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PATIENT INFORMATION	SPECIMEN DETAILS	PROVIDER INFORMATION
NAME:	**SPECIMEN TYPE:** Oracollect DX with preservative	
ACC #:	**COLLECTION DATE:**	
DOB:	**RECEIVED DATE:**	
SEX:	**REPORT DATE:**	

Clinical Health Panel

Current Patient Medications

Pristiq

Pristiq | DESVENLAFAXINE
Normal Sensitivity to Desvenlafaxine (CYP2D6: Intermediate Metabolizer)

ACTIONABLE

Desvenlafaxine can be prescribed at standard label-recommended dosage and administration.

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.

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Risk Management

Antipsychotic-Induced Tardive Dyskinesia

Moderate Risk of Antipsychotic-Induced Tardive Dyskinesia

The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).

The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk for tardive dyskinesia when treated with antipsychotics.

Monitor the patient for any signs of tardive dyskinesia.

Antipsychotic-Induced Hyperprolactinemia

Moderate Risk of Antipsychotic-induced Hyperprolactinemia

The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).

The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk of hyperprolactinemia when treated with antipsychotics.

Monitor patient closely for signs of hyperprolactinemia. An evaluation of the risk-benefit profile of the antipsychotic medication may be required.

Antipsychotic-Induced Weight Gain

Moderate Risk of Antipsychotic-Induced Weight Gain

The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).

The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk for weight gain when treated with antipsychotics.

Monitor patient closely for signs of weight gain.

Type III Hyperlipoproteinemia

Not Associated with Type III Hyperlipoproteinemia

The patient is negative for both the APOE c.388 T>C (Cys130Arg) and c.526 C>T (Arg176Cys) mutations. The patient's genotype is wild-type, which is the most common genotype in the general population (frequency: >60%).

A patient with wild-type genotype does not have a defect in the apolipoprotein E (APOE), which is an integral structure of lipoprotein particles that have critical roles in blood lipid metabolism and transport. The APOE ε3/ε3 genotype is not associated with increased risk of cardiovascular disease.

No action is needed when a patient is normolipidemic.

Hyperhomocysteinemia - Depression

No Increased Risk of Hyperhomocysteinemia

The patient carries one copy of the MTHFR c.665C>T variant (heterozygous). MTHFR enzyme activity is reduced (60% 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. The patient's small reduction in MTHFR activity is not a risk factor for hyperhomocysteinemia.

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, testing for homocysteine levels and serum folate levels may be informative for this patient before prescribing methylfolate as an antidepressant-augmenting agent.

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

No Increased Risk of Hyperhomocysteinemia

The patient carries one copy of MTHFR c.665C>T variant (heterozygous). MTHFR enzyme activity is reduced (60% of normal activity).

The patient's small reduction in MTHFR activity is not a risk factor for hyperhomocysteinemia. Unless other risk factors are present, the patient is not expected to have an increased risk for venous thromboembolism (VTE).

The patient's MTHFR activity is slightly reduced.

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Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Anticancer Agents	Antifolates		Methotrexate (Trexall®)	
	Thiopurines	Azathioprine (Azasan®, Imuran®) Mercaptopurine (Purinethol®, Purixan®) Thioguanine (Tabloid®)		
Cardiovascular	Angiotensin II Receptor Antagonists	Azilsartan (Edarbi®, Edarbyclor®) Candesartan (Atacand®) Eprosartan (Teveten®) Irbesartan (Avapro®) Losartan (Cozaar®, Hyzaar®) Olmesartan (Benicar®) Telmisartan (Micardis®) Valsartan (Diovan®, Entresto®)		
	Antianginal Agents	Ranolazine (Ranexa®)		
	Antiarrhythmics	Amiodarone (Nexterone®, Pacerone®) Disopyramide (Norpace®) Quinidine (Quinidine®) Sotalol (Betapace®, Sorine®, Sotylize®)	Flecainide (Tambocor®) Mexiletine (Mexitil®) Propafenone (Rythmol®)	
	Anticoagulants	Apixaban (Eliquis®) Betrixaban (Bevyxxa®) Dabigatran Etexilate (Pradaxa®) Edoxaban (Savaysa®) Fondaparinux (Arixtra®) Rivaroxaban (Xarelto®)	Warfarin (Coumadin®)	
	Antiplatelets	Prasugrel (Effient®) Ticagrelor (Brilinta®) Vorapaxar (Zontivity®)	Clopidogrel (Plavix®)	
	Beta Blockers	Atenolol (Tenormin®) Bisoprolol (Zebeta®) Carvedilol (Coreg®) Labetalol (Normodyne®, Trandate®) Nebivolol (Bystolic®) Propranolol (Inderal®)	Metoprolol (Lopressor®) Timolol (Timoptic®)	
	Diuretics	Torsemide (Demadex®)		
	Statins	Atorvastatin (Lipitor®) Fluvastatin (Lescol®) Lovastatin (Mevacor®, Altoprev®, Advicor®) Pitavastatin (Livalo®) Pravastatin (Pravachol®) Rosuvastatin (Crestor®) Simvastatin (Zocor®)		

