Medcheck Report

Risk Management

⚠ Antipsychotic-Induced Tardive Dyskinesia

Increased Risk of Antipsychotic-Induced Tardive Dyskinesia

The patient does not carry the Taq1A variant (homozygous for the A2 allele).

The genotype results predict that the patient has normal dopamine receptor DRD2 density and functioning. The patient has increased risk for tardive dyskinesia when treated with antipsychotics.

Closely monitor the patient for signs of tardive dyskinesia.

✓ Antipsychotic-Induced Hyperprolactinemia

Normal Risk of Antipsychotic-Induced Hyperprolactinemia

The patient does not carry the Taq1A variant (homozygous for the A2 allele).

The genotype results predict that the patient has normal dopamine receptor DRD2 density and functioning. The patient has normal risk of hyperprolactinemia when treated with antipsychotics.

Monitor the patients closely for any signs of hyperprolactinemia.

✓ Antipsychotic-Induced Weight Gain

Low Risk of Antipsychotic-Induced Weight Gain

The patient does not carry the Taq1A variant (homozygous for the A2 allele).

The genotype results predict that the patient has normal dopamine receptor DRD2 density and functioning. The patient has a normal risk for weight gain when treated with antipsychotics.

Monitor the patient closely for signs of weight gain.

⚠ Hyperhomocysteinemia - Depression

Increased Risk of Hyperhomocysteinemia

The patient carries two copies of the MTHFR c.665C>T variant (homozygous). MTHFR enzyme activity is severely reduced (30% of normal activity).

Patients diagnosed with depression often have low folate levels and homocysteine is a highly sensitive marker of folate status. Functional folate deficiency is indicated by elevated homocysteine. This patient exhibits significantly reduced MTHFR activity, which is a risk factor for hyperhomocysteinemia. Low MTHFR activity may further exacerbate folate deficiency in patients with depression and may increase the risk of depressive relapse or delay the response to antidepressants.

Patients diagnosed with depression: as lower folate levels are associated with poorer antidepressant response, and baseline levels of folate within the normal range predict antidepressant response, this patient is likely to benefit from methylfolate as an antidepressant-augmenting agent. Testing for homocysteine levels and serum folate levels may be informative for this patient. Although methylfolate may substantially benefit this patient, it should not replace the antidepressant therapy and methylfolate should always be used as an adjuvant to antidepressant medication.

✓ Thrombophilia

Normal Risk of Thrombosis

The patient does not carry the F5 c.1601G>A variant (also known as Factor V Leiden) or the F2 c.*97G>A variant (also known as Factor II 20210G>A).

The patient's risk of thrombosis is not increased (average risk of clotting is about 1 in 1000 for anyone in a year). However, because this test cannot find all of the inherited reasons for abnormal clotting, other factors may affect this risk assessment.

Assess thrombotic risk based on other genetic and/or circumstantial risk factors such as smoking, obesity, malignancy, prolonged immobilization or surgery.

Estrogen-containing contraceptive and hormone replacement therapy: unless other genetic and/or circumstantial risk factors are present, consider standard prescribing and monitoring practices.

⊗ Hyperhomocysteinemia - Thrombosis

Increased Risk of Hyperhomocysteinemia

The patient carries two copies of MTHFR c.665C>T variant (homozygous) and no MTHFR c.1286A>C variant. MTHFR enzyme activity is severely reduced (30% of normal activity).

The patient's significantly reduced MTHFR activity is a risk factor for hyperhomocysteinemia, especially in the presence of low serum folate levels. Mild to moderate hyperhomocysteinemia appears to be associated with an increased risk for venous thromboembolism (VTE).
Testing total plasma homocysteine level may be beneficial. Hyperhomocysteinemia can be treated with nutritional supplementation.

A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.	**ACTIONABLE**	Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA. EMA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as knowledge arises.
Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.		
The medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.	**INFORMATIVE**	There are insufficient or contradictory findings documenting the impact of a given genetic polymorphism or drug interaction. Recommendations are informative and implementation in a clinical setting is optional.

Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Anticancer Agents	Antifolates		Methotrexate	
	Angiotensin II Receptor Antagonists	Azilsartan Irbesartan Losartan		
	Antianginal Agents	Ranolazine		
	Antiarrhythmics		Mexiletine Propafenone	Flecainide
	Anticoagulants		Warfarin	
	Antiplatelets		Clopidogrel	
Cardiovascular	Beta Blockers	Nebivolol Propranolol Timolol		Metoprolol
	Diuretics	Torsemide		
	Statins	Atorvastatin Fluvastatin Lovastatin Pitavastatin Pravastatin Rosuvastatin Simvastatin		
Diabetes	Meglitinides	Nateglinide Repaglinide		
Gastrointestinal	Antiemetics	Dronabinol Metoclopramide	Dolasetron Fosnetupitant / Palonosetron Netupitant / Palonosetron Palonosetron	Ondansetron
	Proton Pump Inhibitors	Esomeprazole Rabeprazole	Dexlansoprazole Lansoprazole Omeprazole Pantoprazole	
Gaucher Disease	Endocrine-Metabolic Agents			Eliglustat
Gynecology	Endometriosis Pain Agents	Elagolix		
Hematology	Hemostatic Agents	Avatrombopag Eltrombopag Lusutrombopag		
Infections	Antifungals			Voriconazole
	Anti-HIV Agents		Efavirenz	
Multiple Sclerosis	Disease-Modifying Agents	Siponimod		
	Muscle Relaxants		Carisoprodol Tizanidine	

