pillcheck

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SAGENE
آزمایشگاه ژنتیک پزشکی ساژن

GYIJAN072019|TEST_SAMPLE_RANDOM|1051|2.1.2|Pillcheck50_04_11_2018|179/179/179

Guide to Using This Report

Welcome to your Pillcheck report! We've created a summary of your report below for you to review. The detailed information in your report is meant to be shared with a doctor and other healthcare professionals in addition to the Pharmacist's Letter that we'll be sending you soon. We find that Pillcheck customers who are taking prescriptions or who are prescribed new drugs get the best results when they share their report and letter with a doctor. Some other notes:

- You may not recognize the names of the drugs in your report because they are 'generic' drug names. If you check the label of your prescriptions, you should be able to find the generic name there, alongside the brand name.
- It's possible that your report will indicate there are no issues with any of the medications you're taking (for example, they're all in the Green category below) yet you may still feel you are having issues. There may be other factors involved in how you metabolize medications and your doctor is the best person to discuss this with.
- We may not be able to determine how you metabolize certain medications because your genetic make-up is highly unique or the test is unable to do so.
- Since your genetic make-up doesn't change, your Pillcheck Report is good for the future too.
- We'll update your report as new information on medications becomes available, and we'll contact you to let you know when your report is updated.
- Please contact us at support@pillcheck.com or 1-877-409-3629 if you have any issues understanding your report.

Meaning of the symbols in your report

Normal drug metabolism and response. No additional dose adjustment needed.

Altered drug metabolism. Can affect clinical response, may require dose adjustment or increased monitoring.

Substantially altered drug metabolism. Requires physicians to adjust dose or consider alternative medications.

Uncertain activity requires caution in drug use. A rare or indeterminate combination of genetic markers is present.

Things you should be aware of

Do not change any medications or dosage prior to consulting your physician or pharmacist, who should determine an appropriate dose. Please note, this report is intended for educational purposes only and does not constitute medical advice.

You may choose to share this information with your family physician or other healthcare provider who may recommend additional clinical testing options.

Additional genetic testing by sequencing might uncover other functional variations that you may carry that also affect the medication response, but were not detected in this analysis.

If you are already taking a medication listed in this report, we encourage you to revisit the drug safety information sheet provided by your pharmacist, as well as other educational resources on drug and food interactions.

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Summary of Your Test

TREATMENT AREA	USE WITH INCREASED CAUTION - CONSIDER ALTERNATIVES	USE WITH CAUTION - MORE FREQUENT MONITORING	USE AS DIRECTED - STANDARD PRECAUTION
Analgesics	Celecoxib Codeine Diclofenac Hydrocodone Oxycodone Piroxicam Tramadol and acetaminophen	Flurbiprofen	Fentanyl Hydromorphone Ketamine Methadone Morphine Naloxone Naltrexone
Antibacterial	Telithromycin		
Antiemetics	Aprepitant Dronabinol Fosaprepitant	Dolasetron Ondansetron Palonosetron Tropisetron	
Antifungals	Itraconazole	Terbinafine	Voriconazole
Antiviral	Fosamprenavir		Atazanavir Boceprevir Daclatasvir Dolutegravir Efavirenz Elbasvir and grazoprevir Ledipasvir and sofosbuvir Nevirapine Ombitasvir, paritaprevir and ritonavir Peginterferon Alpha-2b Simeprevir Sofosbuvir Sofosbuvir and velpatasvir Telaprevir

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Cardiovascular	Amlodipine Atorvastatin Dronedarone Fluvastatin Losartan Lovastatin Metoprolol Pitavastatin Pravastatin Rosuvastatin Sildenafil Simvastatin Tadalafil Vardenafil	Carvedilol Cilostazol Flecainide Irbesartan Nebivolol Propafenone Propranolol Quinidine Ranolazine Timolol	Alirocumab Clopidogrel Evolocumab Prasugrel Ticagrelor
Dermatology and Dental		Cevimeline	
Endocrinology	Eliglustat		
Gastroenterology			Dexlansoprazole Esomeprazole Lansoprazole Omeprazole Pantoprazole Rabeprazole
Gynecology	Desogestrel Ethinylestradiol		
Hematology	Acenocoumarol Apixaban Phenprocoumon Rivaroxaban Warfarin		
Immune therapy	Methotrexate	Cyclosporine Sirolimus Tacrolimus	
Musculoskeletal			Carisoprodol
Neurology	Fosphenytoin Phenytoin Valproic acid / divalproex	Deutetrabenazine Dextromethorphan and quinidine Donepezil Galantamine Midazolam Tetrabenazine Valbenazine	Brivaracetam Caffeine Clobazam Lacosamide Rasagiline

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Oncology	Cabazitaxel	Cisplatin Gefitinib Mercaptopurine Tamoxifen Thioguanine	Belinostat Capecitabine Erlotinib Fluorouracil Irinotecan Nilotinib Pazopanib Tegafur
Other			Flibanserin
Psychiatry	Amitriptyline Buprenorphine Chlordiazepoxide and amitriptyline Clomipramine Clonazepam Desipramine Doxepin Eszopiclone Guanfacine Imipramine Lurasidone Nortriptyline Protriptyline Trazodone Trimipramine Zopiclone	Alprazolam Amphetamine Aripiprazole Atomoxetine Brexpiprazole Clozapine Duloxetine Fluoxetine Fluoxetine and olanzapine Fluvoxamine Haloperidol Iloperidone Mirtazapine Modafinil Nefazodone Paroxetine Perphenazine Pimozide Quetiapine Risperidone Thioridazine Thiothixene Venlafaxine Vortioxetine Zuclopenthixol	Bupropion Chlorpromazine Citalopram Diazepam Escitalopram Lorazepam Olanzapine Oxazepam Sertraline
Pulmonary		Salmeterol	Indacaterol
Rheumatology	Lesinurad	Azathioprine	
Urology		Darifenacin Fesoterodine Tamsulosin Tolterodine	

TREATMENT AREA	USE WITH INCREASED CAUTION - CONSIDER ALTERNATIVES	USE WITH CAUTION - MORE FREQUENT MONITORING	USE AS DIRECTED - STANDARD PRECAUTION

The outcome is uncertain for the following drugs:

Enzalutamide

For Specialist Review Only

Customer Genetic Profile

Marker	Value
ADRB2	GA
CYP1A2	*1A/*1A
CYP2B6	*1/*1
CYP2C19	*1/*1
CYP2C8	*4/*4
CYP2C9	*3/*3
CYP2D6 CYP2D6CNV	*1/*1 3N
CYP3A4	*6/*6
CYP3A5	*1A/*3A
DPYD	*1/*1

Marker	Value
F2	GA
F5	TC
IFNL3	CC
OPRM1	AA
SLCO1B1	*5/*5
TPMT	*1/*2
UGT1A1	*1/*1
UGT2B15	CC
VKORC1	AA

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Technology used in the testing process

Gene	Alleles Tested
ADRB2	rs1042713 A/G
CYP1A2	*1E, *1F, *1J, *1K, *6, *7, *8, *15
CYP2B6	*2, *5, *6, *7, *8, *13, *16, *22, *34
CYP2C19	*2, *3, *4, *6, *8, *10, *17
CYP2C8	*2, *3, *4
CYP2C9	*2, *3, *8, *9, *11, *12, *27
CYP2D6	*3, *4, *5, *6, *7, *10, *17, *29, *41, *64, *69
CYP3A4	*1B, *3, *6, *11, *12, *16, *17, *18, *19, *22
CYP3A5	*2, *3A, *3B, *6
DPYD	*2A, *4, *5, *6, *9A, rs67376798A
F2	rs1799963 A/G
F5	rs6025 C/T
IFNL3	rs12979860 C/T
OPRM1	A118G
SLCO1B1	*1B, *5, *9, *15, *31
TPMT	*2, *3A, *8
UGT1A1	*6, *27, *80
UGT2B15	rs1902023 A/C
VKORC1	c.-1639G>T

Technology: Genotyping was performed using the Applied Biosystems™ QuantStudio™ platform and this report is powered by GeneYouIn Pillcheck technology.

Limitations: This test will not detect all known mutations that result in altered gene activity. *1 or wild-type alleles are reported by default if those listed were not detected. IND values are conservatively assigned to alleles that could not be determined with complete certainty. Only listed mutations are tested for and absence of a detected mutation does not rule out the possibility of sensitivity to a specific drug due to the presence of other mutations or other environmental factors.

Drug Page Index

Drug Recommendations

Acenocoumarol

https://www.pillcheck.ca/C2Z2

Low Vitamin K levels increase the risk of bleeding. Impaired drug clearance and significantly increased risk of serious adverse side effects. Consider low starting dose and check INR. The risk of bleeding may be increased due to slower drug clearance. Consider alternative treatment with Factor X inhibitors. Check INR more frequently. Monitor blood coagulation (INR) when initiating or discontinuing medications that may interact with acenocoumarol.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	B
VKORC1	AA	Low Vitamin K	B

Alirocumab

https://www.pillcheck.ca/N9U3

The variation you carry in the SLCO1B1 gene indicates that you have a high myopathy risk and will be statin-intolerant. Consider treatment with PCSK9 inhibitors.

biomarker	value	interpretation	level of evidence
SLCO1B1	*5/*5	Poor metabolizer	FDA

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Alprazolam

https://www.pillcheck.ca/M5Z7

Increased drug clearance. Patients who express CYP3A5 may have faster clearance rates and increased metabolism of alprazolam as compared to patients who do not express CYP3A5. Other clinical and genetic factors may also influence clearance and metabolism of alprazolam. Strong CYP3A4 inhibitors or inducers may affect disposition of alprazolam.

biomarker	value	interpretation	level of evidence
CYP3A5	*1A/*3A	Intermediate metabolizer	FDA

Amitriptyline

https://www.pillcheck.ca/E3U3

Dosing for Amitriptyline is uncertain due to ultrarapid metabolism of the medication. Another drug should be considered. Utilize therapeutic drug monitoring to guide dose adjustments. TCA's may become abruptly toxic when given a drug inhibiting CYP2D6 activity as concomitant therapy. Quinidine, cimetidine, many other antidepressants, phenothiazines, and the Type 1C antiarrhythmics propafenone and flecainide, as well as fluoxetine, sertraline, and paroxetine inhibit CYP2D6. Caution is indicated in the co-administration of TCAs with any of the SSRIs and also in switching from one class to the other. Sufficient time must elapse before initiating TCA treatment in a patient being withdrawn from fluoxetine, given the long half-life of the parent and active metabolite (at least 5 weeks may be necessary).

