personalized prescribing
next gen pharmacogenetics

Name:	Demo Illustrate	**Sample Type:**	Saliva
Sample ID:	DM0000000005	**Received:**	10-Apr-23
Physician:	Dr. Healer	**Reported:**	27-Apr-23

175 West Beaver Creek, Unit 24
Richmond Hill, ON L4B 1L1

Rx Report™ - Psychiatry - Anxiety & Depression

Pharmacogenomic Test

(Highly Confidential)

Result Summary

Dear Dr. Healer,

Dema Illustrate is experiencing symptoms of anxiety and ADHD. She requested a pharmacogenomic test and a medication review by a clinical pharmacist.

The pharmacogenetic test results and our algorithms indicate:

- The patient is likely to respond to Vortioxetine (Trintellix) 5 mg once daily, with titration to effect.
- The patient may continue to use Bupropion XL (Wellbutrin) and Concerta, if effective and tolerated. (**Note: Bupropion can increase blood levels of Vortioxetine via CYP2D6 inhibition. If taken together, consider not exceeding 10 mg of Vortioxetine and avoiding the maximum daily dose of 20 mg.)

According to a high level of evidence, the patient is a CYP2C19 *1/*2 intermediate metabolizer of Citalopram, Escitalopram, and Sertraline. This means she clears these medications from her body at a slightly slower than normal rate, leading to possible mild accumulation and sensitivity to side-effects. However, no dose adjustment is required. The Clinical Pharmacogenetic Implementation Consortium (CPIC) recommends initiating these medications at their regular starting dose, with a close monitor for side-effects.

According to a high level of evidence, the patient is a CYP2D6 *1/*1 normal metabolizer of antidepressants (Fluoxetine, Fluvoxamine, Paroxetine, Venlafaxine, Duloxetine, and Vortioxetine). This means she has no problems clearing these medications from her body and she is likely to reach normal bloodstream concentrations.

The patient’s ABCB1 gene rs2023583 AA denotes a poor ability for antidepressants to enter the brain due to high expression of the P-glycoprotein pump (P-gp) at the blood-brain barrier. This pump is responsible for expelling any substance from the brain that it recognizes as foreign. Despite this being a generally protective mechanism, many antidepressants have a high affinity for this pump and are easily expelled from the brain into the bloodstream. This may result in rHeduced brain entry and efficacy as well as increased risk of peripheral side effects such as nausea and upset stomach, as serotonin receptors are most densely located in the gut. Antidepressant expected to be able to cross into the brain with ease include: Fluoxetine, Sertraline, Vortioxetine, and Bupropion. Of these medications, she showed the highest likelihood of responding to Vortioxetine (Trintellix). In addition to regulating serotonin activity, Vortioxetine has weak stimulating and pro-cognitive properties by raising levels of other neurotransmitters such as dopamine, noradrenaline, and acetylcholine.

The patient’s gene COMT rs4680 GG status denotes a predisposition to high enzyme degradation of dopamine and norepinephrine in the pre-frontal cortex and thus relatively lower baseline levels of these neurotransmitters. This indicates Helen may benefit from a medication that raises levels of these neurotransmitters to improve her overall mood, energy, motivation, and executive function, such as Bupropion and psychostimulants.

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Summary of Psychiatry - Anxiety & Depression medication

The tested genes have resulted in the following results.

See the last page for an interpretation of the table below.

Drug	Metabolism	Efficacy	Side Effects
5-methylfolate and Vitamin B Complex		Moderate Responder	
Amitriptyline, Clomipramine, Imipramine, Trimipramine, and Doxepin	Intermediate Metabolizer		
Bupropion	Intermediate Metabolizer	Good Responder	**Anxiety**
Citalopram	Normal Metabolizer	Moderate Responder	**Heart Palpitations**; **Memory Loss/Concentration Problems**
Desipramine/Nortriptyline	Intermediate Metabolizer		
Desvenlafaxine		Moderate Responder	**Depression**; **Fatigue**
Duloxetine	Intermediate Metabolizer		
Escitalopram	Normal Metabolizer	Moderate Responder	**Heart Palpitations**; **Memory Loss/Concentration Problems**
Fluoxetine	Intermediate Metabolizer	Moderate Responder	**Insomnia**
Fluvoxamine	Intermediate Metabolizer	Moderate Responder	**Stomach Upset and Nausea**

Levomilnacipran		Moderate Responder	**Anxiety**
Mirtazapine		Moderate Responder	
Nefazodone	Intermediate Metabolizer		
Paroxetine	Intermediate Metabolizer	Moderate Responder	**Nausea - Stomach Upset**
Sertraline	Normal Metabolizer	Good Responder	
SSRIs (Class Effects)		Poor Responder	
Venlafaxine	Intermediate Metabolizer	Moderate Responder	**Increased Depression** **Fatigue**
Vilazodone		Poor Responder	
Vortioxetine	Intermediate Metabolizer	Moderate Responder	

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Pharmacogenomics is a two-part process, pharmacokinetics, and pharmacodynamics.