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PATIENT INFORMATION

SPECIMEN DETAILS

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Pain	NSAIDs	Celecoxib Flurbiprofen Ibuprofen Lornoxicam Meloxicam Piroxicam		
	Opioids	Fentanyl Morphine	Benzhydrocodone Dihydrocodeine Hydrocodone Methadone Oxycodone	Codeine Tramadol
Psychotropic	Antiaddictives	Lofexidine	Bupropion Naltrexone	
	Anti-ADHD Agents	Amphetamine Dextroamphetamine Lisdexamfetamine	Atomoxetine Dexmethylphenidate Methylphenidate	
	Anticonvulsants	Brivaracetam Fosphenytoin Phenobarbital Phenytoin Primidone Zonisamide		
	Antidementia Agents	Galantamine	Donepezil	
	Antidepressants	Desvenlafaxine Fluoxetine Nefazodone Vortioxetine	Amoxapine Fluvoxamine Maprotiline Protriptyline Sertraline	Amitriptyline Citalopram Clomipramine Desipramine Doxepin Escitalopram Imipramine Nortriptyline Paroxetine Trimipramine Venlafaxine
	Antipsychotics	Aripiprazole Brexpiprazole Iloperidone Paliperidone Pimozide Quetiapine Thioridazine	Chlorpromazine Clozapine Olanzapine Perphenazine	Haloperidol Risperidone Zuclopenthixol
	Benzodiazepines	Clobazam	Diazepam Lorazepam Oxazepam	
	Mood Stabilizers	Lithium		
	Other Neurological Agents	Deutetrabenazine Dextromethorphan / Quinidine Flibanserin Valbenazine	Tetrabenazine	

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Anti-Hyperuricemics and Anti-Gout Agents	Allopurinol Lesinurad		
Rheumatology	Immunomodulators	Leflunomide		
	Other Antirheumatic Agents		Sulfasalazine	
Sjogren's Syndrome	Cholinergic Agonists	Cevimeline		
Transplantation	Immunosuppressants	Tacrolimus		
Urologicals	Alpha-Blockers for Benign Prostatic Hyperplasia	Tamsulosin		
	Antispasmodics for Overactive Bladder	Darifenacin Fesoterodine Mirabegron Tolterodine		

Dosing Guidance

Amitriptyline

Possible Decreased Amitriptyline Exposure (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

The patient is predicted to be a CYP2D6 normal or ultra-rapid metabolizer, although the result is not definitive. The patient's possible high CYP2D6 activity is likely to result in a significantly increased metabolism of amitriptyline to less active compounds and a subsequent decrease in amitriptyline exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If amitriptyline is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Neuropathic Pain: Consider an alternative medication. If amitriptyline is warranted titrate dose according to the patient's clinical response and tolerability.

Amitriptyline

Decreased Amitriptyline Exposure (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of amitriptyline to nortriptyline and a subsequent decrease in amitriptyline exposure leading to therapy failure or increased side effects.

Psychiatric Conditions: Consider an alternative medication. If amitriptyline is warranted, consider therapeutic drug monitoring to guide dose adjustments.

Neuropathic Pain: Consider an alternative medication. If amitriptyline is warranted titrate dose according to the patient's clinical response and tolerability.

Citalopram

Insufficient Response to Citalopram (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

At standard label-recommended dosage, citalopram plasma concentrations levels are expected to be low which may result in a loss of efficacy. Consider an alternative medication. If citalopram is warranted, consider increasing the dose to a maximum of 150% and titrate based on the clinical response and tolerability.

Clomipramine

Possible Decreased Clomipramine Exposure (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

The patient is predicted to be a CYP2D6 normal or ultra-rapid metabolizer, although the result is not definitive. The patient's possible high CYP2D6 activity is likely to result in a significantly increased metabolism of clomipramine to less active compounds and a subsequent decrease in clomipramine exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If clomipramine is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Clomipramine

Decreased Clomipramine Exposure (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of clomipramine to desmethyl clomipramine and a subsequent decrease in clomipramine exposure leading to therapy failure or increased side effects.

Psychiatric Conditions: Consider an alternative medication. If clomipramine is warranted, consider therapeutic drug monitoring to guide dose adjustments.

Codeine

Possible Increased Response to Codeine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer. Codeine is converted into its active metabolite morphine by CYP2D6. Since this patient may be a ultra-rapid metabolizer, greatly increased morphine levels may occur, and the patient may be at high risk of toxicity when taking codeine. The ultra-rapid conversion of codeine to morphine in breast feeding mothers can result in high and unsafe levels of morphine in the breast milk potentially causing life threatening respiratory depression in the breastfed infant. Avoid prescribing codeine, and consider an alternative opioid or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

Desipramine

Possible Decreased Desipramine Exposure (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

The patient is predicted to be a CYP2D6 normal or ultra-rapid metabolizer, although the result is not definitive. The patient's possible high CYP2D6 activity is likely to result in a significantly increased metabolism of desipramine to less active compounds and a subsequent decrease in desipramine exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If desipramine is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Doxepin

Possible Decreased Doxepin Exposure (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

The patient is predicted to be a CYP2D6 normal or ultra-rapid metabolizer, although the result is not definitive. The patient's possible high CYP2D6 activity is likely to result in a significantly increased metabolism of doxepin to less active compounds and a subsequent decrease in doxepin exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If doxepin is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Insomnia: Doxepin can be prescribed according to the standard recommended dosage and administration. Monitor patient closely for decreased efficacy.