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	A

Amlodipine

https://www.pillcheck.ca/D1S5

Significantly reduced drug clearance is anticipated, increasing amlodipine systemic exposure. Significantly increased risk of hypotension and edema, especially when amlodipine is coadministered with CYP3A4 inhibitors.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Amphetamine

https://www.pillcheck.ca/B2W4

Enhanced drug clearance may lead to reduced clinical response and lower risk of side effects. Patients with genotype GG of rs510769, which is equivalent to AA in the A118G variant, was associated with significantly increased Stimulation and Euphoria scores after amphetamine.

biomarker	value	interpretation	level of evidence
OPRM1	AA	Normal sensitivity to opioids	C
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	FDA

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Apixaban

https://www.pillcheck.ca/J2P4

Significantly decreased drug metabolism is anticipated, potentially increasing drug exposure and elevated risk of bleeding. Avoid the concurrent use of CYP3A4 and P-glycoprotein inhibitors and apixaban.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Aprepitant

https://www.pillcheck.ca/F7P5

Significantly reduced drug clearance is anticipated. Use alternative antiemetic if risk of drug-drug interactions is a concern. Aprepitant is a moderate CYP3A4 inhibitor and could result in elevated plasma concentrations of concomitant medications metabolized by this enzyme. Avoid concomitant use with docetaxel, irinotecan, ifosfamide, imatinib, vinblastine and vincristine.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Aripiprazole

https://www.pillcheck.ca/M4R2

Potentially decreased response due to accelerated clearance; higher doses might be required to achieve a clinical effect or consider alternative treatment with drugs NOT metabolized by CYP2D6. Adjust dosage at intervals of not less than 2 weeks, the time needed to achieve steady-state concentration. Reduce aripiprazole dosage to half the dosage in patients receiving CYP3A4 or CYP2D6 inhibitors; increase aripiprazole dosage to the usual dosage after discontinuance of the CYP3A4 or CYP2D6 inhibitor. Consider increasing aripiprazole dosage upon initiation of concomitant therapy with drugs that induce CYP3A4 (carbamazepine); decrease aripiprazole dosage if the CYP3A4 inducer is discontinued.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Atazanavir

https://www.pillcheck.ca/N1Q3

Normal UGT1A1 activity and very low likelihood of bilirubin-related discontinuation of atazanavir.

biomarker	value	interpretation	level of evidence
UGT1A1	*1/*1	Normal metabolizer	A

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Atomoxetine

https://www.pillcheck.ca/K6Z4

Ultrafast metabolizers may have reduced clinical benefit for atomoxetine. Select alternative medication not metabolized by CYP2D6. For ADHD patients with hepatic insufficiency (HI), this is the recommended dosage adjustment: For patients with moderate HI (Child-Pugh Class B), initial and target doses should be reduced to 50% of the normal dose. For patients with severe HI (Child-Pugh Class C), initial dose and target doses should be reduced to 25% of normal. In children up to 70 kg body weight administered strong CYP2D6 inhibitors, e.g., paroxetine, fluoxetine, and quinidine, Atomoxentine should be initiated at 0.5 mg/kg/day and only increased to the usual target dose of 1.2 mg/kg/day if symptoms fail to improve after 4 weeks and the initial dose is well tolerated. In children and adolescents over 70 kg body weight administered strong CYP2D6 inhibitors, e.g., paroxetine, fluoxetine, and quinidine, Atomoxentine should be initiated at 40 mg/day and only increased to the usual target dose of 80 mg/day if symptoms fail to improve after 4 weeks and the initial dose is well tolerated.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	A

Atorvastatin

https://www.pillcheck.ca/N6T8

Patients may have low oral clearance and higher plasma concentrations of atorvastatin and therefore, an increased risk of composite adverse effects, like elevated creatinine kinase levels or myopathy. Other genetic and clinical factors may also influence a patient's response to atorvastatin treatment and its pharmacokinetics. Prescribe a lower dose or consider an alternative statin (e.g., pravastatin or rosuvastatin) with routine creatine kinase (CK) surveillance. Consider alternative treatments such as PCSK9 inhibitors

biomarker	value	interpretation	level of evidence
SLCO1B1	*5/*5	Poor metabolizer	FDA

Azathioprine

https://www.pillcheck.ca/N6R1

Moderate to high concentrations of TGN metabolites; low concentrations of methylTIMP. If disease treatment normally starts at the "full dose", consider starting at 30-70% of target dose (e.g., 1-1.5 mg/kg/d), and titrate based on tolerance. Allow 2-4 weeks to reach steady state after each dose adjustment.

biomarker	value	interpretation	level of evidence
TPMT	*1/*2	Intermediate metabolizer	A

Belinostat

https://www.pillcheck.ca/M7S8

Patients with an extensive metabolizer genotype when treated with belinostat may have decreased risk but not absence of dose limiting toxicities. Recent publications suggest lower belinostat dose of 600mg/m2/24h. Other genetic and clinical factors may also influence adverse events associated with belinostat, as additional reduced function alleles may be prevalent in specific populations.

biomarker	value	interpretation	level of evidence
UGT1A1	*1/*1	Normal metabolizer	B

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Boceprevir

https://www.pillcheck.ca/E5U8

Individuals with the CC genotype have a 70% chance of sustained virological response after 48 weeks of PEG-IFN alpha and RBV and a 90% chance of sustained virological response after 24-48 weeks of treatment with protease inhibitor in combination with PEG-IFN alpha and RBV. 80%-90% of patients will be eligible for a shortened therapy of 24-28 weeks of combination treatment.

biomarker	value	interpretation	level of evidence
IFNL3	CC	Normal responder	FDA

Brexpiprazole

https://www.pillcheck.ca/E2P7

Dosage adjustment is recommended in CYP2D6 ultrafast metabolizers, as these patients are expected to have lower Brexpiprazole concentrations than normal metabolizers. Ultrafast CYP2D6 metabolizers should have their dosage increased carefully.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Brivaracetam

https://www.pillcheck.ca/E6T3

Normal drug metabolism is anticipated. Standard drug dosing and monitoring apply. Other genetic and clinical factors may also influence metabolism of brivaracetam.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	B

Buprenorphine

https://www.pillcheck.ca/C2T6

Poor buprenorphine clearance with normal response to opioids is anticipated. May lead to higher buprenorphine exposure, increasing the risk of respiratory depression. Co-administration of CYP3A4 inhibitors may further increase systemic exposure and pose risk of accidental overdose.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA
OPRM1	AA	Normal sensitivity to opioids	C

Bupropion

https://www.pillcheck.ca/L9X6

Normal clearance of bupropion and normal concentrations of hydroxybupropion, the active metabolite, expected. Other genetic and clinical factors may also influence a patient's exposure to bupropion or hydroxybupropion.

biomarker	value	interpretation	level of evidence
CYP2B6	*1/*1	Normal metabolizer	FDA

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Cabazitaxel

https://www.pillcheck.ca/J5P8

Significant drug clearance is anticipated that will significantly increase drug exposure. Concomitant medicinal products that are strong inducers or strong inhibitors of CYP3A should be avoided. However, if patients require co-administration of a strong CYP3A inhibitor, a 25% cabazitaxel dose reduction should be considered. Dose reduction should be considered even in absence of co-administration of a CYP3A inhibitor.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	B

Caffeine

https://www.pillcheck.ca/I5V6

Patients with the normal metabolizer genotype may have a decreased, but not absent, risk of non-fatal myocardial infarction with excessive coffee consumption. Pregnant women with normal caffeine metabolism who consume caffeine may have an increased likelihood of spontaneous abortion as compared to patients with reduced metabolism. Other genetic and clinical factors may also influence the likelihood of non-fatal myocardial infarction and spontaneous abortion.

biomarker	value	interpretation	level of evidence
CYP1A2	*1A/*1A	Normal metabolizer	FDA

Capecitabine

https://www.pillcheck.ca/C6V8

Normal DPD activity and normal risk for fluoropyrimidine toxicity

biomarker	value	interpretation	level of evidence
DPYD	*1/*1	Normal metabolizer	A

Carisoprodol

https://www.pillcheck.ca/D9X9

Normal metabolism of carisoprodol is anticipated; standard dosing and precautions are recommended. No change in therapy.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	B

Carvedilol

https://www.pillcheck.ca/H1R4

Lower risk of dizziness; CYP2D6 inhibitors such as quinidine, fluoxetine, paroxetine, and propafenone increase carvedilol levels, while rifampin may decrease carvedilol levels.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

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Celecoxib

https://www.pillcheck.ca/H7S3

Patients who are known or suspected to be poor metabolizers should be administered celecoxib with caution. Consider starting treatment at 50% of the lowest recommended dose in poor metabolizers. Alternative management should be considered in juvenile rheumatoid arthritis patients identified to be CYP2C9 poor metabolizers

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	B

Cevimeline

https://www.pillcheck.ca/F2P2

Cevimeline should be administered with caution to patients taking beta adrenergic antagonists, because of the possibility of conduction disturbances. Potentially reduced clinical effect at normal doses due to accelerated drug clearance.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Chlordiazepoxide and amitriptyline

https://www.pillcheck.ca/F3V2

Potentially reduced clinical response due to accelerated drug clearance. Consider alternative medications not metabolized by CYP2D6. Avoid concurrent use of selective serotonin reuptake inhibitors (SSRIs), e.g., fluoxetine, sertraline and paroxetine. At least 5 weeks must elapse after fluoxetine withdrawal before initiating TCA treatment.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	FDA

Chlorpromazine

https://www.pillcheck.ca/B9S2

Normal drug clearance is anticipated. Coadministration with CYP1A2 inhibitors like ciprofloxacin, fluvoxamine or vemurafenib can reduce chlorpromazine clearance and hence increase exposure and potentially, adverse side effects. Smoking is expected to reduce chlorpromazine exposure requiring higher doses to achieve adequate clinical response.

biomarker	value	interpretation	level of evidence
CYP1A2	*1A/*1A	Normal metabolizer	FDA

Cilostazol

https://www.pillcheck.ca/L6U4

Increased metabolism of cilostazol as compared to CYP3A5 non-expressors, possibly reducing clinical response. Variations in CYP2C19 and CYP3A4 may also influence metabolism of cilostazol. Consider discontinuation or dosage reduction for cilostazol if coadministration with CYP3A4 or CYP2C19 inhibitors, or if used in poor CYP2C19 or poor CYP3A4 metabolizers.

biomarker	value	interpretation	level of evidence
CYP3A5	*1A/*3A	Intermediate metabolizer	FDA

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Cisplatin

https://www.pillcheck.ca/A7R8

Decreased drug clearance may increase risk of cisplatin-induced ototoxicity, renal toxicity and other side effects. Consider starting with reduced cisplatin doses. Allow 2-4 weeks to reach steady state after each dose adjustment.

biomarker	value	interpretation	level of evidence
TPMT	*1/*2	Intermediate metabolizer	FDA

Citalopram

https://www.pillcheck.ca/L7T1

Normal metabolism of citalopram is anticipated; standard dosing and precautions are recommended.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	A

Clobazam

https://www.pillcheck.ca/C1T4

Normal metabolism of Clobazam is anticipated; standard dosing and precautions are recommended. Titrate according to weight. If necessary and based upon clinical response, an additional titration to the maximum dose (20 mg/day or 40 mg/day, depending on the weight group) may be started on day 14.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	C

Clomipramine

https://www.pillcheck.ca/H7X7

Select alternative drug (e.g., citalopram, sertraline) or monitor (desmethyl) clomipramine plasma concentration. Monitor TCA plasma levels whenever an agent of the tricyclic antidepressant class including Anafranil is going to be co-administered with another drug known to be an inhibitor of CYP2D6.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Clonazepam

https://www.pillcheck.ca/E1S2

Significantly reduced drug clearance is anticipated, increasing the risk of side effects. Estimated dose requirement for low CYP3A4 expresser patients is 0.029 mg/kg bodyweight. Co-administration of CYP3A4 inhibitors may increase drug exposure and risk of side effects.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

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Clopidogrel

https://www.pillcheck.ca/J6R1

Normal platelet inhibition; normal residual platelet aggregation. Initiate clopidogrel with a single 300 mg oral loading dose and then continue at 75 mg once daily, usually in combination with aspirin (75-325 mg once daily).

