higher systemic concentrations and higher adverse reaction risk.	<u>FDA</u>
A	Pimozide	Orap	CYP2D6	Poor Metabolizer	Results in higher systemic concentrations. Dosages should not exceed 0.05 mg/kg in children or 4 mg/day in adults who are poor metabolizers and dosages should not be increased earlier than 14 days.	<u>FDA</u>

Psychostimulants

	Generic name	Brand names	Gene	Your gene phenotype	Implication	Source
A	Amphetamine	Adzenys ER	CYP2D6	Poor Metabolizer	May affect systemic concentrations and adverse reaction risk. Consider lower starting dosage or use alternative agent.	<u>FDA</u>
A	Atomoxetine	Strattera	CYP2D6	Poor Metabolizer	 CPIC: Significantly decreased metabolism of atomoxetine may result in higher concentrations as compared to non- poor metabolizers. This may increase the occurrence of treatment-emergent side effects, but also a greater improvement of ADHD symptoms as compared with non- poor metabolizers in those who tolerate treatment. Poor metabolizer status is associated with lower final dose requirements as compared to non- poor metabolizers. FDA: Results in higher adverse reaction risk. Adjust titration interval and increase dosage if tolerated. Refer to FDA labeling for specific dosing recommendations. 	<u>CPIC</u> , FDA

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Drugs with Typical Response

Based on your genetics, you are likely to respond normally to medications listed in this section.

Antidepressants - SSRI

	Generic name	Brand names	Gene	Your gene phenotype	Implication	Source
<	Citalopram	Celexa, Cipralex, Lexapro	CYP2C19	Intermediate Metabolizer	CPIC: Reduced metabolism when compared to extensive metabolizers.FDA: No FDA guidance for your genotype	<u>CPIC, FDA</u>
⊘	Escitalopram	Lexapro	CYP2C19	Intermediate Metabolizer	Reduced metabolism when compared to extensive metabolizers.	<u>CPIC</u>
⊘	Sertraline	Zoloft	CYP2C19	Intermediate Metabolizer	Reduced metabolism when compared to extensive metabolizers.	<u>CPIC</u>

Frequently Asked Questions

What do I do now?

If you find that you may have an atypical response to a medication you take or are considering taking it is important that you first consult with your healthcare provider or a genetic counselor before making any changes. The guidelines linked next to each finding (either CPIC or FDA) provide therapeutic guidance that include treatment recommendations.

Should I change medications or dosage based on my report?

No! Do not alter your medication dosage or stop taking your medication without first consulting your healthcare provider. Direct-toconsumer data is not clinical grade, so anything included in the report should be used as a conversation starter with your healthcare provider to seek the appropriate clinical laboratory test. Again, do not alter your medication dosage or stop taking your medication without first consulting your healthcare provider.

Why shouldn't I change my medication based on this report?

Our service relies on the genetic information provided to you by the direct-to-consumer service you paid for. Unfortunately, directto-consumer data is not clinical grade, so anything included in the report should be used as a conversation starter with your healthcare provider to seek the appropriate clinical laboratory test. DO NOT alter your medication dosage or stop taking your medication without first consulting your healthcare provider. Read more <u>here</u> and read primary research <u>here</u>.

Are these expert annotations?

Yes, The Clinical Pharmacogenetics Implementation Consortium (CPIC®) is a group of PGx experts that volunteer their time to curate genetic guidance for drug response, based on the most recent research. They have high standards for the evidence required to include a drug-gene guideline. The US Food and Drug Administration (FDA) has evaluated all pharmacogenetic associations presented in this report and believes there is sufficient scientific evidence to provide clinical guidance for prescribing practices. Read more <u>here</u>.

Why would my PGx annotations change?

While your genetics don't change over the course of your life, research is an ongoing process and what we know about how an individual's genetics influences their drug response changes over time. As new research is conducted and published, the CPIC guidelines and FDA drug labels are updated accordingly. These updates only happen once new research meets strict validation requirements and experts agree its time for a guideline change. Gene2Rx provides the most recent CPIC and FDA guidance at the time of the report.

I don't see my medication in the report. Why not?

Not all drugs are influenced by pharmacogenetics, and some need more research to verify an association. If you don't see you medication listed, it means that there is not yet a CPIC guideline for providing clinical guidance for pharmacogenetic dosing.

Does Gene2Rx determine structural variants for CYP2D6?

Structural variations for CYP2D6 are not called and may affect your response to drugs metabolized by CYP2D6.

More questions?

Contact us at contact@gene2rx.com.

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