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
Diabetes	Meglitinides	Nateglinide (Starlix®) Repaglinide (Prandin®, Prandimet®)		
	Sulfonylureas	Chlorpropamide (Diabinese®) Glimepiride (Amaryl®) Glipizide (Glucotrol®) Glyburide (Micronase®) Tolbutamide (Orinase®)		
Gastrointestinal	Antiemetics	Aprepitant (Emend-oral®) Dolasetron (Anzemet®) Dronabinol (Marinol®) Fosaprepitant (Emend-i.v®) Fosnetupitant / Palonosetron (Akynzeo-i.v®) Granisetron (Sancuso®, Sustol®) Netupitant / Palonosetron (Akynzeo-oral®) Ondansetron (Zofran®, Zuplenz®) Palonosetron (Aloxi®) Rolapitant (Varubi®)	Metoclopramide (Reglan®)	
	Proton Pump Inhibitors	Dexlansoprazole (Dexilant®, Kapidex®) Esomeprazole (Nexium®) Lansoprazole (Prevacid®) Omeprazole (Prilosec®) Pantoprazole (Protonix®) Rabeprazole (Aciphex®)		
Gaucher Disease	Endocrine-Metabolic Agents	Eliglustat (Cerdelga®) Imiglucerase (Cerezyme®) Miglustat (Zavesca®) Taliglucerase alfa (Elelyso®) Velaglucerase alfa (Vpriv®)		
Hematology	Hemostatic Agents	Avatrombopag (Doptelet®) Eltrombopag (Promacta®) Lusutrombopag (Mulpleta®)		
Infections	Antifungals	Amphotericin B (AmBisome®, Abelcet®) Anidulafungin (Eraxis®) Caspofungin (Cancidas®) Fluconazole (Diflucan®) Isavuconazonium (Cresemba®) Itraconazole (Sporanox®) Micafungin (Mycamine®) Posaconazole (Noxafil®)		Voriconazole (Vfend®)
	Anti-HIV Agents	Dolutegravir (Tivicay®, Triumeq®) Doravirine (Pifeltro®) Efavirenz (Sustiva®) Etravirine (Edurant®) Raltegravir (Isentress®, Dutrebis®) Rilpivirine (Intelence®)		
	Antimalarials	Proguanil (Malarone®)		

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Pain	Fibromyalgia Agents	Milnacipran (Savella®)		
	Muscle Relaxants	Cyclobenzaprine (Flexeril®, Amrix®) Metaxalone (Skelaxin®) Methocarbamol (Robaxin®)	Carisoprodol (Soma®) Tizanidine (Zanaflex®)	
	NSAIDs	Celecoxib (Celebrex®) Diclofenac (Voltaren®) Flurbiprofen (Ansaid®) Ibuprofen (Advil®, Motrin®) Indomethacin (Indocin®) Ketoprofen (Orudis®) Ketorolac (Toradol®) Meloxicam (Mobic®) Nabumetone (Relafen®) Naproxen (Aleve®) Piroxicam (Feldene®) Sulindac (Clinoril®)		
	Opioids	Alfentanil (Alfenta®) Buprenorphine (Butrans®, Buprenex®) Dihydrocodeine (Synalgos-DC®) Fentanyl (Actiq®) Hydromorphone (Dilaudid®, Exalgo®) Levorphanol (Levo Dromoran®) Meperidine (Demerol®) Methadone (Dolophine®) Oxymorphone (Opana®, Numorphan®) Sufentanil (Sufenta®) Tapentadol (Nucynta®)	Benzhydrocodone (Apadaz®) Codeine (Codeine; Fioricet® with Codeine) Hydrocodone (Vicodin®) Morphine (MS Contin®) Oxycodone (Percocet®, Oxycontin®) Tramadol (Ultram®)	
	Antiaddictives	Lofexidine (Lucemyra®)	Bupropion (Wellbutrin®, Zyban®, Aplenzin®, Contrave®) Naltrexone (Vivitrol®, Contrave®)	
	Anti-ADHD Agents	Amphetamine (Adderall®, Evekeo®) Clonidine (Kapvay®) Dexmethylphenidate (Focalin®) Dextroamphetamine (Dexedrine®) Guanfacine (Intuniv®) Lisdexamfetamine (Vyvanse®) Methylphenidate (Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®)	Atomoxetine (Strattera®)	