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	A

Clozapine

https://www.pillcheck.ca/I3S5

Clinical effect of clozapine does not appear to depend on CYP2D6 genotype. Drugs that are metabolized by CYP2D6 may inhibit the activity of this isozyme, and thus may make normal metabolizers resemble poor metabolizers. Concomitant use of clozapine with other drugs metabolized by CYP2D6 including antidepressants, phenothiazines, carbamazepine, and Type 1C antiarrhythmics (e.g., propafenone, flecainide and encainide), or that inhibit this enzyme (e.g., quinidine), may require lower doses.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Codeine

https://www.pillcheck.ca/M6Q5

Increased formation of morphine following codeine administration, leading to a higher risk of toxicity. Avoid codeine use due to the potential for toxicity. Alternatives that are not affected by this CYP2D6 phenotype include morphine and non-opioid analgesics. Tramadol, and to a lesser extent hydrocodone and oxycodone, are not good alternatives because their metabolism is affected by CYP2D6 activity.

biomarker	value	interpretation	level of evidence
OPRM1	AA	Normal sensitivity to opioids	D
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	A

Cyclosporine

https://www.pillcheck.ca/L1V6

Patients with the CYP3A5 *1/*3 (CYP3A5 expressors) may require a higher dose of cyclosporine to reach target blood concentration as compared to patients with the *3/*3 diplotype, although this is contradicted in some studies. Other genetic and clinical factors may also influence dose of cyclosporine. Individuals expressing CYP3A5 exhibited enhanced formation of AM19 and AM1c9, secondary metabolites of CsA that have been associated with an increased risk of CsA-induced nephrotoxicity. The same phenotype influenced the apparent urinary clearance of CsA, suggesting the presence of significant intra-renal CsA metabolism for individuals that carry the functional CYP3A5*1 allele.

biomarker	value	interpretation	level of evidence
CYP3A5	*1A/*3A	Intermediate metabolizer	C

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Daclatasvir

https://www.pillcheck.ca/M2T2

Patients with genotype CC may have increased response to Daclatasvir, peginterferon alpha-2a, peginterferon alpha-2b and Ribavirin compared to genotypes CT or TT. Other genetic and clinical factors may also influence the response to Daclatasvir therapy.

biomarker	value	interpretation	level of evidence
IFNL3	CC	Normal responder	FDA

Darifenacin

https://www.pillcheck.ca/C4Z1

Be aware that there may be increased metabolism to less active compound, resulting in lower plasma concentrations and reduced response. There are no darifenacin dosing recommendations for ultrarapid metabolizers of CYP2D6.

biomarker	value	interpretation	level of evidence
CYP2D6	*1/*1	Ultrarapid metabolizer	FDA
CYP2D6CNV	3N		

Desipramine

https://www.pillcheck.ca/H5V6

Greatly enhanced metabolism of tricyclics to less active compounds as compared with extensive metabolizers. Avoid tricyclic use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6 or increase starting dose if TCA is warranted. Use therapeutic drug monitoring to guide dose adjustments. Avoid concurrent use of selective serotonin reuptake inhibitors (SSRIs), e.g., fluoxetine, sertraline and paroxetine. At least 5 weeks must elapse after fluoxetine withdrawal before initiating TCA treatment

biomarker	value	interpretation	level of evidence
CYP2D6	*1/*1	Ultrarapid metabolizer	B
CYP2D6CNV	3N		

Desogestrel

https://www.pillcheck.ca/H3Z8

Significantly reduced conversion of desogestrel to active metabolites which may lead to therapeutic failure. Increased risk of estradiol induced thrombosis due to presence of F2 and F5 mutations. Avoid use of estradiol containing medications and tamoxifen.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	FDA
F2	GA	Heterozygous carrier	FDA
F5	TC	Heterozygous carrier	FDA

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Deutetrabenazine

https://www.pillcheck.ca/L2V8

Enhanced drug clearance is anticipated potentially affecting clinical response. The starting dose is 6 mg once daily. Titrate up at weekly intervals by 6 mg per day to a tolerated dose that reduces chorea, up to a maximum recommended daily dosage of 48 mg (24 mg twice daily). Administer total daily dosages of 12 mg or above in two divided doses. A clinically relevant QT prolongation may occur in some patients treated with Deutetrabenazine when co-administered with a strong CYP2D6 inhibitor.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	FDA

Dexlansoprazole

https://www.pillcheck.ca/M4Q6

Normal metabolism is anticipated; standard dosing and precautions are recommended.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	B

Dextromethorphan and quinidine

https://www.pillcheck.ca/K5W4

The Quinidine component of Dextromethorphan/Quinidine is intended to inhibit CYP2D6 so that higher exposure to dextromethorphan can be achieved compared to when dextromethorphan is given alone. Quinidine may have reduced contribution to the effectiveness of Dextromethorphan/Quinidine in ultrafast metabolizers.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Diazepam

https://www.pillcheck.ca/B7Y4

Normal metabolism is anticipated; standard dosing and precautions are recommended.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	C

Diclofenac

https://www.pillcheck.ca/L1Z8

Significantly reduced drug clearance is anticipated. Significantly increased risk of GI bleeding and other side effects, requiring reduced doses or alternative treatment. Celecoxib and other NSAIDs are also affected.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	C

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Dolasetron

https://www.pillcheck.ca/C7P6

Enhanced CYP2D6 metabolism of the active metabolite, hydrodolasetron, may decrease response. The decreased response could lead to a higher risk of vomiting after chemotherapy or anesthesia. No significant associations have been observed for nausea. Select an alternative drug less dependent of CYP2D6 metabolism (i.e. granisetron).

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Dolutegravir

https://www.pillcheck.ca/I1W7

Subject expected to show normal oral clearance. Other genetic and clinical factors may affect oral clearance of dolutegravir.

biomarker	value	interpretation	level of evidence
UGT1A1	*1/*1	Normal metabolizer	B

Donepezil

https://www.pillcheck.ca/M4P6

Significantly enhanced drug clearance is expected based on the CYP2D6 metabolic status, leading to 24% faster clearance. Be alert to lack of efficacy and side effects. Population pharmacokinetic analysis showed that in the presence of concomitant CYP2D6 inhibitors, donepezil AUC was increased by approximately 17% to 20% in patients with Alzheimer's Disease taking ARICEPT 10 and 23 mg.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Doxepin

https://www.pillcheck.ca/K4T5

Select alternative drug (citalopram, sertraline) or increase dose by 100%. Adjust maintenance dose in response to (nor)doxepin plasma concentration.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Dronabinol

https://www.pillcheck.ca/L8T8

Poor drug clearance. Published data indicate a 2- to 3-fold higher dronabinol exposure in individuals carrying genetic variants associated with diminished CYP2C9 function. Monitor for increased dronabinol-related adverse reactions when it is co-administered with inhibitors of CYP2C9 and CYP3A4 enzymes.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	FDA

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Dronedarone

https://www.pillcheck.ca/F6V1

Significantly reduced drug clearance is anticipated leading to high risk of QT interval prolongation and induction of Torsade de Pointes. Dronedarone can further increase propranolol and metoprolol exposure. Other CYP2D6 substrates, including other beta blockers, tricyclic antidepressants, and SSRIs may have increased exposure upon co-administration with dronedarone.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Duloxetine

https://www.pillcheck.ca/K6Q4

Significantly enhanced duloxetine clearance by CYP2D6 is anticipated, affecting clinical response. Both CYP1A2 and CYP2D6 are responsible for Duloxetine metabolism. Inhibition of CYP1A2 or CYP2D6 may significantly increase drug exposure. Avoid coadministration of duloxetine with CYP2D6 inhibitors or CYP1A2 inhibitors including orcimetidine, ciprofloxacin, enoxacin, and fluvoxamine. Among CYP1A2 inducers, smoking is probably the most important, but the usual enzyme inducers such as rifampin and barbiturates can also substantially increase CYP1A2 activity and affect response to duloxetine.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Efavirenz

https://www.pillcheck.ca/M9U1

Reduced risk for Efavirenz induced CNS toxicity. Efavirenz enhances the clearance of coadministered drugs metabolized by CYP3A4. This induction is most pronounced in extensive metabolizers requiring a dose adjustment. Dose optimization by Metabolic Status and weight is critical.

biomarker	value	interpretation	level of evidence
CYP2B6	*1/*1	Normal metabolizer	A

Elbasvir and grazoprevir

https://www.pillcheck.ca/B6X4

Patients with the CC genotype may have increased response to peginterferon alpha-2a, peginterferon alpha-2b, Ribavirin therapy compared to patients with genotype CT or TT. However, the role of the IFNL3 genotype is modest for Elbasvir and Grazoprevir therapy as compared to PEG-IFN/RBV therapy. Other genetic and clinical factors may also influence the response to Elbasvir and Grazoprevir-based therapy.

biomarker	value	interpretation	level of evidence
IFNL3	CC	Normal responder	FDA

Eliglustat

https://www.pillcheck.ca/L5V1

Eliglustat should not be used in patients who are CYP2D6 ultra-rapid metabolizers as they may not achieve adequate concentrations of eliglustat to achieve a therapeutic effect.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

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Enzalutamide

https://www.pillcheck.ca/E3R8

Rare diplotype of unknown clinical significance. Assess enzatumaide and N-desmethyl enzalutamide levels. Avoid strong CYP2C8 inhibitors, as they can increase the plasma exposure. If co-administration is necessary, reduce enzalutamide dose. Enzalutamide is a strong inducer of CYP3A4. Avoid strong or moderate CYP3A4 or CYP2C8 inducers as they can alter the plasma exposure.