Doxepin

Decreased Doxepin Exposure (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of doxepin to desmethyl doxepin and a subsequent decrease in doxepin exposure leading to therapy failure or increased side effects.

Psychiatric Conditions: Consider an alternative medication. If doxepin is warranted, consider therapeutic drug monitoring to guide dose adjustments.

Insomnia: Doxepin can be prescribed according to the standard recommended dosage and administration.

Eliglustat

Decreased Exposure to Eliglustat (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: The genotype result indicates that the patient is likely to have significantly reduced eliglustat exposure. The patient may not reach adequate concentrations of eliglustat to achieve a therapeutic effect. Consider an alternative medication.

Escitalopram

Insufficient Response to Escitalopram (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

At standard label-recommended dosage, escitalopram plasma concentrations levels are expected to be low which may result in a loss of efficacy. Consider an alternative medication. If escitalopram is warranted, consider increasing the dose to a maximum of 150% and titrate based on the clinical response and tolerability.

Flecainide

Decreased Exposure to Flecainide (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: The patient's genotype may be associated with a decreased flecainide exposure following standard dosing. For therapeutic indications, consider titrating carefully and consider adjusting dose in response to plasma concentration and ECG monitoring. An alternative medication such as sotalol, disopyramide, quinidine or amiodarone may also be considered.

Dose adjustments are not required when flecainide is utilized for diagnostic uses.

Haloperidol

Possible Decreased Exposure to Haloperidol (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: The patient's genotype may be associated with a decreased haloperidol exposure following standard dosing. Consider an alternative medication or prescribe haloperidol at the standard dose and adjust dosage to achieve a favorable clinical response. Be alert to decreased haloperidol exposure.

Imipramine

Possible Decreased Imipramine Exposure (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

The patient is predicted to be a CYP2D6 normal or ultra-rapid metabolizer, although the result is not definitive. The patient's possible high CYP2D6 activity is likely to result in a significantly increased metabolism of imipramine to less active compounds and a subsequent decrease in imipramine exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If imipramine is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Imipramine

Decreased Imipramine Exposure (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of imipramine to desipramine and a subsequent decrease in imipramine exposure leading to therapy failure or increased side effects.

Psychiatric Conditions: Consider an alternative medication. If imipramine is warranted, consider therapeutic drug monitoring to guide dose adjustments.

Metoprolol

Possible Decreased Exposure to Metoprolol (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: The patient's genotype may be associated with a decreased metoprolol exposure following standard dosing. Consider an alternative beta-blocker such as bisoprolol or carvedilol. If use of metoprolol is warranted, use the maximum dose for the prescribed indication. If response is still not adequate, increase the dose to 250% of the standard dose.

Nortriptyline

Possible Decreased Nortriptyline Exposure (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

The patient is predicted to be a CYP2D6 normal or ultra-rapid metabolizer, although the result is not definitive. The patient's possible high CYP2D6 activity is likely to result in a significantly increased metabolism of nortriptyline to less active compounds and a subsequent decrease in nortriptyline exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If nortriptyline is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Ondansetron

Possible Non-Response to Ondansetron (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: a substantially decreased antiemetic effect has been reported in these patients when taking standard doses of this medication. Consider prescribing an alternative drug not metabolized by CYP2D6 such as granisetron.

Paroxetine

Possible Reduced Response to Paroxetine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: there is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. Consider an alternative medication.

Risperidone

Reduced Exposure to Risperidone (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: The patient's genotype may be associated with a decreased risperidone exposure and increased active metabolite (paliperidone) exposure following standard dosing. Consider an alternative medication.

Tramadol

Possible Increased Exposure to Tramadol (CYP2D6: Ultra-Rapid or Normal Metabolizer) ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: The patient's genotype may be associated with an increased conversion of tramadol to an active metabolite with higher activity. If an alternative is not available, consider reducing the dose by 60% and monitor for opioid side effects (such as drowsiness, confusion, constipation, nausea and vomiting, respiratory depression or urine retention). Alternatively, try an analgesic not as dependent on CYP2D6 metabolism (fentanyl, morphine, hydromorphone, oxymorphone or tapentadol) or try a non-opioid analgesic such as a NSAID or a COX-2 inhibitor.

Warning: Breastfeeding is not recommended when taking tramadol due to the risk of serious adverse reactions in breastfed infants.

Trimipramine

Possible Decreased Trimipramine Exposure (CYP2D6: Ultra-Rapid or Normal Metabolizer) INFORMATIVE

The patient is predicted to be a CYP2D6 normal or ultra-rapid metabolizer, although the result is not definitive. The patient's possible high CYP2D6 activity is likely to result in a significantly increased metabolism of trimipramine to less active compounds and a subsequent decrease in trimipramine exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If trimipramine is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Trimipramine

Decreased Trimipramine Exposure (CYP2C19: Ultra-Rapid Metabolizer) INFORMATIVE

The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of trimipramine to desmethyl trimipramine and a subsequent decrease in trimipramine exposure leading to therapy failure or increased side effects.