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Psychotropic	**Anticonvulsants**	Brivaracetam (Briviact®) Cannabidiol (Epidiolex®) Carbamazepine (Tegretol®, Carbatrol®, Epitol®) Eslicarbazepine (Aptiom®) Ethosuximide (Zarontin®) Ezogabine (Potiga®) Felbamate (Felbatol®) Fosphenytoin (Cerebyx®) Gabapentin (Neurontin®) Lacosamide (Vimpat®) Lamotrigine (Lamictal®) Levetiracetam (Keppra®) Oxcarbazepine (Trileptal®, Oxtellar XR®) Perampanel (Fycompa®) Phenobarbital (Luminal®) Phenytoin (Dilantin®) Pregabalin (Lyrica®) Primidone (Mysoline®) Rufinamide (Banzel®) Tiagabine (Gabitril®) Topiramate (Topamax®) Valproic Acid (Depakote®, Depakene®) Vigabatrin (Sabril®) Zonisamide (Zonegran®)		
	Antidementia Agents	Donepezil (Aricept®) Galantamine (Razadyne®) Memantine (Namenda®)		
	Antidepressants	Desvenlafaxine (Pristiq®) Duloxetine (Cymbalta®) Fluoxetine (Prozac®, Sarafem®) Fluvoxamine (Luvox®) Levomilnacipran (Fetzima®) Mirtazapine (Remeron®) Nefazodone (Serzone®) Paroxetine (Paxil®, Brisdelle®) Trazodone (Oleptro®) Vilazodone (Viibryd®) Vortioxetine (Trintellix®)	Amoxapine (Amoxapine®) Desipramine (Norpramin®) Maprotiline (Ludiomil®) Nortriptyline (Pamelor®) Protriptyline (Vivactil®) Sertraline (Zoloft®)	Amitriptyline (Elavil®) Citalopram (Celexa®) Clomipramine (Anafranil®) Doxepin (Silenor®) Escitalopram (Lexapro®) Imipramine (Tofranil®) Trimipramine (Surmontil®) Venlafaxine (Effexor®)

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	Antipsychotics	Aripiprazole (Abilify®, Aristada®) Asenapine (Saphris®) Brexpiprazole (Rexulti®) Cariprazine (Vraylar®) Chlorpromazine (Thorazine®) Fluphenazine (Prolixin®) Haloperidol (Haldol®) Loxapine (Loxitane®, Adasuve®) Lurasidone (Latuda®) Paliperidone (Invega®) Pimavanserin (Nuplazid®) Pimozide (Orap®) Quetiapine (Seroquel®) Risperidone (Risperdal®) Thiothixene (Navane®) Trifluoperazine (Stelazine®) Ziprasidone (Geodon®)	Clozapine (Clozaril®) Iloperidone (Fanapt®) Olanzapine (Zyprexa®) Perphenazine (Trilafon®)	Thioridazine (Mellaril®)
	Benzodiazepines	Alprazolam (Xanax®) Clobazam (Onfi®) Clonazepam (Klonopin®)	Diazepam (Valium®) Lorazepam (Ativan®) Oxazepam (Serax®)	
	Other Neurological Agents	Deutetrabenazine (Austedo®) Dextromethorphan / Quinidine (Nuedexta®) Flibanserin (Addyi®) Valbenazine (Ingrezza®)	Tetrabenazine (Xenazine®)	
Rheumatology	Anti-Hyperuricemics and Anti-Gout Agents	Colchicine (Mitigare®) Febuxostat (Uloric®)		
	Immunomodulators	Apremilast (Otezla®) Leflunomide (Arava®) Tofacitinib (Xeljanz®)		
Sjogren's Syndrome	Cholinergic Agonists	Cevimeline (Evoxac®)		
Transplantation	Immunosuppressants		Tacrolimus (Prograf®)	
Urologicals	5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	Dutasteride (Avodart®) Finasteride (Proscar®)		
	Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin (UroXatral®) Doxazosin (Cardura®) Silodosin (Rapaflo®) Tamsulosin (Flomax®) Terazosin (Hytrin®)		
	Antispasmodics for Overactive Bladder	Darifenacin (Enablex®) Fesoterodine (Toviaz®) Mirabegron (Myrbetriq®) Oxybutynin (Ditropan®) Solifenacin (Vesicare®) Tolterodine (Detrol®) Trospium (Sanctura®)		

