May 9, 2022

Dear Physician,

Re: Patient Name

Your patient has elected to receive information about his/her pharmacogenetic profile using the Pillcheck™ service. I am a consulting clinical pharmacist providing a review of your patient's pharmacogenetic profile and the medical information provided by the patient. This letter outlines considerations for current and/or future medication therapy where applicable.

Patient-reported medical conditions:

Depression, PPPD

Patient-reported medications:

Medication	Dosage	Date Started	Side Effects	Still Take
Amitriptyline	20 mg	Aug 2021	Nausea, tremors	Yes
TRINTELLIX	20mg	Jan 2021	Nausea, tremors	Yes

Considerations for current therapy:

vortioxetine - metabolized by CYP2D6 (ultrarapid metabolizer)

- due to increased metabolism, can see lower than expected drug levels and reduced response
- recommend considering alternative agent; see below "considerations for future therapy"

amitriptyline - metabolized by CYP2C19 (intermediate metabolizer) and CYP2D6 (ultrarapid metabolizer)

- due to CYP2D6 status, likely to see significantly increased clearance and reduced therapeutic response
- recommend considering alternative agent; see below "considerations for future therapy"

Considerations for current conditions:

PPPD - vertigo associated with PPPD has been successfully treated with certain antidepressants (SSRIs) resulting in decreased frequency and severity of vertigo attacked see section below "antidepressants"

Migraines

- Topiramate - metabolism not affected by CYP450 standard dosing and precautions recommended
- nadolol - metabolism not affected by CYP450

- Off label use in the treatment of migraines
- According to the American Academy of Neurology and the American Headache Society, the use of nadolol has been shown to be effective in the treatment of migraines
- Standard dosing and precautions recommended

AVOID

- amitriptyline, nortriptyline, duloxetine - metabolized by CYP2D6 (ultrarapid metabolizer) ▪ see comments above for vortioxetine

Antidepressants

RECOMMENDED

- desvenlafaxine - normal CYP3A4 metabolizer; standard dosing and precautions recommended
- vilazodone - normal CYP3A4 metabolizer (major metabolic pathway)
  minor metabolic pathways include CYP2C19 (intermediate metabolizer) and unlikely that genetic variation will affect drug metabolism and response; standard dosing and precautions recommended
- Bupropion - normal CYP2B6 metabolizer; standard dosing and precautions recommended

USE WITH CAUTION

- citalopram, escitalopram, sertraline - intermediate CYP2C19 metabolizer; as a result of somewhat decreased metabolism, may see slightly increased drug levels (compared to normal metabolizers) this may manifest as efficacy at lower doses, or an increased risk of side effects, especially with doses on the higher end of the therapeutic range

AVOID
fluoxetine, paroxetine, duloxetine, vortioxetine, venlafaxine, fluvoxamine, mirtazapine, amitriptyline, nortriptyline - metabolized by CYP2D6 (ultrarapid metabolizer) ▪ see comments for vortioxetine above

Pharmacogenetic implications for psychiatry:

*Desvenlafaxine is one of the medications that is not impacted by genetic variations in the CYP2D6 and CYP2C19 and can be used at regular doses for depression and other mental health conditions.

Biomarker	Function	Summary
CYP2C19	Intermediate metabolizer	Reduced metabolism of citalopram, escitalopram and sertraline is anticipated which may lead to enhanced response. Initiate therapy with recommended starting dose and be alert to signs of side effects. Amitriptyline, doxepin and imipramine are partly metabolized by CYP2C19. Verify CYP2D6 metabolism, if CYP2D6 metabolism is normal, for CYP2C19 intermediate metabolizers, no empiric dose adjustments are recommended however suggest to monitor closely

		for side effects. Reduced metabolism of clobazam may lead to a higher risk for adverse effects, but also a better response to treatment. Consider starting at lower doses and proceed slowly with dose titration. Patients receiving diazepam for preoperative anxiety may have reduced clearance and may therefore take longer time to emerge from anaesthesia.
CYP2D6	Ultrarapid metabolizer	Reduced response to tricyclic antidepressants, certain other antidepressants (fluoxetine, fluvoxamine, paroxetine, venlafaxine), certain antipsychotic medications (aripiprazole, clozapine, haloperidol, sertindole, zuclopenthixol), stimulants (atomoxetine and amphetamine). Avoid use of CYP2D6 dependent antidepressants and antipsychotics if possible; if not, suggest close monitoring for possible decreased efficacy. Possible decreased response to donepezil and amphetamine.
UGT2B15	Poor metabolizer	Significantly reduced clearance of lorazepam and oxazepam is anticipated, consider alternative treatment or starting at lower doses.
CYP1A2	Ultrarapid metabolizer	Increased clearance of rasagiline, olanzapine and chlorpromazine, which may lead to reduced clinical response and potential need to increase dosage. Pregnant women with ultrarapid CYP1A2 metabolism who consume caffeine may have an increased likelihood of spontaneous abortion as compared to patients with reduced metabolism.

Pillcheck follows drug dosage guidelines from US FDA drug monographs and Clinical Pharmacogenetic Implementation Consortium (CPIC), which publishes the latest peer-reviewed guidelines for clinical practice (cpicpgx.org). More information about Pillcheck is available at pillcheck.ca/providers.

Attached for your reference is a summary table of Pillcheck-tested medications for your patient. Patients may grant their healthcare provider direct online access to their full results by sending Pillcheck their **provider's name, email and phone number**.

I hope you will find this information useful in the continued care of your patient. Please feel free to contact me with questions.

Sincerely,

Pharmacist Name, PharmD, OCP #2XXXXX
Clinical Pharmacist
tel: 555-555-XXXX
email@mailaddress.com