biomarker	value	interpretation	level of evidence
CYP2C8	*4/*4	Unknown metabolizer	FDA

Erlotinib

https://www.pillcheck.ca/C2V7

Erlotinib is a strong inhibitor of glucuronidation by UGT1A1 in-vitro. The inhibition of glucuronidation may cause interactions with medicinal products which are substrates of UGT1A1 and exclusively cleared by this pathway.

biomarker	value	interpretation	level of evidence
UGT1A1	*1/*1	Normal metabolizer	FDA

Escitalopram

https://www.pillcheck.ca/A4Q9

Normal drug clearance is anticipated.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	A

Esomeprazole

https://www.pillcheck.ca/H4Z5

Coadministration of esomeprazole 30 mg and diazepam, a CYP2C19 substrate, resulted in a 45% decrease in the clearance of diazepam. Concomitant administration of esomeprazole and a combined inhibitor of CYP2C19 and CYP3A4, such as voriconazole, may result in more than doubling of the esomeprazole exposure. Dose adjustment of esomeprazole is not normally required. Esomeprazole is a CYP2C19 competitive inhibitor; avoid concomitant use with clopidogrel, St. John's Wort or rifampin. Interaction with Methotrexate and Tacrolimus were reported.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	B

Eszopiclone

https://www.pillcheck.ca/D7S6

Significantly reduced clearance is anticipated, increasing exposure to eszopiclone and the risk of side effects risk. Consider dose reduction or alternative medication not metabolized by CYP3A4. In elderly patients the starting dose of eszopiclone should be further decreased, as well as in patients with impaired liver function.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

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Ethinylestradiol

https://www.pillcheck.ca/E1X9

Carrier of F2 and F5 mutations that pose high risk venous or arterial thrombosis in women taking estradiol containing medications. Avoid use of estradiol containing medications and tamoxifen.

biomarker	value	interpretation	level of evidence
F2	GA	Heterozygous carrier	FDA
F5	TC	Heterozygous carrier	FDA

Evolocumab

https://www.pillcheck.ca/B7V4

The variation you carry in the SLCO1B1 gene indicates that you have a high myopathy risk and will be statin-intolerant. Consider treatment with PCSK9 inhibitors.

biomarker	value	interpretation	level of evidence
SLCO1B1	*5/*5	Poor metabolizer	FDA

Fentanyl

https://www.pillcheck.ca/D1P5

Individuals with the AA genotype may experience increased efficacy of opioids for pain management, may be less susceptible to opioid addiction, and may require a decreased dose of opioids as compared to individuals with the GG genotype. However, this has been contradicted in some studies. Other genetic and clinical factors may also influence a patient's response to opioid drugs.

biomarker	value	interpretation	level of evidence
OPRM1	AA	Normal sensitivity to opioids	C

Fesoterodine

https://www.pillcheck.ca/D7W1

Be aware of lower plasma fesoterodine concentrations and reduced response. There are no fesoterodine dosing recommendations for ultrarapid metabolizers of CYP2D6.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Flecainide

https://www.pillcheck.ca/H1P6

Record ECG and monitor plasma concentration or select alternative drug e.g., sotalol, disopyramide, quinidine, amiodarone.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

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Flibanserin

https://www.pillcheck.ca/M7S5

Normal drug clearance by CYP2C19 is anticipated. Flibanserin is also metabolized by CYP3A4, CYP2D6 and CYP2C9. Poor metabolizers of CYP2D6 and poor CYP2C9 metabolizers may have slightly decreased drug exposure. Severe hypotension and syncope can occur when Flibanserin is used with moderate or strong CYP3A4 inhibitors or in patients with hepatic impairment; therefore, Flibanserin use in these settings is contraindicated. Risk of hypotension is elevated for women with reduced CYP3A4 function.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	C

Fluorouracil

https://www.pillcheck.ca/D1P3

Normal metabolism of Fluorouracil is anticipated; standard dosing and precautions are recommended. Note that there is a normal risk of unanticipated myelosuppression, arrhythmia and death.

biomarker	value	interpretation	level of evidence
DPYD	*1/*1	Normal metabolizer	A

Fluoxetine

https://www.pillcheck.ca/A7S5

Enhanced drug clearance may affect clinical response at regular doses. Fluoxetine inhibits CYP2D6 and may make individuals with normal CYP2D6 activity resemble a poor metabolizer. Coadministration of fluoxetine with drugs that are metabolized by CYP2D6 (TCAs, phenothiazines and atypicals), and antiarrhythmics (propafenone, flecainide) should be approached with caution. Drugs metabolized by the CYP2D6 should be initiated at the low end of the dose range if a patient is receiving fluoxetine or has taken it in the previous 5 weeks - dosing requirements as for poor metabolizers. If fluoxetine is added to a drug metabolized by CYP2D6 decrease dose of the original medication. Thioridazine should not be administered with fluoxetine or within a minimum of 5 weeks after fluoxetine has been discontinued due to the risk of ventricular arrhythmias and sudden death.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Fluoxetine and olanzapine

https://www.pillcheck.ca/C1U5

Potentially reduced clinical response due to enhanced fluoxentine clearance. Fluoxetine inhibits CYP2D6 and may make individuals with normal CYP2D6 activity resemble a poor metabolizer. Coadministration of fluoxetine with other drugs that are metabolized by CYP2D6 (TCAs, phenothiazines and most atypicals, antiarrhythmics) should be approached with caution. Therapy with drugs metabolized by the CYP2D6 system should be initiated at the low end of the dose range if a patient is receiving fluoxetine or has taken it in the previous 5 weeks. If fluoxetine is added to the treatment regimen of a patient already receiving a drug metabolized by CYP2D6 (including but not limited to, flecainide, propafenone, vinblastine, and TCAs), the need for a decreased dose of the original medication should be considered. Agents inducing CYP1A2 or glucuronyl transferase enzymes (omeprazole, rifampin) may cause an increase in olanzapine clearance.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

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Flurbiprofen

https://www.pillcheck.ca/I7V9

Patients who are poor metabolizers should be administered flurbiprofen with caution as they may have abnormally high plasma levels due to reduced metabolic clearance.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	B

Fluvastatin

https://www.pillcheck.ca/L4V8

Significantly increased risk of statin-induced myopathy. Consider alternative treatment options such ask PCSK9 inhibitors.

biomarker	value	interpretation	level of evidence
SLCO1B1	*5/*5	Poor metabolizer	FDA

Fluvoxamine

https://www.pillcheck.ca/M8U9

Enhanced metabolism. Lower plasma concentraiton may decrease clinical effect due to enhanced drug clearance. Fluvoxamine inhibits the CYP1A2, 2C9, 3A4, 2C19 isozymes and affects metabolism of multiple drugs including Warfarin, Alprazolam, Omeprazole, Theophyllin and many other medications.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	A

Fosamprenavir

https://www.pillcheck.ca/G3Q9

Significantly reduced drug clearance is anticipated, affecting total exposure and increasing risk of side effects. Consider alternative treatment.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Fosaprepitant

https://www.pillcheck.ca/N9Y6

Fosaprepitant is a prodrug that is rapidly converted by numerous organs to its active metabolite, aprepitant. Significantly reduced aprepitant clearance is anticipated. Use alternative antiemetic due to risk of drug-drug interactions. Aprepitant is a moderate CYP3A4 inhibitor and could result in elevated plasma concentrations of concomitant medications metabolized by this enzyme. Avoid concomitant use with docetaxel, irinotecan, ifosfamide, imatinib, vinblastine and vincristine.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

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Fosphenytoin

https://www.pillcheck.ca/G7Z4

Significantly reduced metabolism of phenytoin, the active metabolite of fosphenytoin. Higher plasma concentrations will increase the probability of toxicities. Consider a 50% reduction of the recommended starting maintenance dose. Subsequent doses should be adjusted according to therapeutic drug monitoring and response. Patients of Chinese ancestry have found a strong association between the risk of developing SJS/TEN and the presence of HLA-B*1502.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	FDA

Galantamine

https://www.pillcheck.ca/C6R1

CYP2D6 and CYP3A4 are major enzymes needed for galantamine metabolism. Enhanced drug clearance may reduce clinical effect. The dose of drug is individually titrated to tolerability.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	D

Gefitinib

https://www.pillcheck.ca/J7Q1

Enhanced drug clearance with reduced exposure and decreased risk for rash or hepatotoxicity. Higher clearance can affect clinical response. Increased clearance of gefitinib in patients receiving a strong CYP3A4 inducer, requiring dose increase. Avoid coadministration of CYP3A4 Inhibitors. Avoid concomitant use of gefitinib with proton pump inhibitors. Possible hemorrhage in patients taking warfarin: Monitor changes in prothrombin time or INR.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	FDA

Guanfacine

https://www.pillcheck.ca/H6Q7

Significantly reduced drug clearance is anticipated. Consider alternative treatment due to significantly increased exposure. When discontinuing, taper the dose in decrements of no more than 1 mg every 3 to 7 days.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Haloperidol

https://www.pillcheck.ca/L9Z6

Be alert to decreased haloperidol plasma concentration and adjust maintenance dose in response or select alternative drug e.g., pimozide, flupenthixol, fluphenazine, olanzapine, clozapine.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

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Hydrocodone

https://www.pillcheck.ca/I9V2

Increased formation of hydromorphone formation following hydrocodone administration, leading to a higher risk of toxicity. Avoid hydrocodone use due to the potential for toxicity. Alternatives that are not affected by this CYP2D6 phenotype include morphine and non-opioid analgesics. Tramadol, oxycodone are not good alternatives because their metabolism is affected by CYP2D6 activity.

biomarker	value	interpretation	level of evidence
OPRM1	AA	Normal sensitivity to opioids	C
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	FDA

Hydromorphone

https://www.pillcheck.ca/H3Q1

Hydromorphone is not metabolized by CYP2D6 and can be prescribed to patients with altered CYP2D6 metabolism. Individuals with the AA genotype may experience increased efficacy of opioids for pain management, may be less susceptible to opioid addiction, and may require a decreased dose of opioids as compared to individuals with the GG genotype. However, this has been contradicted in some studies. Other genetic and clinical factors may also influence a patient's response to opioid drugs.

biomarker	value	interpretation	level of evidence
OPRM1	AA	Normal sensitivity to opioids	C

Iloperidone

https://www.pillcheck.ca/K6R2

CYP2D6 and CYP3A4 are the major enzymes needed for Iloperidone metabolism. Potentially reduced clinical response due to enhanced drug clearance. Dose adjustment may be required.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Imipramine

https://www.pillcheck.ca/H8W8

Increased metabolism of tricyclics to less active compounds as compared with extensive metabolizers. Lower plasma concentrations will increase probability of pharmacotherapy failure. Avoid tricyclic use due to potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6. If a tricyclic is warranted, consider increasing the starting dose. Use therapeutic drug monitoring to guide dose adjustments