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CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
	Phosphodiesterase Inhibitors for Erectile Dysfunction	Avanafil (Stendra®) Sildenafil (Viagra®) Tadalafil (Cialis®) Vardenafil (Levitra®)		

Dosing Guidance

Amitriptyline
Elavil®

Decreased Amitriptyline Exposure (CYP2C19: 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
Celexa®

Insufficient Response to Citalopram (CYP2C19: 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
Anafranil®

Decreased Clomipramine Exposure (CYP2C19: 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.

Doxepin
Silenor®

Decreased Doxepin Exposure (CYP2C19: 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.

Escitalopram
Lexapro®

Insufficient Response to Escitalopram (CYP2C19: 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.

Imipramine
Tofranil®

Decreased Imipramine Exposure (CYP2C19: 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.

Thioridazine
Mellaril®

Increased Sensitivity to Thioridazine (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

Reduced cytochrome CYP2D6 activity results in elevated plasma levels of thioridazine, would be expected to augment the prolongation of the QTc interval associated with thioridazine, and may increase the risk of serious, potentially fatal, cardiac arrhythmias, such as Torsades de pointes-type arrhythmias. Such an increased risk may result also from the additive effect of coadministering thioridazine with other agents that prolong the QTc interval. Therefore, thioridazine is contraindicated in patients with reduced levels of CYP2D6 activity.

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Trimipramine
Surmontil®

Decreased Trimipramine Exposure (CYP2C19: 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
Effexor®

Increased Exposure to Venlafaxine (CYP2D6: Intermediate Metabolizer) — **ACTIONABLE**

The patient has a decreased CYP2D6 activity which may result in elevated plasma concentrations of venlafaxine at standard doses. Consider an alternative medication or consider prescribing venlafaxine at a reduced dose and be extra alert for adverse events; adjust the dose based on tolerability 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
Vfend®

Non-Response to Voriconazole (CYP2C19: 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.

Amoxapine
Amoxapine®

Possible Increased Amoxapine Exposure (CYP2D6: Intermediate 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. Decreased CYP2D6 activity may result in higher amoxapine concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased CYP2D6 function; therapy must be initiated cautiously and adjusted according to the patient's response.

Atomoxetine
Strattera®

Possible Atomoxetine Overexposure Leading to Toxicity (CYP2D6: Intermediate Metabolizer) — **ACTIONABLE**

The genotype result indicates that the patient is likely to have an increased risk of adverse events following standard dosing. Consider the following dosing strategy:

- Initiate treatment at 40 mg/day.
- If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider a dose increase to 80 mg/day.
- If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider therapeutic drug monitoring 2-4 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
Apadaz®

Possible Altered Response to Benzhydrocodone (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

Benzhydrocodone is a prodrug of hydrocodone and is converted to active hydrocodone by intestinal enzymes. Decreased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 intermediate metabolizers. However, there is insufficient evidence whether these patients have decreased analgesia when taking benzhydrocodone. Adequate pain relief can be achieved by increasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 may also be considered (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone).

Bupropion
Wellbutrin®, Zyban®, Aplenzin®, Contrave®

Decreased Response to Bupropion for Smoking Cessation (ANKK1: Altered DRD2 function) — **INFORMATIVE**

Smoking Cessation: The patient's genotype result is associated with a positive response to nicotine replacement therapy and a lesser response to bupropion treatment.

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Carisoprodol
Soma®

Altered Sensitivity to Carisoprodol (CYP2C19: 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.

Clopidogrel
Plavix®

Increased Response to Clopidogrel (CYP2C19: 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
Clozaril®

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

Smokers may be at 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 may increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.