Psychiatric Conditions: Consider an alternative medication. If trimipramine is warranted, consider therapeutic drug monitoring to guide dose adjustments.

Venlafaxine

Possible Decreased Exposure to Venlafaxine (CYP2D6: Ultra-Rapid or Normal Metabolizer) ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: the patient is unlikely to achieve adequate serum levels of venlafaxine and O-desmethylvenlafaxine when taking standard doses of venlafaxine. Consider an alternative medication or consider increasing the venlafaxine dose to a maximum of 150% of the normal dose and adjust the dose based on clinical response and therapeutic monitoring.

If therapeutic drug monitoring is utilized, the sum of venlafaxine and O-desmethylvenlafaxine (an active metabolite) plasma concentrations should be used for efficacy. While the sum of the parent and the active metabolite are informative for efficacy, a higher parent (venlafaxine) concentration may be associated with higher side effects, including QT prolongation.

Voriconazole

Non-Response to Voriconazole (CYP2C19: Ultra-Rapid Metabolizer) ACTIONABLE

Voriconazole plasma concentrations are expected to be low if a standard dose is used, increasing the risk of loss of response and effectiveness and subsequent disease progression. Consider an alternative medication that is not dependent on CYP2C19 metabolism, such as isavuconazole, liposomal amphotericin B or posaconazole.

Zuclopenthixol

Possible Decreased Exposure to Zuclopenthixol (CYP2D6: Ultra-Rapid or Normal Metabolizer) INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: The patient's genotype may be associated with a decreased zuclopenthixol exposure following standard dosing. This patient may be at risk of therapy failure when taking zuclopenthixol at standard dosage. Consider using this drug with close monitoring of plasma concentrations and titrate dose in response to the clinical effect or consider an alternative medication. Examples of alternative medications include flupenthixol, clozapine, olanzapine or quetiapine.

Amoxapine

Possible Decreased Amoxapine Exposure (CYP2D6: Ultra-Rapid or Normal Metabolizer) INFORMATIVE

Like other tricyclic and tetracyclic antidepressants, amoxapine is metabolized by CYP2D6. However, the overall contribution of this enzyme in the metabolism of this drug is not well documented. Based on the genotype result, this patient may be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: patients with increased CYP2D6 function may metabolize amoxapine more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations. There are no established dosing adjustments for patients with increased CYP2D6 function; therapy must be initiated cautiously and adjusted according to the patient's response.

Atomoxetine

Possible Atomoxetine Underexposure Leading to Decreased Response (CYP2D6: Ultra-Rapid or Normal Metabolizer) ACTIONABLE

The genotype result indicates that the patient is likely to have an insufficient response due to inadequate drug exposure following standard dosing. Consider the following dosing strategy:

- Initiate treatment at 40 mg/day, increase to 80 mg/day after 3 days and maintain dose.
- If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider a dose increase to 100 mg/day.
- If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider therapeutic drug monitoring 1-2 hours post dose. If the plasma concentration is less than 200 ng/ml consider a dose increase to a target of 400 ng/ml. Doses greater than 100 mg/day may be needed to achieve a targeted therapeutic concentration. (Therapeutic range: 200-1000 ng/ml).

Benzhydrocodone

Possible Altered Response to Benzhydrocodone (CYP2D6: Ultra-Rapid or Normal Metabolizer) INFORMATIVE

Benzhydrocodone is a prodrug of hydrocodone and is converted to active hydrocodone by intestinal enzymes. Increased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 ultrarapid metabolizers. Based on the genotype result, this patient MAY be a CYP2D6 ultrarapid metabolizer. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Bupropion

Altered Bupropion Exposure (CYP2B6: Intermediate Metabolizer) INFORMATIVE

The genotype result indicates that the patient is likely to have increased bupropion exposure, but decreased exposure to the active metabolite (hydroxybupropion). This metabolite contributes to the therapeutic effects of bupropion when used as a smoking cessation agent or as an antidepressant. This decrease in exposure of hydroxybupropion may result in decreased therapeutic efficacy.

Smoking Cessation: There is insufficient data to allow calculation of dose adjustment. Consider standard prescribing and closer monitoring.

Major Depressive Disorder and Prevention of Seasonal Affective Disorder: There is insufficient data to allow calculation of dose adjustment. Therapeutic monitoring of bupropion-hydroxybupropion levels may be considered to guide dosing adjustments.

Carisoprodol

Altered Sensitivity to Carisoprodol (CYP2C19: Ultra-Rapid Metabolizer) INFORMATIVE

There is insufficient data to allow calculation of dose adjustment. If carisoprodol is prescribed, it is recommended to use a lower dose, and to carefully monitor the patient for side effects.

Chlorpromazine

Possible Non-Response to Chlorpromazine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Chlorpromazine is metabolized by CYP2D6, CYP3A4 and flavin-containing monooxygenases. Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: subjects with increased CYP2D6 function will metabolize chlorpromazine more rapidly which can result in sub-therapeutic drug concentrations. Consider a standard dose and adjust dosage according to the patient's tolerability and response. Higher doses may be necessary to achieve efficacy.

Clopidogrel

Increased Response to Clopidogrel (CYP2C19: Ultra-Rapid Metabolizer) — ACTIONABLE

Clopidogrel can be prescribed at standard label-recommended dosage. Individuals with the *17 allele may have an increased risk of bleeding while taking clopidogrel.

