

## How can I use the clinical considerations to help interpret the GeneSight® Psychotropic report?

### Introduction

Pharmacogenomic reports contain a lot of useful information. Sometimes there is so much information the report can seem overwhelming. To overcome this issue and to increase the clarity of the results for both healthcare providers and patients, the GeneSight test employs a user-friendly software-based product to report the results in an easy-to-read way. The GeneSight report categorizes medications into intuitive, color-coded categories based on an individual's genetic results. These include the green "Use as Directed," yellow "Moderate Gene-Drug Interaction," and red "Significant Gene-Drug Interaction" categories.

### What are clinical considerations and what is their clinical significance?

All medications start out in the green category on the GeneSight test. Based on an individual's genetic variation, a medication may be moved out of this category, and into the yellow or red category, depending on how significantly the variation is expected to impact outcomes with that medication. Medications on the GeneSight report are labeled with one or more of the ten possible clinical considerations, which explain the rationale for a medication's classification and can be used to help inform treatment decisions.

### How do I interpret each clinical consideration?

#### CLINICAL CONSIDERATIONS:

1: Serum level may be too high, lower doses may be required.  
 2: Serum level may be too low, higher doses may be required.  
 3: Difficult to predict dose adjustments due to conflicting variations in metabolism.

Clinical considerations 1 and 2 reflect an issue with how the medication is metabolized. This means that the individual has variation in one or more of their pharmacokinetic genes. This may affect how much medication is in an individual's system and may require a lower or higher dose, respectively. Clinical consideration 3 indicates that there are conflicting variations in the metabolism of that medication, thus making it difficult to predict a dose adjustment. The most common example is when there are two genes that contribute a relatively similar amount to the overall metabolism of the medication, but one has increased activity and the other has decreased activity.

4: Genotype may impact drug mechanism of action and result in moderately reduced efficacy.

Medications labeled with clinical consideration 4 are affected by a pharmacodynamic gene, and thus reflect an issue with the drug's mechanism of action. Variation in these genes predicts a moderately reduced response to certain medications. Since pharmacodynamic genes do not affect metabolism, it is unlikely that adjusting the dose will improve efficacy.

5: CYP2D6 genotype indicates that this patient may experience increased frequency of side effects but also greater symptom improvement in those who find the treatment tolerable.

Clinical consideration 5 specifically applies to atomoxetine (Strattera®) when a patient is a CYP2D6 poor metabolizer. This is based on evidence which shows that CYP2D6 poor metabolizers treated with atomoxetine experienced an increased frequency of side effects but also significantly greater improvement in ADHD symptoms compared to extensive (normal) metabolizers.<sup>1</sup>

6: Use of this drug may increase risk of side effects.

Clinical consideration 6 indicates that an individual may have an increased risk for side effects when taking this medication. This can be due to variation in one or more pharmacokinetic genes that may predict slower than normal metabolism of certain medications, which may result in higher levels of medication in the system. It could also be due to an effect caused by one of the pharmacodynamic genes.

7: Smoking status changes the results of this medication. See next section labeled Smokers for smoking results.

Clinical consideration 7 specifically applies to individuals who have the highly inducible variant of the CYP1A2 gene, which may result in increased activity for CYP1A2 when the patient is a smoker. This increased activity may change how this medication is metabolized. For individuals who are smokers, it is important to refer to the results in the following section labeled Smokers.

8: FDA label identifies a potential gene-drug interaction for this medication.  
9: Per FDA label, this medication is contraindicated for this genotype.

When medications are labeled with clinical consideration 8, it alerts the healthcare provider and patient that the FDA has made a statement in the package insert that may have pharmacogenomic implications for a person with this genotype taking this medication. Clinical consideration 9 indicates that the FDA has declared this medication contraindicated for a person with this genotype.

10: While this medication does not have clinically proven genetic markers that allow it to be categorized, it may be an effective choice based on other clinical factors.

Clinical consideration 10 is associated with medications in the gray "No Proven Genetic Markers" category, meaning that genetic markers have not yet been discovered to reliably predict which genes are involved in the metabolism and/or therapeutic efficacy of these medications. Due to this lack of evidence, we are not currently able to categorize them or provide actionable recommendations.

## Conclusions

Clinical considerations provide valuable information about a medication's classification. Healthcare providers can rely on these to help them think about how to potentially use a medication that is affected by genetic variation. Clinical considerations can also be used to help guide discussions with patients about treatment decisions.

---

For more information, contact the Assurex Health Medical Information Department at:

**PHONE:** 855.891.9415

**EMAIL:** [medinfo@assurexhealth.com](mailto:medinfo@assurexhealth.com)

## References

1. Michelson, D. et al. CYP2D6 and clinical response to atomoxetine in children and adolescents with ADHD. *J Am Acad Child Adolesc Psychiatry.* 46(2), 242-251 (2007).