Codeine
Codeine; Fioricet® with Codeine

Possible Non-Response to Codeine (CYP2D6: Intermediate Metabolizer) — **ACTIONABLE**

Reduced morphine levels are anticipated, and the patient may or may not experience adequate pain relief with codeine. Codeine can be prescribed at standard label-recommended dosage and administration, with monitoring for symptoms of insufficient pain relief. Other opioids not metabolized by CYP2D6 may also be considered (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone).

Desipramine
Norpramin®

Increased Desipramine Exposure (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of desipramine to less active compounds and a subsequent increase in desipramine exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Diazepam
Valium®

Possible Altered Sensitivity to Diazepam (CYP2C19: 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.

Flecainide
Tambocor®

Increased Exposure to Flecainide (CYP2D6: Intermediate Metabolizer) — **ACTIONABLE**

The patient's genotype may be associated with an increased flecainide exposure following standard dosing. Consider prescribing a lower flecainide dose for therapeutic indications. When compared to a CYP2D6 normal metabolizer, an intermediate metabolizer may require a 25% dose reduction. Careful titration with ECG recording and monitoring of flecainide plasma concentrations are recommended until a favorable clinical response is achieved.

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

Hydrocodone
Vicodin®

Possible Altered Response to Hydrocodone (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

Decreased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 intermediate metabolizers. However, there is insufficient evidence whether these patients have decreased analgesia when taking hydrocodone. Adequate pain relief can be achieved by increasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 may also be considered (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone).

Iloperidone
Fanapt®

Moderate Sensitivity to Iloperidone (CYP2D6: Intermediate Metabolizer) — **ACTIONABLE**

Because iloperidone is associated with QTc prolongation, caution is warranted when prescribing the drug in patients with reduced CYP2D6 activity. Iloperidone must be titrated slowly from a low starting dose to avoid orthostatic hypotension. If patients taking iloperidone experience symptoms that could indicate the occurrence of cardiac arrhythmias (e.g., dizziness, palpitations, or syncope), the prescriber should initiate further evaluation, including cardiac monitoring.

Lorazepam
Ativan®

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
Ludiomil®

Possible Increased Maprotiline Exposure (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

Like other tricyclic and tetracyclic antidepressants, maprotiline is metabolized by CYP2D6 as well as CYP1A2. Decreased CYP2D6 activity results in higher maprotiline concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased 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.

Methotrexate
Trexall®

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

The patient carries one copy of the MTHFR c.665C>T variant resulting in a reduced MTHFR activity. **Malignancy:** Leukemia or lymphoma patients who are treated with methotrexate standard regimens might have an increased likelihood of treatment interruptions due to methotrexate toxicity. 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.

Metoclopramide
Reglan®

Possible Sensitivity to Metoclopramide (CYP2D6: Intermediate Metabolizer) — **INFORMATIVE**

There is no data documenting the changes in plasma concentrations of metoclopramide in CYP2D6 intermediate metabolizers. Metoclopramide can be prescribed at standard label-recommended dosage and administration with careful monitoring for possible increase of side effects.

Metoprolol
Lopressor®

Increased Exposure to Metoprolol (CYP2D6: Intermediate Metabolizer) — **ACTIONABLE**

The patient's genotype may be associated with an increased metoprolol exposure following standard dosing. When compared to a normal metabolizer, an intermediate metabolizer may require a 50% dose reduction. If metoprolol is prescribed, be alert to adverse events (e.g., bradycardia or cold extremities).

Mexiletine
Mexitil®

Increased Sensitivity to Mexiletine (CYP2D6: Intermediate Metabolizer) — **ACTIONABLE**

Consider prescribing a lower mexiletine dose. A slow titration with ECG recording and monitoring of mexiletine plasma concentrations are recommended until a favorable clinical response is achieved.

Morphine
MS Contin®

Altered Response to Morphine (COMT: High/Normal COMT Activity) — **INFORMATIVE**

The patient does not carry the COMT Val158Met variant. The patient may require higher doses of morphine for adequate pain control. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.

Naltrexone
Vivitrol®, Contrave®

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.

Nortriptyline
Pamelor®

Increased Nortriptyline Exposure (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of nortriptyline to less active compounds and a subsequent increase in nortriptyline exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Olanzapine
Zyprexa®

Possible Non-Response to Olanzapine (CYP1A2: Normal Metabolizer- Possible 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.

Oxazepam
Serax®

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
Percocet®, Oxycontin®

Possible Altered Response to Oxycodone (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

Decreased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 intermediate metabolizers. However, there is insufficient evidence whether these patients have decreased analgesia when taking oxycodone. Adequate pain relief can be achieved by increasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 may also be considered (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone).