Pharmacokinetics is what the body does to the drug.

How it absorbs it, metabolizes it to its active component, circulates it and most importantly, clears it through the liver.

Patients can be one of the following:

Extensive Metabolizers are expected to clear these medications normally.
Intermediate Metabolizers have a slightly reduced ability to clear these medications from the body and may be more sensitive to their dose-related side-effects.
Poor Metabolizers have an increased inability to clear the medication and could result in serious side effects.
Ultra-Rapid Metabolizers clear these drugs too fast such that the drug is ineffective.

Pharmacodynamics is what the drug does to the body.

Drugs have mechanisms of action that include attaching to target genes, and by doing that, they might inhibit their function or might boost their function or another activity.

If most of the target genes are receptive, the drug succeeds, if some genes are receptive and others are not, the drugs does not respond too well, and if most of the genes are non-responsive, the drug fails.

Patients may respond to a medication in one of the following:

Good Responders:	This is an indication that the patient is likely to respond well to the medication.	**Proceed**
Moderate Responders:	This is an indication that the patient is likely to respond moderately well to the medication.	**Use with caution if cannot find a Good Response medication**
Poor Responders:	This is an indication that the patient is likely to respond poorly to the medication.	**Avoid**

Pharmacodynamics also can indicate side effects: The drug might attach to other genes that are not intended, which results in side effects.

Please do feel free to contact me if you have any questions.

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The Rx Report™ is aimed to provide genetic information to individuals and to their healthcare professionals that may help in selecting the appropriate medications for individuals struggling with mental illness medications. The report is based on patient assessment, including correct diagnosis, clinical history, relevant lifestyle factors, family history, co-morbidities, medications, and other factors. The Result Summary by a pharmacist is derived based on individual's genetic variations (SNPs) that are relevant to drug metabolism, transport, and target receptor binding for efficacy and side effects as per Personalized Prescribing Inc. (PPI) proprietary algorithm.

DISCLAIMER

The result summary is not intended to be diagnostic but to indicate drugs that are more likely to be effective for individuals. Any decision to prescribe or change medications should only be made by individual's treating physician based on their professional judgement and considering patients' medical history and other relevant information available in clinical literature, practice guidelines, FDA-approved drug labelling, indications, warnings, precautions etc.

The genes included in the report are based on the most recent literature available in public platforms such as FDA, Clinical Pharmacogenetic Implementation Consortium (CPIC), PharmGKB, and peer-reviewed medical literature. Any periodic updates on gene-drug interactions by PPI because of continuous changes in the availability of pharmacogenomic information, will be reflected in patients' genetic profiles, however, no updated Result Summary will be sent if not requested by patients or their physicians.

Discussion with PPI Pharmacist

Healthcare professionals/ psychiatrists/ physicians interested to discuss about PPI pharmacogenomics testing service, patient report interpretation etc. can contact PPI psychopharmacists. Please send an email to pharmacist@personalizedprescribing.com or call 647-943-0210 ext.1 to schedule an appointment with a psychopharmacist.

Test Methodology

The test was developed and validated in Personalized Prescribing Inc. (PPI) laboratory. PPI use in-house designed primers and assay reagents from Agena Bioscience, USA to perform the analysis. The test is used for clinical purpose, not for investigational use. PPI laboratory is certified by College of American Pathology (CAP) for performing high complexity testing. Rx Report-Psychiatry & Pain test by PPI has not been approved by the U.S. Food and Drug Administration (FDA).

Limitation of Test Process

The test methodology has limitations. The quality and quantity of DNA extracted from patients are depended on saliva sample collection process, for example dietary or microbial influence which can impact the test process. PCR process can be influenced by exogenous enzymes or PCR inhibitors that may affect the assay result. SLC6A4 is a very delicate assay that is developed and validated and interpreted based on currently available scientific evidence. The result interpretation may vary if rs255331 is not considered in addition to Long (L) and Short (S) alleles. There are a couple of SNPs that have repeat bases, amplification of DNA samples can be deterred due to repeat bases. As the test does not include sequencing of whole genome, there could be undetected genetic variants that may influence the phenotype. Non-genetic factors such as drug-drug interactions that are unknown could also limit the interpretation of the test. Rx report- Psychiatry & Pain test report is based on available resources in scientific platforms like PharmGKB, FDA, DPWG and CPIC. PPI geneticists and pharmacists conduct in-house research to understand the clinical relevance of the variant identified, phenotypes, and recurrent risks.

References

There are references for our developed algorithms listed at our website: www.personalizedprescribing.com/references/