Clozapine

Non-Response to Clozapine (CYP1A2: Normal Metabolizer - Higher Inducibility) — INFORMATIVE

Smokers have a high risk for non-response at standard doses and may require higher doses. There is an association between high clozapine doses and the risk of seizures, and therefore careful monitoring is recommended during dosing adjustment. Smoking cessation will increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.

Dexlansoprazole

Decreased Exposure to Dexlansoprazole (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

The patient's genotype is associated with a decreased dexlansoprazole exposure following standard dosing. Be alert for insufficient response, consider increasing the recommended dose by 100% and monitor for efficacy.

Dexmethylphenidate

Decreased Response to Dexmethylphenidate (COMT: Intermediate COMT Activity) — INFORMATIVE

The patient's genotype result predicts a less optimal response to dexmethylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

Diazepam

Possible Altered Sensitivity to Diazepam (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

CYP2C19 rapid and ultra-rapid metabolizers metabolize diazepam and nordiazepam more rapidly than normal metabolizers. However, there is insufficient data to allow calculation of dose adjustment when diazepam is prescribed. Monitor the patient's response and adjust the dose accordingly.

Dihydrocodeine

Possible Altered Response to Dihydrocodeine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: Increased conversion of dihydrocodeine to the more active metabolite dihydromorphine is expected in CYP2D6 ultra-rapid metabolizers. This may result in an exaggerated response. Adequate pain relief can be achieved by decreasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if signs of overdose (excessive sleepiness, confusion, or shallow breathing) are reported.

Dolasetron

Possible Altered Response to Dolasetron (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

The reduction of dolasetron to its active metabolite hydrodolasetron is mediated by a carbonyl reductase. Hydrodolasetron is further eliminated by multiple routes, including renal excretion and by glucuronidation or hydroxylation by CYP2D6. Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower hydroxydolasetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Dolasetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Donepezil

Possible Altered Exposure to Donepezil (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: when compared to a normal metabolizer, a ultra-rapid metabolizers has a 24% increase in donepezil clearance. The clinical significance of this increase is not well documented. Consider using a standard dosing regimen and adjust dosage in response to clinical response and tolerability.

Efavirenz

Increased Efavirenz Exposure (CYP2B6: Intermediate Metabolizer) — ACTIONABLE

The genotype result indicates that the patient is likely to have higher dose-adjusted trough concentrations of efavirenz following standard dosing. This may result in increased risk of CNS adverse events. Consider initiating efavirenz with a decreased dose of 400 mg/day. If therapeutic drug monitoring is available and a decreased efavirenz dose is prescribed, consider obtaining steady-state plasma efavirenz concentrations to ensure concentrations are in the suggested therapeutic range (~1 to 4 µg/mL).

Fluvoxamine

Possible Reduced Response to Fluvoxamine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: there is insufficient data documenting fluvoxamine exposure for this phenotype. If a standard dose is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug may occur. An alternative medication not metabolized by CYP2D6 may also be considered.

Fosnetupitant / Palonosetron

Possible Altered Response to Fosnetupitant-Palonosetron (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Fosnetupitant: Fosnetupitant is converted to netupitant via metabolic hydrolysis. Netupitant is extensively metabolized to three major metabolites (desmethyl, N-oxide and a hydroxy-methyl derivatives). Metabolism is mediated primarily by CYP3A4 and to a lesser extent by CYP2C9 and CYP2D6. No genetically guided drug selection or dosing recommendations are available for this drug. Fosnetupitant can be prescribed at standard label-recommended dosage and administration.
Palonosetron: Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Hydrocodone

Possible Altered Response to Hydrocodone (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer. Increased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 ultra-rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower hydrocodone doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Lansoprazole

Decreased Exposure to Lansoprazole (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

The patient's genotype is associated with a decreased lansoprazole exposure following standard dosing. Be alert for insufficient response, consider increasing the recommended dose by 100% and monitor for efficacy.

Lorazepam

Possible Altered Response to Lorazepam (UGT2B15: Intermediate Metabolizer) — INFORMATIVE

Lorazepam clearance may be reduced in this patient. However, there is insufficient evidence whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

Maprotiline

INFORMATIVE

Possible Decreased Maprotiline Exposure (CYP2D6: Ultra-Rapid or Normal Metabolizer)

Like other tricyclic and tetracyclic antidepressants, maprotiline is metabolized by CYP2D6 as well as CYP1A2. Patients with increased CYP2D6 function may metabolize maprotiline more rapidly which can result in sub-therapeutic drug concentrations; these patients may require higher doses to achieve adequate plasma concentrations. There are no established dosing adjustments for patients with increased CYP2D6 function. Seizures have been associated with the use of maprotiline especially at high doses. Therefore, therapy must be initiated at a standard dose and gradually increased in small increments according to the patient's response.

⚠ Methadone

Increased Methadone Exposure (CYP2B6: Intermediate Metabolizer) INFORMATIVE

The patient's genotype may be associated with an increased methadone exposure following standard dosing.

For Addiction Treatment: There is limited evidence indicating that intermediate metabolizers require lower doses, therefore, a dose adjustment cannot be calculated.

For Pain Management: There are no studies documenting the effect of CYP2B6 genetic variations on methadone exposure when this drug is used as an analgesic. Consider standard prescribing and monitoring practices.