Perphenazine
Trilafon®

Possible Sensitivity to Perphenazine (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

Patients with a decreased CYP2D6 function will eliminate perphenazine more slowly, which can result in higher drug concentrations and possibly more adverse events (extrapyramidal symptoms). Consider close monitoring and dose reduction to avoid toxicity.

Propafenone
Rythmol®

Increased Exposure to Propafenone (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

The patient's genotype may be associated with an increased 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
Vivactil®

Possible Increased Protriptyline Exposure (CYP2D6: Intermediate Metabolizer) — INFORMATIVE

Like other tricyclic and tetracyclic antidepressants, protriptyline is metabolized by CYP2D6. Decreased CYP2D6 activity results in higher protriptyline concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased 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
Zoloft®

Possible Reduced Response to Sertraline (CYP2C19: 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.

Tacrolimus
Prograf®

Insufficient Response to Tacrolimus (CYP3A5: Intermediate Metabolizer) — ACTIONABLE

The genotype result predicts that the patient expresses the CYP3A5 protein. Therefore, the patient may metabolize tacrolimus more rapidly, resulting in low tacrolimus trough levels. Studies have shown patients with this genotype may be at increased risk for acute transplant rejection while taking a standard dose of tacrolimus. Therefore, increasing starting dose 1.5 to 2 times recommended starting dose with close monitoring is strongly recommended to achieve therapeutic effect. Total starting dose should not exceed 0.3mg/kg/day.

Tetrabenazine
Xenazine®

Normal Sensitivity to Tetrabenazine (CYP2D6: Intermediate 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 intermediate metabolizers of CYP2D6 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.

Timolol
Timoptic®

Possible Sensitivity to Timolol (CYP2D6: Intermediate Metabolizer) — INFORMATIVE

Potentiated systemic beta-blockade (e.g., bradycardia) has been reported during timolol treatment by patients with decreased CYP2D6 activity. Monitor patient for treatment-related adverse effects.

Tizanidine
Zanaflex®

Possible Non-Response to Tizanidine (CYP1A2: Normal Metabolizer- Possible 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.

Tramadol
Ultram®

Possible decreased exposure to Tramadol (CYP2D6: Intermediate Metabolizer) — ACTIONABLE

The patient's genotype may be associated with a reduced conversion of tramadol to an active metabolite with higher activity. Consider monitoring for reduced effectiveness and titrate the dose if analgesia is not achieved. If titration fails, choose an alternative 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.

Warfarin
Coumadin®

Dosing Adjustments are Expected (CYP2C9 *1/*1; VKORC1 -1639G>A A/A; CYP4F2 1347G>A G/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 3-4 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.

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.

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PATIENT INFORMATION

NAME:
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DOB:
SEX:

Test Details

Gene	Genotype	Phenotype	Clinical Consequences
ANKK1/DRD2	DRD2:Taq1A A/G	Altered DRD2 function	Consistent with a reduced dopamine receptor D2 function.
Apolipoprotein E	ε3/ε3	Normal APOE function	Not associated with type III hyperlipoproteinemia - No increased risk of cardiovascular disease
COMT	Val158Met G/G	High/Normal COMT Activity	Consistent with a normal catechol O-methyltransferase (COMT) function.
CYP1A2	*1F/*1V	Normal Metabolizer- Possible Inducibility	Consistent with a typical CYP1A2 activity in absence of inducing substances. Rapid metabolism may occur in presence of inducers such as barbiturates, cruciferous vegetables, carbamazepine, rifampin and smoking.
CYP2B6	*1/*1	Normal Metabolizer	Consistent with a typical CYP2B6 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2C19	*1/*17	Rapid Metabolizer	Consistent with a significant increase in CYP2C19 activity. Potential risk for side effects or loss of efficacy with drug substrates.
CYP2C9	*1/*1	Normal Metabolizer	Consistent with a typical CYP2C9 activity. This test did not identify risks for side effects or loss of efficacy with drug substrates.
CYP2D6	*3/*41	Intermediate Metabolizer	Consistent with moderate to substantial deficiency in CYP2D6 activity. Increased risk for side effects or loss of efficacy with drug substrates.
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	*1/*3	Intermediate Metabolizer	Consistent with an intermediate CYP3A5 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.
CYP4F2	1347G>A G/G	Homozygous for the G allele (rs2108622)	Normal CYP4F2 protein levels resulting in normal 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.
HTR2A	-1438G>A C/T	Heterozygous for the T Allele (rs6311)	The patient carries one copy of the variant allele at rs6311 which may be associated with greater serotonin 2A receptor gene expression.
HTR2A	rs7997012 A/G	Heterozygous for the A allele (rs7997012)	Reduced response to citalopram and escitalopram
MTHFR	c.665C>T GA	Reduced MTHFR Activity	The patient carries one MTHFR C677T mutation (heterozygous) and the patient's MTHFR activity is reduced slightly. This is not associated with an increased risk of hyperhomocysteinemia.
MTHFR	c.1286A>C TT c.665C>T GA	No Increased Risk of Hyperhomocysteinemia	The patient MTHFR function is reduced slightly. This is not associated with an increased risk for venous thromboembolism.
NUDT15	*1/*1	Normal Metabolizer	Consistent with a typical NUDT15 activity and a typical risk of side effects with conventional doses of thiopurines.
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. The patient's risk for statin-induced myopathy is not increased.
TPMT	*1/*1	Normal Metabolizer	Consistent with a typical TPMT activity and a typical risk of side effects with conventional doses of thiopurines.
UGT2B15	*1/*2	Intermediate Metabolizer	Consistent with a moderately decreased UGT2B15 glucuronidation function. Potential risk for side effects with drug substrates.