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

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Indacaterol

https://www.pillcheck.ca/N9Y5

Normal drug clearance. Steady-state AUC and Cmax of indacaterol were 1.2-fold higher in the (TA)/(TA)7 genotype, suggesting no relevant effect of UGT1A1 genotype on indacaterol exposure.

biomarker	value	interpretation	level of evidence
UGT1A1	*1/*1	Normal metabolizer	FDA

Irbesartan

https://www.pillcheck.ca/K9Y9

Individuals with poor CYP2C9 metabolism may have significantly decreased clearance of Irbesartan, which may result in increased exposure as compared to patients with normal metabolism, resulting in greater reduction in blood pressure. Other clinical and genetic factors may also influence the metabolism of Irbesartan. Excessive exposure to the medication can also increase the risk of side effects.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	FDA

Irinotecan

https://www.pillcheck.ca/F1W4

Irinotecan frequently causes diarrhea and myelosuppression. Normal metabolism anticipated. Early diarrhea may be accompanied by cholinergic symptoms which may be prevented or ameliorated by atropine. Late diarrhea can be life threatening and should be treated promptly with loperamide. Monitor patients with diarrhea and give fluid and electrolytes as needed. Institute antibiotic therapy if patients develop ileus, fever, or severe neutropenia. Interrupt and reduce subsequent doses if severe diarrhea occurs. Severe myelosuppression may also occur.

biomarker	value	interpretation	level of evidence
UGT1A1	*1/*1	Normal metabolizer	A

Itraconazole

https://www.pillcheck.ca/F6W9

Significantly reduced drug clearance is anticipated, significantly increasing the plasma concentrations of drugs metabolized by CYP3A4 including itraconazole. Avoid concomitant use of cisapride, pimozide, levacetylmethadol and quinidine with itraconazole due to serious risk of significant cardiovascular events, including QT prolongation, torsades de pointes, ventricular tachycardia, cardiac arrest, and/or sudden death.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Ketamine

https://www.pillcheck.ca/I5V7

Normal drug clearance anticipated. Average risk of side effects including drowsiness, hallucinations, dizziness and confusion. Use of ketamine is associated with emergence phenomena outcome characterized by vivid dreams, euphoria, illusions, delirium, and hallucinations, schizophrenia-like symptoms, or as a floating sensation.

biomarker	value	interpretation	level of evidence
CYP2B6	*1/*1	Normal metabolizer	FDA

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Lacosamide

https://www.pillcheck.ca/I6W9

Normal plasma concentrations of the lacosamide O-desmethyl metabolite is expected. As lacosamide is also metabolized by CYP2C9, poor metabolizers of CYP2C9 might have increased exposure to lacosamide.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	FDA

Lansoprazole

https://www.pillcheck.ca/M8V4

Normal metabolism of lansoprazole is anticipated; standard dosing and precautions are recommended. Concomitant administration of lansoprazole and tacrolimus may increase whole blood levels of tacrolimus, especially in transplant patients who are intermediate or poor metabolizers of CYP2C19.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	B

Ledipasvir and sofosbuvir

https://www.pillcheck.ca/I9U8

Patients with the CC genotype may have increased response to peginterferon alpha-2a, peginterferon alpha-2b, Ribavirin therapy compared to patients with genotype CT or TT. However, the role of the IFNL3 genotype is modest for Ledipasvir and Sofosbuvir therapy as compared to PEG-IFN/RBV therapy. Other genetic and clinical factors may also influence the response to Ledipasvir and Sofosbuvir-based therapy.

biomarker	value	interpretation	level of evidence
IFNL3	CC	Normal responder	FDA

Lesinurad

https://www.pillcheck.ca/J9Q8

Lesinurad exposure is increased in CYP2C9 poor metabolizers. At the 400 mg dose, lesinurad exposure was approximately 1.8-fold higher in CYP2C9 poor metabolizers compared to CYP2C9 extensive metabolizers. Lesinurad should be used with caution in patients who are CYP2C9 poor metabolizers.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	C

Lorazepam

https://www.pillcheck.ca/G1V1

Normal drug clearance is anticipated. Lorazepam may have abuse potential, especially in patients with a history of drug or alcohol abuse. In patients with depression, benzodiazepines should not be used without adequate antidepressant therapy. Use with caution in patients with COPD or sleep apnea. Elderly or debilitated patients may be more susceptible to the sedative effects. Therefore, these patients should be monitored frequently and have their dosage adjusted according to patient response; the initial dosage should not exceed 2 mg.

biomarker	value	interpretation	level of evidence
UGT2B15	CC	Normal metabolizer	FDA

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Losartan

https://www.pillcheck.ca/M8W4

Individuals may have significantly decreased metabolism of Losartan, as indicated by decreased plasma concentration of the active metabolite, E-3174. Subjects may show significantly higher Losartan/E3174 metabolic ratios, which may result in significantly reduced clinical response to this medication. Other genetic and clinical factors may also influence Losartan metabolism and response.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	FDA

Lovastatin

https://www.pillcheck.ca/H5U2

The genotype is associated with increased exposure but decreased response to lovastatin as measured by decreases in triglycerides. The increased exposure may increase the probability of side effects, like elevated creatinine kinase levels or myopathy. The concomitant use of lovastatin with strong inhibitors of CYP3A4 can also increase levels of lovastatin in plasma, increasing risk of myopathy. Prescribe a lower dose or consider an alternative statin (e.g., pravastatin or rosuvastatin) with routine creatine kinase (CK) surveillance. Consider alternative treatments such as PCSK9 inhibitors.

biomarker	value	interpretation	level of evidence
SLCO1B1	*5/*5	Poor metabolizer	FDA

Lurasidone

https://www.pillcheck.ca/K2R7

Significantly reduced drug metabolism is anticipated will affect clinical response and risk of side effects. Lurasidone is metabolized mainly via CYP3A4 into two active metabolites (ID-14283 and ID-14326) and two major non-active metabolites (ID-20219 and ID-20220). Avoid coadministration with a strong CYP3A4 inhibitor (e.g., ketoconazole) and inducer (e.g., rifampin). Dose adjustment is recommended for moderate CYP3A4 inhibitors (e.g. diltiazem).

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Mercaptopurine

https://www.pillcheck.ca/C7V4

Increased risk of drug sensitivity. Moderate to high concentrations of TGN metabolites. Start with reduced doses (reduce by 30-50%) and adjust doses of mercaptopurine based on degree of myelosuppression and disease-specific guidelines. Allow 2-4 weeks to reach steady state after each dose adjustment. In setting of myelosuppression, and depending on other therapy, emphasis should be on reducing mercaptopurine over other agents.

biomarker	value	interpretation	level of evidence
TPMT	*1/*2	Intermediate metabolizer	A

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Methadone

https://www.pillcheck.ca/C8P7

Clinical response to methadone is strongly related to prior use. Multiple doses versus single dose, body weight, history of cocaine dependence and ethnicity (Asian>Caucasian>African) were independently associated with methadone dose in multiple regression analysis.

biomarker	value	interpretation	level of evidence
OPRM1	AA	Normal sensitivity to opioids	C
CYP2B6	*1/*1	Normal metabolizer	B

Methotrexate

https://www.pillcheck.ca/G8W2

Significantly reduced drug clearance by OATP1B1 transporter is anticipated. Substantially increased risk of methotrexate toxicity. Assess variations in MTHFR and MTRR; adjust dosage accordingly.

biomarker	value	interpretation	level of evidence
SLCO1B1	*5/*5	Poor metabolizer	C

Metoprolol

https://www.pillcheck.ca/L3V4

Enhanced drug metabolism; select alternative drug (e.g., bisoprolol, carvedilol) or titrate dose to a maximum of 250% of the normal dose in response to efficacy and ADE. Caution should be exercised when coadministering potent CYP2D6 inhibitors such as fluoxetine, paroxetine or bupropion, antipsychotics, antiarrhythmics, antiretrovirals, antihistamines, antimalarials, antifungals and cimetidine.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Midazolam

https://www.pillcheck.ca/A4Z9

Increased drug clearance. Patients who express CYP3A5 may have faster clearance rates and increased metabolism of midazolam as compared to patients who do not express CYP3A5. Other clinical and genetic factors may also influence clearance and metabolism of midazolam.

biomarker	value	interpretation	level of evidence
CYP3A5	*1A/*3A	Intermediate metabolizer	C

Mirtazapine

https://www.pillcheck.ca/I3U9

Enhanced drug clearance is anticipated. Increased metabolism is associated with decreased response to mirtazapine in people with Mood Disorders. Other genetic and clinical factors may also influence a patient's metabolism of mirtazapine

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	FDA

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Modafinil

https://www.pillcheck.ca/J7Y3

Significantly enhanced drug metabolism; select alternative treatment. In tricyclic-treated patients, particularly Ultrafast CYP2D6 Metabolizers, the amount of metabolism by CYP2C19 may be substantially decreased. Modafinil may cause elevation of the levels of the tricyclics in this subset of patients. Do not use Modafinil in patients with reduced CYP2C19 or 2D6 metabolism.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Morphine

https://www.pillcheck.ca/G7Q5

Individuals with the AA genotype may experience increased efficacy of opioids for pain management, may be less susceptible to opioid addiction, and may require a decreased dose of opioids as compared to individuals with the GG genotype. However, this has been contradicted in some studies. Other genetic and clinical factors may also influence a patient's response to opioid drugs.

biomarker	value	interpretation	level of evidence
OPRM1	AA	Normal sensitivity to opioids	C

Naloxone

https://www.pillcheck.ca/H8U5

Patients with the AA genotype who are treated with naloxone may have lower cortisol response to opioid blockade as compared to patients with the AG or GG genotype. Other genetic and clinical factors may also influence the response to naloxone.

biomarker	value	interpretation	level of evidence
OPRM1	AA	Normal sensitivity to opioids	C

Naltrexone

https://www.pillcheck.ca/I3Q7

Patients with the AA genotype who are treated with naltrexone may have a decreased 1) response to naltrexone, 2) blunting of alcohol craving, 3) severity of intoxication when exposed to ethanol and naltrexone as compared to patients with the AG or GG genotype, 4) may experience increased efficacy of opioids for pain and opioid related drugs to treat addiction. The association with naltrexone response has been contradicted in other studies. Other genetic and clinical factors may also influence a patient's response to naltrexone.

biomarker	value	interpretation	level of evidence
OPRM1	AA	Normal sensitivity to opioids	C

Nebivolol

https://www.pillcheck.ca/J6X3

Enhanced drug clearance, compared to Normal Metabolizers, is anticipated which may result in decreased response to Nebivolol. Other genetic and clinical factors may also influence a patient's metabolism of Nebivolol.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	FDA