⚠ Methotrexate

Increased Risk for Methotrexate Toxicity (MTHFR: Reduced MTHFR Activity) INFORMATIVE

The patient carries two copies of the MTHFR c.665C>T variant, resulting in a significantly reduced MTHFR activity. **Malignancy:** Leukemia or lymphoma patients who are treated with methotrexate standard regimens may have an increased risk of overall toxicity (including mucositis, thrombocytopenia, and hepatic toxicity), and an increased severity of mucositis. Monitor the patient closely for increased side effects and adjust the dose accordingly. Other genetic and clinical factors may also influence the patient's risk for toxicity and response to methotrexate treatment. **Nonmalignant conditions:** a limited number of studies found an association between individuals carrying the MTHFR c.665C>T variant and methotrexate-induced toxicity in rheumatoid arthritis patients. However, there is insufficient data to calculate dose adjustment. Monitor patient closely for increased side effects and adjust the dose accordingly. Other genetic and clinical factors may also influence the patient's risk for toxicity and response to methotrexate treatment.

⚠ Methylphenidate

Decreased Response to Methylphenidate (COMT: Intermediate COMT Activity) INFORMATIVE

The patient's genotype result predicts a less optimal response to methylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

⚠ Mexiletine

Altered Response to Mexiletine (CYP2D6: Ultra-Rapid or Normal Metabolizer) INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: because mexiletine plasma concentrations may be decreased, consider adjusting dose in response to mexiletine plasma concentration and ECG monitoring, until a favorable response in achieved.

⚠ Naltrexone

Altered Response to Naltrexone (OPRM1: Normal OPRM1 Function) INFORMATIVE

Treatment of alcohol dependence: the patient has the OPRM1 118AA wild-type genotype that is associated with a poorer outcome with naltrexone therapy. Naltrexone-treated patients not carrying the OPRM1 118A>G G allele are less likely to respond to this drug, and may have higher relapse rates than those who are carriers of this allele. This association has not been reported consistently across studies.

⚠ Netupitant / Palonosetron

Possible Altered Response to Netupitant-Palonosetron (CYP2D6: Ultra-Rapid or Normal Metabolizer) INFORMATIVE

Netupitant: Netupitant is extensively metabolized to three major metabolites (desmethyl, N-oxide and a hydroxy-methyl derivatives). Metabolism is mediated primarily by CYP3A4 and to a lesser extent by CYP2C9 and CYP2D6. No genetically guided drug selection or dosing recommendations are available for this drug. Netupitant can be prescribed at standard label-recommended dosage and administration.
Palonosetron: Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Olanzapine

Non-Response to Olanzapine (CYP1A2: Normal Metabolizer - Higher Inducibility) INFORMATIVE

There is little evidence regarding the impact of CYP1A2 genetic variants on olanzapine response. Smokers may be at risk for non-response at standard doses. Careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Omeprazole

Decreased Exposure to Omeprazole (CYP2C19: Ultra-Rapid Metabolizer) INFORMATIVE

The patient's genotype is associated with a decreased omeprazole exposure following standard dosing. Be alert for insufficient response, consider increasing the recommended dose by 100% and monitor for efficacy.

Oxazepam

Possible Altered Response to Oxazepam (UGT2B15: Intermediate Metabolizer) INFORMATIVE

Oxazepam clearance may be reduced in this patient. However, there is insufficient evidence whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

Oxycodone

Possible Altered Response to Oxycodone (CYP2D6: Ultra-Rapid or Normal Metabolizer) ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer. Increased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 ultra-rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower oxycodone doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Palonosetron

Possible Altered Response to Palonosetron (CYP2D6: Ultra-Rapid or Normal Metabolizer) INFORMATIVE

Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Pantoprazole

Decreased Exposure to Pantoprazole (CYP2C19: Ultra-Rapid Metabolizer) INFORMATIVE

The patient's genotype is associated with a decreased pantoprazole exposure following standard dosing. Be alert for insufficient response, consider increasing the recommended dose by 100% and monitor for efficacy.

Perphenazine

Possible Non-Response to Perphenazine (CYP2D6: Ultra-Rapid or Normal Metabolizer) INFORMATIVE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: subjects with increased CYP2D6 function will metabolize perphenazine more rapidly, which can result in sub-therapeutic drug concentrations. Consider a dose increase with close monitoring until a favorable response is achieved.

Propafenone

Possible Decreased Exposure to Propafenone (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. The following recommendations apply for CYP2D6 ultra-rapid metabolizers: The patient's genotype may be associated with a decreased propafenone exposure following standard dosing. There is insufficient data to allow calculation of dose adjustment. Titrate carefully and adjust the dose in response to plasma concentration and ECG monitoring. An alternative medication such as sotalol, disopyramide, quinidine or amiodarone may also be considered.

Dose adjustments with co-medications: concurrent use of propafenone along with CYP3A4 inhibitors and CYP2D6 inhibitors may significantly increase the plasma concentration of propafenone increasing the risk of proarrhythmia and other adverse events. Therefore, avoid simultaneous use of propafenone with both a CYP2D6 inhibitor and a CYP3A4 inhibitor.