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VKORC1	-1639G>A A/A	**High Warfarin Sensitivity**	VKORC1 is the site of action of warfarin. The patient may require a substantial decrease in warfarin dose.

Alleles Tested: ANKK1/DRD2 DRD2:Taq1A; **Apolipoprotein E** ε2, ε4, (ε3 is reference); **COMT** Val158Met; **CYP1A2** *1C, *1D, *1F, *1K, *1L, *1V, *1W; **CYP2B6** *6, *9; **CYP2C19** *2, *3, *4, *4B, *5, *6, *7, *8, *9, *17; **CYP2C9** *2, *3, *4, *5, *6, *8, *11; **CYP2D6** *2, *3, *4, *4M, *6, *7, *8, *9, *10, *12, *14A, *14B, *17, *29, *35, *41, *5 (gene deletion), XN (gene duplication); **CYP3A4** *22; **CYP3A5** *3, *3C, *6, *7; **CYP4F2** 1347G>A; **Factor II** rs1799963; **Factor V Leiden** rs6025; **HTR2A** -1438G>A, rs7997012; **MTHFR** c.1286A>C, c.665C>T; **NUDT15** *2, *3, *5; **OPRM1** A118G; **SLCO1B1** 521T>C; **TPMT** *2, *3A, *3B, *3C, *4; **UGT2B15** *2; **VKORC1** -1639G>A

Disclaimer: Resolve Molecular Diagnostics developed the genotyping-based test. The performance characteristics of this test were determined by Resolve Molecular Diagnostics. It has not been cleared or approved by the U.S. Food and Drug Administration (FDA).

Resolve Molecular Diagnostics performed the genotyping-based test per the request of Advanced Biomedical.

Only a qualified healthcare professional should advise a patient on how to interpret the results and information found in this report. Resolve Molecular Diagnostics will not make any recommendations based on the results of the test performed, therefore, please seek advice from your healthcare provider.

Methodology: All single nucleic polymorphism (SNP) genotyping was performed using Applied BiosystemsTM TaqMan® chemistry on the QuantStudioTM 12K Flex Real-Time PCR System from ThermoFisher Scientific. Array based assays detects listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%.

Limitations: 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.

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.

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PATIENT INFORMATION

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SEX:

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.

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REPORT DETAILS

Patient:
DOB:
ACC #:

Pharmacogenetic Test Summary

CYP2C19	*1/*17	Rapid Metabolizer
CYP2C9	*1/*1	Normal Metabolizer
CYP2D6	*3/*41	Intermediate Metabolizer
CYP3A4	*1/*1	Normal Metabolizer
CYP3A5	*1/*3	Intermediate Metabolizer

MTHFR	c.665C>T GA	Reduced MTHFR Activity
MTHFR	c.1286A>C TT c.665C>T GA	No Increased Risk of Hyperhomocysteinemia
VKORC1	-1639G>A A/A	High Warfarin Sensitivity

For a complete report contact Resolve Molecular Diagnostics

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