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Nefazodone

https://www.pillcheck.ca/A3Y4

Potentially reduced clinical effect due to enhanced drug clearance. Nefazodone has been shown in vitro to be an inhibitor of CYP3A4. Interactions have been observed between nefazodone and triazolam, alprazolam, buspirone, atorvastatin, and simvastatin. CYP2D6 poor metabolizers have a higher risk of interactions with debrisoquine, dextromethorphan, and the tricyclic antidepressants.

biomarker	value	interpretation	level of evidence
CYP2D6	*1/*1	Ultrarapid metabolizer	FDA
CYP2D6CNV	3N		

Nevirapine

https://www.pillcheck.ca/N7R4

Reduced risk for Nevirapine induced toxicity. Nevirapine enhances the clearance of coadministered drugs metabolized by CYP3A4. This induction is most pronounced in extensive metabolizers requiring dose adjustment.

biomarker	value	interpretation	level of evidence
CYP2B6	*1/*1	Normal metabolizer	B

Nilotinib

https://www.pillcheck.ca/B9X9

Normal metabolism is anticipated; standard dosing and precautions are recommended. Nilotinib can increase bilirubin levels.

biomarker	value	interpretation	level of evidence
UGT1A1	*1/*1	Normal metabolizer	C

Nortriptyline

https://www.pillcheck.ca/E5U6

Select alternative drug (e.g., citalopram, sertraline) if possible. If not, consider increasing the dose and monitor nortriptyline + 10-hydroxynortriptyline plasma concentrations. Drugs inhibiting the activity of CYP2D6 make normal metabolizers resemble poor metabolizers. TCA may become abruptly toxic when given one of these inhibiting drugs as concomitant therapy. Quinidine, cimetidine, many other antidepressants, phenothiazines, and the Type 1C antiarrhythmics propafenone and flecainide, as well as fluoxetine, sertraline, and paroxetine also inhibit CYP2D6. Sufficient time must elapse before initiating TCA treatment in a patient being withdrawn from fluoxetine, given the long half-life of the parent and active metabolite (at least 5 weeks may be necessary).

biomarker	value	interpretation	level of evidence
CYP2D6	*1/*1	Ultrarapid metabolizer	A
CYP2D6CNV	3N		

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Olanzapine

https://www.pillcheck.ca/B5Y6

Normal drug metabolism is anticipated. A decrease in the dose of Olanzapine should be considered if treatment with an inhibitor of CYP1A2 is initiated. Fluvoxamine, a CYP1A2 inhibitor results in a 54% mean increase in Olanzapine Cmax in female non-smokers and 77% in male smokers. Other genetic and clinical factors may also influence a patient's response to Olanzapine.

biomarker	value	interpretation	level of evidence
CYP1A2	*1A/*1A	Normal metabolizer	D

Ombitasvir, paritaprevir and ritonavir

https://www.pillcheck.ca/L5Z2

Patients with the CC genotype may have increased response to peginterferon alpha-2a, peginterferon alpha-2b, Ribavirin therapy compared to patients with genotype CT or TT. However, the role of the IFNL3 genotype is modest for Ombitasvir, Paritaprevir, and Ritonavir therapy as compared to PEG-IFN/RBV therapy. Other genetic and clinical factors may also influence the response to Ombitasvir, Paritaprevir, and Ritonavir-based therapy.

biomarker	value	interpretation	level of evidence
IFNL3	CC	Normal responder	FDA

Omeprazole

https://www.pillcheck.ca/G3R4

Normal metabolism is anticipated; standard dosing and precautions are recommended. Omeprazole is a CYP2C19 competitive inhibitor; avoid concomitant use with clopidogrel, St. John's Wort or rifampin. Interactions with Methotrexate and Tacrolimus have been reported.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	B

Ondansetron

https://www.pillcheck.ca/L1T9

CYP2D6 Ultrarapid Metabolizers are more likely to have a decreased response to Ondansetron as compared to other metabolizer groups. This decreased response leads to a higher risk of vomiting after chemotherapy or anesthesia. No significant associations have been observed for nausea. Select an alternative drug not predominantly metabolized by CYP2D6 (i.e. granisetron)

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	A

Oxazepam

https://www.pillcheck.ca/A1W2

Normal drug clearance is anticipated. Usual adult dose for anxiety 10 to 15 mg orally, 3 or 4 times per day. Management of mild-to-moderate anxiety syndromes, agitation, or anxiety associated with depression, tension, irritability, agitation, as well as for alcohol withdrawal 15 to 30 mg orally, 3 or 4 times / day. For geriatric population usual dose is 10 mg orally, 3 times / day; if needed, increase cautiously to 15 mg orally, 3 or 4 times / day.

biomarker	value	interpretation	level of evidence
UGT2B15	CC	Normal metabolizer	D

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Oxycodone

https://www.pillcheck.ca/J5W5

Increased formation of oxymorphone formation following oxycodone administration, leading to higher risk of toxicity. Avoid oxycodone use due to potential for toxicity. Alternatives that are not affected by this CYP2D6 phenotype include morphine and non-opioid analgesics. Tramadol and hydrocodone are not good alternatives because their metabolism is affected by CYP2D6 activity.

biomarker	value	interpretation	level of evidence
OPRM1	AA	Normal sensitivity to opioids	C
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	A

Palonosetron

https://www.pillcheck.ca/L1Y4

Enhanced CYP2D6 metabolism may decrease response to palonosetron. Therefore, similar to ondansetron, CYP2D6 Ultrarapid metabolizer are more likely to have a decreased response as compared to other metabolizer groups. The decreased response could lead to a higher risk of vomiting after chemotherapy or anesthesia. Select an alternative drug not predominantly metabolized by CYP2D6 (i.e. granisetron)

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Pantoprazole

https://www.pillcheck.ca/B5R8

Normal metabolism is anticipated; standard dosing and precautions are recommended.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	B

Paroxetine

https://www.pillcheck.ca/M2Q9

Increased metabolism to less active compounds when compared to extensive metabolizers. Lower/undetectable plasma concentrations may increase probability of pharmacotherapy failure. Select alternative drug not predominantly metabolized by CYP2D6. Coadministration of paroxetine with other drugs that are metabolized by CYP2D6, including certain drugs effective in the treatment of major depressive disorder should be avoided. Due to the risk of serious ventricular arrhythmias and sudden death potentially associated with elevated plasma levels of thioridazine, paroxetine, and thioridazine should not be coadministered. Tamoxifen is a pro-drug requiring metabolic activation by CYP2D6. Inhibition of CYP2D6 by paroxetine may lead to reduced plasma concentrations of an active metabolite (endoxifen) and hence reduced efficacy of tamoxifen.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	A

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Pazopanib

https://www.pillcheck.ca/M4X4

Patients with an extensive metabolizer genotype when treated with pazopanib may have decreased risk, but not absence, of hyperbilirubinemia. Other genetic and clinical factors may also influence adverse events associated with pazopanib. Co-administration of pazopanib with strong inhibitors of CYP3A4 (e.g., ketoconazole, ritonavir, clarithromycin) increases pazopanib concentrations and should be avoided. If co-administration of a strong CYP3A4 inhibitor is warranted, reduce the dose of pazopanib to 400 mg.

biomarker	value	interpretation	level of evidence
UGT1A1	*1/*1	Normal metabolizer	B

Peginterferon Alpha-2b

https://www.pillcheck.ca/K2S8

Patients with the CC genotype and Hepatitis C genotype 1 may have increased response when administered peginterferon alpha (2a, 2b) and Ribavirin as compared to patients with the CT or TT genotype. Patients with the CC genotype may also have higher spontaneous clearance in acute HCV infections than patients with the CT or TT genotype. Other genetic and clinical factors may also influence a patient's response to peginterferon and Ribavirin.

biomarker	value	interpretation	level of evidence
IFNL3	CC	Normal responder	A

Perphenazine

https://www.pillcheck.ca/G5T2

Potentially reduced clinical effect due to enhanced drug clearance.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Phenprocoumon

https://www.pillcheck.ca/N3U3

High risk of side effects; consider alternative anticoagulants such as Factor X inhibitors. Check INR more frequently. Symptoms of overdose include suspected or overt abnormal bleeding (e.g., appearance of blood in stools or urine, hematuria, excessive menstrual bleeding, melena, petechiae, excessive bruising or persistent oozing from superficial injuries). Monitor INR when initiating or discontinuing medications may affect the metabolism of phenprocoumon.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	B
VKORC1	AA	Low Vitamin K	B

Phenytoin

https://www.pillcheck.ca/B9Y4

Standard loading dose. Reduce maintenance dose by 50%. Evaluate response and serum concentration after 7-10 days. Be alert to ADEs (e.g., ataxia, nystagmus, dysarthria, sedation). Patients of Chinese ancestry have found a strong association between the risk of developing SJS/TEN and the presence of HLA-B*1502.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	A

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Pimozide

https://www.pillcheck.ca/H9X4

Enhanced drug clearance expected; be alert to reduced clinical efficacy.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Piroxicam

https://www.pillcheck.ca/B8Q7

Consider a dose reduction as poor CYP2C9 metabolizers may have abnormally high plasma levels due to reduced metabolic clearance. Data from published studies show that CYP2C9 poor metabolizers have 5.3-fold higher piroxicam systemic levels and 8.8-fold higher mean elimination half-life values than subjects who are normal metabolizer.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	FDA

Pitavastatin

https://www.pillcheck.ca/B6U4

This genotype is associated with significantly increased pitavastatin plasma concentrations (AUC) and Cmax. Patient may have high myopathy risk. Other genetic and clinical factors may also influence a patient's pitavastatin pharmacokinetics. Prescribe a lower dose or consider routine CK surveillance.

biomarker	value	interpretation	level of evidence
SLCO1B1	*5/*5	Poor metabolizer	C

Prasugrel

https://www.pillcheck.ca/F6W8

Normal clopidogrel metabolism is anticipated. Studies have shown that prasugrel active metabolite levels were higher in patients older than 75 years compared with a younger group. In clinical pharmacology studies, after adjusting for body weight, the AUC of the active metabolite was approximately 19% higher in Chinese, Japanese, and Korean subjects than in Caucasian subjects. Prasugrel increases the risk of intracranial bleeding in patients with a history of TIA or stroke.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	FDA

Pravastatin

https://www.pillcheck.ca/F2U3

Patients may have increased bioavailability and increased pravastatin plasma concentrations. Other genetic and clinical factors may also influence the pharmacokinetics of pravastatin. European-Americans had significantly higher pravastatin AUC and Cmax than African-Americans.

biomarker	value	interpretation	level of evidence
SLCO1B1	*5/*5	Poor metabolizer	C