Protriptyline

Possible Decreased Protriptyline Exposure (CYP2D6: Ultra-Rapid or Normal Metabolizer) — INFORMATIVE

Like other tricyclic and tetracyclic antidepressants, protriptyline is metabolized by CYP2D6. Based on the genotype result, this patient MAY be a CYP2D6 ultra-rapid metabolizer, although the result is not definitive. There are no established dosing adjustments for patients with abnormal CYP2D6 function. Therefore, therapy must be initiated at a low dosage and gradually adjusted according to the patient's response. The lowest effective dosage should always be considered during maintenance therapy.

Sertraline

Possible Reduced Response to Sertraline (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

Sertraline can be prescribed at standard label-recommended dosage and administration. If patient does not respond to recommended maintenance dosing, consider an alternative medication.

Sulfasalazine

Decreased Response to Sulfasalazine For the Treatment of Rheumatoid Arthritis (ABCG2: Normal Function) — INFORMATIVE

Rheumatoid Arthritis: The patient carries two copies of ABCG2 rs2231142 C allele. Preliminary data suggests that this genotype may be associated with decreased plasma levels of sulfasalazine which may decrease the likelihood of response to this drug.

Tetrabenazine

Unknown Sensitivity to Tetrabenazine (CYP2D6: Ultra-Rapid or Normal Metabolizer) — ACTIONABLE

For treating chorea associated with Huntington's disease: Individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. **The maximum daily dose in CYP2D6 ultra-rapid metabolizers is not defined. The maximum daily dose in normal metabolizers is 100 mg with a maximum single dose of 37.5 mg**. If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.

Tizanidine

Possible Non-Response to Tizanidine (CYP1A2: Normal Metabolizer - Higher Inducibility) — INFORMATIVE

There is little evidence regarding the impact of CYP1A2 genetic variants on tizanidine response. Smokers may be at risk for non-response and may require higher doses. There is an association between high tizanidine plasma concentrations and the risk of hypotension and excessive sedation. Therefore, careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to excessive hypotension and sedation. Careful monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

Warfarin

Dosing Adjustments are Expected (CYP2C9 *1/*1; VKORC1 -1639G>A G/A; CYP4F2 c.1297G>A A/G) — ACTIONABLE

When initiating warfarin treatment for indications with a target INR of 2-3, consider one of the following methods to estimate dosing requirements:

FDA Label: CYP2C9 and VKORC1 genotype results indicate an expected therapeutic dose of 5-7 mg/day.

Pharmacogenomics algorithms/calculators available at www.warfarindosing.org:

Caucasians and Asians: Use the patient's demographics and other clinical factors along with CYP2C9 and VKORC1 genotypes to calculate the expected therapeutic dose. Consider an additional 5-10% increase to the calculated dose.

Africans and African Americans: Use the patient's demographics and other clinical factors along with CYP2C9 and VKORC1 genotypes to calculate the expected therapeutic dose.

The provided recommendations in Africans and African Americans apply only when all the following CYP2C9 alleles are tested: *5, *6, *8, *11.

Test Details

Gene	Genotype	Phenotype	Clinical Consequences
ABCG2	421C>A C/C	**Normal Function**	Consistent with a normal ABCG2 transporter function. The patient's risk for statin-induced adverse events is normal.
ADRA2A	C-1291G G/G	**Homozygous for G Allele**	Carriers of the G allele of ADRA2A C-1291G variant, show greater reduction of inattentive symptoms when administered Methylphenidate or Dexmethylphenidate.
ANKK1/DRD2	DRD2:Taq1A C/C	**Unaltered DRD2 function**	Consistent with a normal dopamine receptor D2 function.
BDNF	434C>T C/T	**Heterozygous for rs6265 T allele**	Consistent with reduced activity-dependent secretion of BDNF from neurons and impaired BDNF signaling.
COMT	Val158Met A/G	**Intermediate COMT Activity**	Consistent with a reduced catechol O-methyltransferase (COMT) function.
CYP1A2	*1A/*1F	**Normal Metabolizer - Higher Inducibility**	Consistent with a typical CYP1A2 activity in absence of inducing substances. Rapid Metabolism occurs in presence of inducers such as barbiturates, cruciferous vegetables, carbamazepine, rifampin and smoking.
CYP2B6	*1/*6	**Intermediate Metabolizer**	Consistent with a moderate deficiency in CYP2B6 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP2C19	*17/*17	**Ultra-Rapid Metabolizer**	Consistent with a significant increase in CYP2C19 enzyme activity. Exercise caution if CYP2C19 drug substrates are prescribed.
CYP2C9	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP2C9 enzyme activity.
CYP2D6	*1/*10 XN	**Ultra-Rapid or Normal Metabolizer**	Consistent with a typical or significant increase in CYP2D6 enzyme activity. Exercise caution if CYP2D6 drug substrates are prescribed.
CYP3A4	*1/*1	**Normal Metabolizer**	Consistent with a typical CYP3A4 activity. Caution is advised when prescribing narrow therapeutic index drugs. Alternative drugs or dose adjustment may be required if CYP3A inhibitors or inducers are co-prescribed.
CYP3A5	*3/*3	**Poor Metabolizer**	Consistent with an absence of CYP3A5 enzyme expression (Non-Expresser). This phenotype is the most common in the general population.
CYP4F2	c.1297G>A A/G	**Reduced Activity**	Consistent with a deficiency in CYP4F2 protein expression, resulting in reduced vitamin K metabolism.
F2 **F5**	rs1799963 GG rs6025 CC	**Normal Risk of Thrombosis**	Unless other genetic or circumstantial risk factors are present, the patient is not expected to have an increased risk for thrombosis.
MC4R	g.60215554C>A C/A	**Heterozygous for A allele (rs489693)**	Altered MC4R function
MTHFR	c.665C>T AA	**Reduced MTHFR Activity**	The patient carries two copies of the MTHFR c.665C>T variant (homozygous). MTHFR enzyme activity is severely reduced (30% of normal activity) and the risk of hyperhomocysteinemia is severely increased.
MTHFR	c.1286A>C TT c.665C>T AA	**Increased Risk of Hyperhomocysteinemia**	The patient has a significantly reduced MTHFR function, leading to mild to moderate hyperhomocysteinemia. This appears to be associated with an increased risk for venous thromboembolism.
OPRM1	A118G A/A	**Normal OPRM1 Function**	Consistent with a normal OPRM1 receptor signaling efficiency induced by exogenous opioids. This is associated with a good analgesia following standard opioid doses and a poor response to naltrexone.
SLCO1B1	521T>C T/T	**Normal Function**	Consistent with a typical SLCO1B1 transporter function.
UGT2B15	*1/*2	**Intermediate Metabolizer**	Consistent with a moderately decreased UGT2B15 glucuronidation function. Potential risk for side effects with drug substrates.
VKORC1	-1639G>A G/A	**Intermediate Warfarin Sensitivity**	Consistent with a moderately decreased VKORC1 expression. Exercise caution with coumarin anticoagulants.