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Propafenone

https://www.pillcheck.ca/C8S8

Enhanced drug clearance. Propafenone is used to treat cardiac arrhythmia, but should be used only if the condition is thought to be life-threatening. Propafenone is metabolized by CYP2D6, CYP3A4 and CYP1A2 enzymes. The combination of propafenone and inhibition of CYP3A4 and/or CYP2D6 could be hazardous. Desipramine, paroxetine, ritonavir, sertraline block CYP2D6; ketoconazole, erythromycin, saquinavir, and grapefruit juice inhibit CYP3A4 and should be avoided. Amiodarone inhibits CYP1A2 and can cause increased plasma levels of propafenone.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Propranolol

https://www.pillcheck.ca/D5U8

Enhanced CYP2D6 activity can decrease S-propranolol plasma concentration when treated with propranolol as compared to extensive metabolizers.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Protriptyline

https://www.pillcheck.ca/G3T6

Enhanced Drug clearance. Ultrafast CYP2D6 metabolizers will have lower than expected plasma concentrations of tricyclic antidepressants (TCAs) when given the usual doses. Certain drugs that inhibit the activity of the CYP2D6 isozyme can make normal metabolizers resemble poor metabolizers. A patient who is stable on a given dose of TCA may experience abrupt toxicity when given one of these inhibiting drugs as concomitant therapy. CYP2D6 inhibiting drugs include quinidine, cimetidine and many other antidepressants, phenothiazines, and the Type 1C antiarrhythmics, propafenone and flecainide.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Quetiapine

https://www.pillcheck.ca/L6Q5

Reduced plasma concentrations are observed for CYP3A5 expressors. Significantly reduced clinical response is anticipated.

biomarker	value	interpretation	level of evidence
CYP3A5	*1A/*3A	Intermediate metabolizer	FDA

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Quinidine

https://www.pillcheck.ca/H2R2

Quinidine is not metabolized by CYP2D6, but it inhibits the action of cytochrome CYP2D6, effectively converting extensive metabolizers into poor metabolizers. May have lower impact in Ultrafast CYP2D6 metabolizers. Caution must be exercised whenever quinidine is prescribed together with drugs metabolized by CYP2D6.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Rabeprazole

https://www.pillcheck.ca/I6Y9

Normal drug response is anticipated. Rabeprazole is less affected by CYP2C19 variation than Omeprazole.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	B

Ranolazine

https://www.pillcheck.ca/E4Z6

There are no dosage guidelines for Ranolazine for subjects who are Ultrarapid metabolizers of CYP2D6. Enhanced drug clearance may reduce clinical response at standard doses.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	FDA

Rasagiline

https://www.pillcheck.ca/M1V3

Normal drug clearance is anticipated. Patients with mild hepatic impairment or concomitant use of ciprofloxacin or other CYP1A2 inhibitors should not exceed a dose of 0.5 mg rasagiline, once daily. Avoid concomitant use of meperidine, tramadol, methadone, propoxyphene, dextromethorphan, St. John's wort, cyclobenzaprine, or other MAO inhibitor. Avoid rasagiline use in patients with moderate or severe hepatic impairment.

biomarker	value	interpretation	level of evidence
CYP1A2	*1A/*1A	Normal metabolizer	FDA

Risperidone

https://www.pillcheck.ca/M6Z2

Enhanced drug clearance may affect clinical response. Select an alternative drug or be extra alert to adverse drug events (ADR). Although extensive metabolizers have lower risperidone and higher 9- hydroxyrisperidone concentrations than poor metabolizers, the pharmacokinetics of risperidone and 9-hydroxyrisperidone combined, after single and multiple doses, are similar in extensive and poor metabolizers. Adjust risperidone dose to clinical response.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

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Rivaroxaban

https://www.pillcheck.ca/F5Q9

Significantly reduced drug metabolism is anticipated, which may lead to increased drug exposure and risk of bleeding. Inhibitors of CYP3A4 can further decrease metabolism while CYP3A4 inducers can increase the metabolism of rivaroxaban. P-glycoprotein inhibitors can increase the absorption of rivaroxaban, while inducers can reduce the absorption of rivaroxaban. Agents that interfere with both P-glycoprotein and CYP3A4 are likely to cause more significant interactions with rivaroxaban than agents that interfere with P-glycoprotein or CYP3A4 alone. Avoid use of combined P- glycoprotein and strong CYP3A4 inhibitors or inducers. If strong inhibitors are co-administered in Poor metabolizers of CYP3A4, use rivaroxaban with caution or avoid use.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Rosuvastatin

https://www.pillcheck.ca/C5U9

Patients may have low oral clearance and higher plasma concentrations of rosuvastatin. The higher plasma concentrations of drug may increase the probability of side effects, like elevated creatinine kinase levels or myopathy. To avoid toxicity in Asian patients, lower doses should be considered. Pharmacokinetic studies show an approximately two-fold increase in peak plasma concentration and AUC in Asian patients (Filipino, Chinese, Japanese, Korean, Vietnamese, or Asian-Indian descent) compared to Caucasians patients. Consider alternative treatments including PCSK9 inhibitors.

biomarker	value	interpretation	level of evidence
SLCO1B1	*5/*5	Poor metabolizer	B

Salmeterol

https://www.pillcheck.ca/H3S9

Somewhat reduced response to salmeterol or salbutamol is anticipated (as measured by a decreased risk of asthma excerbations and higher quality of life scores). This association does not seem to apply to lung function measurements such as peak expiratory flow rate or FEV1. Other genetic and clinical factors may also influence a patient's response to treatment. Salmeterol may increase the risk of asthma-related death and should only be used as additional therapy for patients with asthma who are currently taking but are inadequately controlled on a long-term asthma control medication, such as an inhaled corticosteroid.

biomarker	value	interpretation	level of evidence
ADRB2	GA	Intermediate responder	C

Sertraline

https://www.pillcheck.ca/J2V3

Initiate therapy with recommended starting dose.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	B

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Sildenafil

https://www.pillcheck.ca/I9P2

Significantly reduced drug clearance is anticipated. Substantially increased risk of decreased blood pressure, syncope, and prolonged erection due to higher sildenafil exposures. Concomitant use of alpha-blockers or amlodipine produces additive blood pressure lowering effects. In patients taking strong CYP3A4 inhibitors, such as ritonavir, sildenafil exposure is increased and a decrease in sildenafil dosage is strongly recommended.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Simeprevir

https://www.pillcheck.ca/K6W4

Patients with the CC genotype may have increased response to Simeprevir and peginterferon alpha-2a, peginterferon alpha-2b, Ribavirin therapy compared to patients with genotype CT or TT. However, the role of the IFNL3 genotype is modest for Simeprevir therapy as compared to PEG-IFN/RBV therapy. Other genetic and clinical factors may also influence the response to Simeprevir-based therapy.

biomarker	value	interpretation	level of evidence
IFNL3	CC	Normal responder	FDA

Simvastatin

https://www.pillcheck.ca/E7P5

High myopathy risk. Prescribe a lower dose or consider an alternative statin. Monitor creatine kinase (CK) levels routinely.

biomarker	value	interpretation	level of evidence
SLCO1B1	*5/*5	Poor metabolizer	C

Sirolimus

https://www.pillcheck.ca/N5V8

Higher dose requirement is anticipated. Patients with CYP3A5 expresser genotype (*1/*3) who are recipients of transplants may have increased metabolism of sirolimus and require a higher dose as compared to patients with the CYP3A5 non-expresser genotype (*3/*3). Other genetic and clinical factors may influence a patient's sirolimus dose requirements. Sirolimus metabolism is strongly affected by drugs inhibiting CYP3A4. Therapeutic monitoring and dose adjustments are recommended when sirolimus is coadministrated with strong CYP3A inhibitors or inducers.

biomarker	value	interpretation	level of evidence
CYP3A5	*1A/*3A	Intermediate metabolizer	C

Sofosbuvir

https://www.pillcheck.ca/L6V8

Patients with the CC genotype may have increased response to peginterferon alpha-2a, peginterferon alpha-2b, Ribavirin therapy compared to patients with genotype CT or TT. However, the role of the IFNL3 genotype is modest for Sofosbuvir therapy as compared to PEG-IFN/RBV therapy. Other genetic and clinical factors may also influence the response to Sofosbuvir-based therapy.

biomarker	value	interpretation	level of evidence
IFNL3	CC	Normal responder	FDA

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Sofosbuvir and velpatasvir

https://www.pillcheck.ca/I1S5

Patients with the CC genotype may have increased response to peginterferon alpha-2a, peginterferon alpha-2b, Ribavirin therapy compared to patients with genotype CT or TT. However, the role of the IFNL3 genotype is modest for Sofosbuvir and Velpatasvir therapy as compared to PEG-IFN/RBV therapy. Other genetic and clinical factors may also influence the response to Sofosbuvir and Velpatasvir based therapy.

biomarker	value	interpretation	level of evidence
IFNL3	CC	Normal responder	FDA

Tacrolimus

https://www.pillcheck.ca/N7S6

Organ recipients with an intermediate metabolizer phenotype (CYP3A5 expressor) will generally require an increased dose of tacrolimus to achieve therapeutic drug concentrations. Increase starting dose 1.5 to 2 times recommended starting dose. Total starting dose should not exceed 0.3mg/kg/day. Follow with therapeutic drug monitoring given the risk of arterial vasoconstriction, hypertension and nephrotoxicity that can occur with supratherapeutic tacrolimus concentrations. Further dose adjustments or selection of alternative therapy may be necessary due to other clinical factors (medication interactions, or hepatic function).

biomarker	value	interpretation	level of evidence
CYP3A5	*1A/*3A	Intermediate metabolizer	A

Tadalafil

https://www.pillcheck.ca/N9W7

Significantly reduced drug clearance is anticipated. Substantially increased risk of decreased blood pressure, syncope, and prolonged erection due to higher tadalafil exposures. Consider dose reduction or alternative treatment. Concomitant administration of alpha-blockers or amlodipine produces additive blood pressure lowering effects. Avoid use of CYP3A4 inhibitors.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Tamoxifen

https://www.pillcheck.ca/J9S2

There are no therapeutic dose recommendations for Ultrarapid CYP2D6 metabolizers. Be alert to adverse drug events: QTc prolongation, INR increase < 4.5 and kinetic effect.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	A

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Tamsulosin

https://www.pillcheck.ca/F1T5

Enhanced clearance of tamsulosin is expected, which may affect clinical response at normal doses. Concomitant treatment with paroxetine, which is strong CYP2D6 inhibitor, results in an increase in the Cmax and AUC of tamsulosin by a factor of 1.3 and 1.6, respectively. Tamsulosin 0.4 mg capsules should not be used in combination with strong inhibitors of CYP3A4 (e.g., ketoconazole).

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Tegafur

https://www.pillcheck.ca/J7T4

Normal DPYD activity and "normal" risk for fluoropyrimidine toxicity. Use label-recommended dosage and administration.

biomarker	value	interpretation	level of evidence
DPYD	*1/*1	Normal metabolizer	C

Telaprevir

https://www.pillcheck.ca/I1V6

In patients who have Hepatitis C genotype 1, those with the CC genotype may have higher response rates (SVR) to triple therapy (Telaprevir, peginterferon alpha-2a/b and Ribavirin) as compared to patients with the CT or TT genotype. Patients with the CC genotype are also more likely to be eligible for shortened therapy (24 weeks instead of the standard 48 weeks). The impact of the IL28B genotype may be dampened in patients with prior PegIFN/RBV treatment failure. Other genetic and clinical factors may also influence a patient's response to HCV triple therapy.

biomarker	value	interpretation	level of evidence
IFNL3	CC	Normal responder	FDA

Telithromycin

https://www.pillcheck.ca/L2W8

Significantly reduced clearance of telithromycin increases the risk of side effects, especially upon co-administration of CYP3A4 inhibitors. Due to a potential to increase the QT interval, Telithromycin should be used with care in patients with coronary heart disease, a history of ventricular arrhythmias, uncorrected hypokalaemia and/or hypomagnesaemia, or bradycardia (<50 bpm), during concomitant administration of Telithromycin with QT interval prolonging agents, or in patients concomitantly treated with potent CYP3A4 inhibitors such as protease inhibitors or azole antifungals (e.g. ketoconazole, fluconazole). Avoid concomitant administration with medicinal products that prolong the QT interval and are CYP3A4 substrates, such as cisapride, pimozide, astemizole, terfenadine, dronedarone, and saquinavir. Treatment with simvastatin, atorvastatin, and lovastatin should be interrupted during Telithromycin treatment. Avoid concomitant administration with ergot alkaloid derivatives (such as ergotamine and dihydroergotamine).

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

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Terbinafine

https://www.pillcheck.ca/N5P7

Enhanced drug clearance may affect clinical response. Terbinafine is an inhibitor of CYP2D6 isozyme and has an effect on metabolism of desipramine, cimetidine, fluconazole, cyclosporine, rifampin, and caffeine. Drugs predominantly metabolized by the CYP2D6 isozyme include the following drug classes: tricyclic antidepressants, selective serotonin reuptake inhibitors, beta-blockers, antiarrhythmics class 1C (e.g., flecainide and propafenone) and monoamine oxidase inhibitors Type B. Coadministration of terbinafine should be done with careful monitoring and may require a reduction in dose of the 2D6-metabolized drug

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Tetrabenazine

https://www.pillcheck.ca/E8W2

There are no Tetrabenazine dosage guidelines for Ultrarapid metabolizers of CYP2D6. Be alert to symptoms of insufficient therapeutic effects. Potentially reduced risk of toxicity. Titrate drug dose weekly. CYP2D6 inhibitors (paroxetine, fluoxetine, quinidine) markedly increase exposure to alpha-HTBZ and beta-HTBZ, requiring a dose reduction of Tetrabenzine.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Thioguanine

https://www.pillcheck.ca/I6V5

Moderate to high concentrations of TGN metabolites; but note that TGN after thioguanine are 5-10x higher than TGN after mercaptopurine or azathioprine. Start with reduced doses (reduce by 30-50%) and adjust doses of thioguanine based on degree of myelosuppression and disease-specific guidelines. Allow 2-4 weeks to reach steady state after each dose adjustment. In the setting of myelosuppression, and depending on other therapy, emphasis should be on reducing thioguanine over other agents.

biomarker	value	interpretation	level of evidence
TPMT	*1/*2	Intermediate metabolizer	A

Thioridazine

https://www.pillcheck.ca/E8R4

Enhanced drug clearance may affect clinical response. Thioridazine may increase the risk of Torsades de pointes and/or sudden death in association with the use of drugs that prolong the QTc interval. Certain circumstances may increase this risk, including 1) bradycardia, 2) hypokalemia, 3) concomitant use of other drugs that prolong the QTc interval, 4) presence of congenital prolongation of the QT interval, and 5) for thioridazine coadministration with drugs that may inhibit P450 2D6 or by some other mechanism interfere with the clearance of thioridazine.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

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Thiothixene

https://www.pillcheck.ca/J5W4

Enhanced drug clearance is anticipated potentially affecting clinical response. Use of CYP2D6 inhibitors can affect thiothixene exposure.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	FDA

Ticagrelor

https://www.pillcheck.ca/C1T9

Normal response to clopidogrel is anticipated. Normal response to ticagrelor is also expected and can be used. Ticagrelor should not be given to patients with a history of severe hepatic impairment or intracranial bleeding. Possible interaction with simvastatin. Monitor digoxin levels with initiation of, or any change in ticagrelor therapy. Ticagrelor is metabolized by CYP3A4/5. Avoid use with strong CYP3A inhibitors as well as potent CYP3A inducers, such as rifampin, dexamethasone, phenytoin, carbamazepine and phenobarbital.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	FDA

Timolol

https://www.pillcheck.ca/G3Z2

Enhanced drug clearance may affect clinical response. Lower risk of side effects such as decreased heart rate (i.e., systemic beta-blockade).

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

Tolterodine

https://www.pillcheck.ca/E8P3

Enhanced drug metabolism of tolterodine to its active metabolite DD01 (5-HM). However, since tolterodine and DD01 (5-HM) have similar pharmacological effects, the net activity of tolterodine is expected to be similar regardless of CYP2D6 metabolizer status. Proceed with caution in patients with a known history of QT prolongation or patients who are taking Class IA (e.g., quinidine, procainamide) or Class III (e.g., amiodarone, sotalol) antiarrhythmic medications.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	FDA

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Tramadol and acetaminophen

https://www.pillcheck.ca/F1W5

Increased formation of O-desmethyltramadol (M1) formation following tramadol administration, leading to higher risk of toxicity. Avoid Tramadol use due to potential for toxicity. Alternatives that are not affected by this CYP2D6 phenotype include morphine and non-opioid analgesics. Hydrocodone and oxycodone are not good alternatives because their metabolism is affected by CYP2D6 activity.

biomarker	value	interpretation	level of evidence
OPRM1	AA	Normal sensitivity to opioids	C
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	A

Trazodone

https://www.pillcheck.ca/E8U2

Significantly reduced drug clearance is anticipated, increasing the risk of side effects. Avoid concomitant use with a CYP3A4 inhibitor. Adverse reactions may occur upon discontinuation; gradually reduce the dosage rather than stopping trazodone abruptly. Concomitant use of aspirin, NSAIDS, other antiplatelet drugs, warfarin, and other anticoagulants may increase the risk of bleeding events.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Trimipramine

https://www.pillcheck.ca/G9T3

Avoid tricyclic use due to the potential lack of efficacy. Consider alternative drug not metabolized by CYP2D6. Consider increasing starting dose if the use of TCA is warranted. Use therapeutic drug monitoring to guide dose adjustments. Check CYP2C19 metabolic status: for CYP2C19 poor metabolizers consider a 50% reduction of recommended starting dose; for CYP2C19 ultrafast metabolizers, consider alternative medications.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Tropisetron

https://www.pillcheck.ca/J8Z5

In Ultrarapid Metabolizers, there is increased metabolism of Tropisetron to less active compounds when compared to normal metabolizers, and this is associated with decreased response. Select an alternative drug that is not predominantly metabolized by CYP2D6 (i.e. Granisetron).

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	A

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Valbenazine

https://www.pillcheck.ca/H4T1

Enhanced drug clearance may affect clinical response. Decreased exposure to valbenazine's active metabolite is anticipated thus decreasing the risk of exposure-related adverse reactions. For patients who are taking a strong CYP2D6 inhibitor, dose reduction may be necessary. The initial dose is 40 mg once daily. The recommended dose for patients with moderate or severe hepatic impairment is 40 mg once daily.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	FDA

Valproic acid / divalproex

https://www.pillcheck.ca/F7Q1

Significantly reduced clearance anticipated; use non-VPA therapy for the children with two mutated CYP2C9 alleles.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	B

Vardenafil

https://www.pillcheck.ca/K5R5

Significantly reduced drug clearance is anticipated. Substantially increased risk of syncope, decreased blood pressure, and prolonged erection. Avoid vardenafil in patients also taking CYP3A4 inhibitors.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Venlafaxine

https://www.pillcheck.ca/G5Y8

Be alert to decreased venlafaxine and increased (O-desmethyl) venlafaxine plasma concentration. Titrate dose to a maximum of 150% of the normal dose or select an alternative drug (e.g., citalopram, sertraline). Venlafaxine is metabolized to its active metabolite, ODV, by CYP2D6. CYP2D6 inhibitors such as quinidine would be expected to reduce venlafaxine metabolism to ODV and affect clinical efficacy.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Voriconazole

https://www.pillcheck.ca/G9X4

For pediatric or adult patients: initiate therapy with recommended standard dosing. Further dose adjustments or selection of alternative therapy may be necessary due to other clinical factors, such as drug interactions, hepatic function, renal function, species, site of infection, TDM and co-morbidities.

biomarker	value	interpretation	level of evidence
CYP2C19	*1/*1	Normal metabolizer	A

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Vortioxetine

https://www.pillcheck.ca/F1Z5

In CYP2D6 ultra-rapid metabolizers, there is an increased drug clearance; the plasma concentration of vortioxetine administered at 10 mg/day were between those obtained in extensive metabolizers at 5 mg/day and 10 mg/day. Therefore, depending on individual patient response, a dose adjustment may be considered.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	B

Warfarin

https://www.pillcheck.ca/A3W1

Recommended starting dose is in the range of 0.5-2mg. Low warfarin initiation dose and frequent blood coagulation (INR) monitoring are required when initiating or discontinuing medications that may influence the metabolism of warfarin. Warfarin dose will need to be adjusted according to your health status, age, body weight, dietary habits and other medications you are taking. Consider alternative treatment with Factor X inhibitors.

biomarker	value	interpretation	level of evidence
CYP2C9	*3/*3	Poor metabolizer	A
VKORC1	AA	Low Vitamin K	A

Zopiclone

https://www.pillcheck.ca/L8W4

Significantly reduced clearance is anticipated increasing total exposure and clinical response. Avoid use in elderly adults. Consider dose reduction or alternative medication not metabolized by CYP3A4. Patients with impaired liver function also may exhibit increased exposure to zopiclone.

biomarker	value	interpretation	level of evidence
CYP3A4	*6/*6	Poor metabolizer	FDA

Zuclopenthixol

https://www.pillcheck.ca/C9T2

Be alert to low zuclopenthixol plasma concentrations or select alternative drug e.g. flupenthixol, olanzapine, clozapine.

biomarker	value	interpretation	level of evidence
CYP2D6 CYP2D6CNV	*1/*1 3N	Ultrarapid metabolizer	C

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End of Pillcheck™ Report

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