Alleles Tested: **ABCG2** 421C>A; **ADRA2A** C-1291G; **ANKK1/DRD2** DRD2:Taq1A; **BDNF** 434C>T; **COMT** Val158Met; **CYP1A2** *1F, *1K; **CYP2B6** *6, *9, *11, *16, *18; **CYP2C19** *2, *3, *4A, *4B, *6, *7, *8, *9, *10, *17; **CYP2C9** *2, *3, *4, *5, *8, *11, *27; **CYP2D6** *2, *4, *4M, *7, *8, *10, *12, *14, *17, *29, *35, *41, *114, *5 (gene deletion), XN (gene duplication); **CYP3A4** *3, *12, *17, *22; **CYP3A5** *3, *6; **CYP4F2** c.1297G>A; **Factor II** rs1799963; **Factor V Leiden** rs6025; **MC4R** g.60215554C>A; **MTHFR** c.1286A>C, c.665C>T; **OPRM1** A118G; **SLCO1B1** 521T>C; **UGT2B15** *2; **VKORC1** -1639G>A

Limitation: This test will not detect all the known alleles that result in altered or inactive tested genes. This test does not account for all individual variations in the individual tested. Absence of a detectable gene mutation does not rule out the possibility that a patient has different phenotypes due to the presence of an undetected polymorphism or due to other factors such as drug-drug interactions, comorbidities and lifestyle habits.

Methodology: Array based assays detect listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%.

Lab Disclaimer: DNAlysis Biotechnology developed the Genotype test. The performance characteristics of this test were determined by DNAlysis Biotechnology. It has not been cleared or approved by the U.S. Food and Drug Administration.

Translational Software Disclaimer: The information presented on this report is provided as general educational health information. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of the medications prescribed.

The pharmacogenetic assay involves use of reporting software and genotype-phenotype associations performed by Translational Software (www.translationalsoftware.com). The software has not been evaluated by the Food and Drug Administration. The software, and the report generated by the software, is not intended to diagnose, treat, cure, or prevent any disease. A qualified designee within the lab uses Translational Software to generate and subsequently review the report. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

Approved By: Laboratory Manager
Thenusha Naidoo
MS 0000990

Patient Information Card

This is a summary genetic report for your patient to share with other healthcare providers. The card can be cut out along the dashed line and carried with the patient.

REPORT DETAILS

Pharmacogenetic Test Summary

ABCG2	421C>A C/C	Normal Function
ADRA2A	C-1291G G/G	Homozygous for G Allele
ANKK1/DRD2	DRD2:Taq1A C/C	Unaltered DRD2 function
BDNF	434C>T C/T	Heterozygous for rs6265 T allele
COMT	Val158Met A/G	Intermediate COMT Activity
CYP1A2	*1A/*1F	Normal Metabolizer - Higher Inducibility
CYP2B6	*1/*6	Intermediate Metabolizer
CYP2C19	*17/*17	Ultra-Rapid Metabolizer
CYP2C9	*1/*1	Normal Metabolizer
CYP2D6	*1/*10 XN	Ultra-Rapid or Normal Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*3/*3	Poor Metabolizer
CYP4F2	c.1297G>A A/G	Reduced Activity
Factor II	rs1799963 GG	Normal Thrombosis Risk
Factor V Leiden	rs6025 CC	Normal Thrombosis Risk
MC4R	g.60215554C>A C/A	Heterozygous for A allele (rs489693)
MTHFR	c.1286A>C TT	Normal MTHFR Activity
MTHFR	c.665C>T AA	Reduced MTHFR Activity
OPRM1	A118G A/A	Normal OPRM1 Function
SLCO1B1	521T>C T/T	Normal Function
UGT2B15	*1/*2	Intermediate Metabolizer
VKORC1	-1639G>A G/A	Intermediate Warfarin Sensitivity

For a complete report contact DNAlysis Biotechnology
www.dnalysis.co.za