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Alpha Genomix Comprehensive Extended Created for: Johnny Doe

Patient:	Johnny Doe	DOB:	7/18/1969
Accession #:	41001501237465	Gender:	Male
Collection Date:	9/28/2015	Received Date:	9/29/2015
Ordered By:	Dr. El Shawa	Report Generated:	10/1/2015

Current Patient Medications

Current Medication List: Celexa, Oxycodone, Haldol, Lipitor, Soma

Medications Affected by Patient Genetic Results

Lipitor (Atorvastatin)

Increased Myopathy Risk (SLCO1B1 521T>C CC Low Transporter Function) Evidence Level: **Informative**

The reduced SLCO1B1 function may result in elevated atorvastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high atorvastatin doses in this patient should be avoided. If atorvastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Soma (Carisoprodol)

Moderate Sensitivity to Carisoprodol (CYP2C19 *2/*17 Intermediate Metabolizer) Evidence Level: **Informative**

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

Celexa (Citalopram)

Delayed Response to Citalopram (SLC6A4 S/La Decreased Serotonin Transporter Expression) Evidence Level: **Informative**

The genotype predicts a decreased serotonin transporter levels. A longer titration period may be required to achieve maximal antidepressant response. The patient may respond to citalopram more slowly (up to 12 weeks).

Haldol (Haloperidol)

Increased Sensitivity to Haloperidol (CYP2D6 *4/*5 Poor Metabolizer) Evidence Level: **Actionable**

Haloperidol is metabolized by CYP2D6, CYP3A4, and other enzymes. **Decreased CYP2D6 activity results in higher haloperidol concentrations, potentially leading to more adverse events.** Consider an alternative drug, or prescribe haloperidol at 50% of the usual starting dose, then adjust dosage to achieve a favorable clinical response.

Oxycodone (Percocet, Oxycontin)

Possible Altered Response to Oxycodone (CYP2D6 *4/*5 Poor Metabolizer) Evidence Level: **Actionable**

Decreased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 poor metabolizers. However, there is insufficient evidence whether poor metabolizers 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).

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Guidance Levels

Based upon the patient's genotype, a medication has potentially reduced efficacy or increased toxicity or the patient has an increased risk for the indicated condition.

Based upon the patient's genotype, guidelines exist for adjusting dosage or increased vigilance or the patient has a moderate risk for the indicated condition.

Based on this patient's genotype, the medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.

Evidence Levels

Actionable - Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA. EMEA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as new knowledge arises.
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.

Additional Risk Factors

Hyperlipidemia/Atherosclerotic Cardiovascular Disease

No increased risk of hyperlipidemia/atherosclerotic vascular disease

The patient is negative for the APOE 388 T>C (Arg112Cys) and 526 C>T (Cys158Arg) 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. Defects in APOE can increase a person's risk for developing atherosclerosis and cardiovascular disease.

No action is needed when a patient is normolipidemic.

Thrombophilia

No Increased Risk of Thrombosis

The patient does not carry the Factor V Leiden G1691A mutation or Factor II G20210A mutation (wild-type).

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.

Unless other genetic and/or circumstantial risk factors are present (e.g., smoking or obesity…), estrogen-containing contraceptive and hormone replacement therapy can be used by the patient.

Hyperhomocysteinemia

No Increased Risk of Hyperhomocysteinemia

The patient carries one MTHFR C677T mutation and one A1298C mutation (compound heterozygous). MTHFR enzyme activity is reduced.

The patient's reduced 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).

Testing total plasma homocysteine level may be beneficial. Hyperhomocysteinemia can be treated with nutritional supplementation.

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Potentially Impacted Medications for: Johnny Doe

Category	Standard Precautions	Use With Caution	Consider Alternatives
5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	Dutasteride (Avodart) Finasteride (Proscar)		
Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin (UroXatral) Doxazosin (Cardura) Silodosin (Rapaflo) Terazosin (Hytrin)	Tamsulosin (Flomax)	
Angiotensin II Receptor Antagonists	Irbesartan (Avapro)		
Antiaddictives	Bupropion (Wellbutrin, Zyban, Aplenzin, Contrave) Naltrexone (Vivitrol)		
Anti-ADHD Agents	Amphetamine (Adderall) Clonidine (Kapvay) Dextroamphetamine (Dexedrine) Guanfacine (Intuniv) Lisdexamfetamine (Vyvanse)	Atomoxetine (Strattera) Dexmethylphenidate (Focalin) Methylphenidate (Ritalin)	
Antianginal Agents		Ranolazine (Ranexa)	
Antiarrhythmics		Flecainide (Tambocor) Mexiletine (Mexitil) Propafenone (Rythmol)	
Anticoagulants	Apixaban (Eliquis) Dabigatran Etexilate (Pradaxa) Edoxaban (Savaysa) Fondaparinux (Arixtra) Rivaroxaban (Xarelto)	Warfarin (Coumadin)	
Anticonvulsants	Carbamazepine (Tegretol, Carbatrol) Eslicarbazepine (Aptiom) Ethosuximide (Zarontin) Ezogabine (Potiga) Felbamate (Felbatol) Fosphenytoin (Cerebyx) Gabapentin (Neurontin) Lacosamide (Vimpat) Lamotrigine (Lamictal) Levetiracetam (Keppra) Oxcarbazepine (Trileptal) Perampanel (Fycompa) Phenytoin (Dilantin) Pregabalin (Lyrica) Rufinamide (Banzel) Tiagabine (Gabitril) Topiramate (Topamax) Valproic Acid (Depakote, Depakene) Vigabatrin (Sabril)	Phenobarbital (Luminal) Primidone (Mysoline) Zonisamide (Zonegran)	
Antidementia Agents	Memantine (Namenda)	Donepezil (Aricept) Galantamine (Razadyne)	

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Category	Standard Precautions	Use With Caution	Consider Alternatives
Antidepressants	Desvenlafaxine (Pristiq) Fluoxetine (Prozac, Sarafem) Levomilnacipran (Fetzima) Mirtazapine (Remeron) Sertraline (Zoloft) Vilazodone (Viibryd)	Amoxapine (Amoxapine) Citalopram (Celexa) Duloxetine (Cymbalta) Escitalopram (Lexapro) Fluvoxamine (Luvox) Maprotiline (Ludiomil) Nefazodone (Serzone) Vortioxetine (Brintellix)	Amitriptyline (Elavil) Clomipramine (Anafranil) Desipramine (Norpramin) Doxepin (Silenor) Imipramine (Tofranil) Nortriptyline (Pamelor) Paroxetine (Paxil, Brisdelle) Protriptyline (Vivactil) Trimipramine (Surmontil) Venlafaxine (Effexor)
Antiemetics	Dolasetron (Anzemet) Ondansetron (Zofran) Palonosetron (Aloxi)	Metoclopramide (Reglan)	
Antifolates		Methotrexate (Trexall)	
Antifungals	Voriconazole (Vfend)		
Antiplatelets	Prasugrel (Effient) Ticagrelor (Brilinta) Vorapaxar (Zontivity)		Clopidogrel (Plavix)
Antipsychotics	Asenapine (Saphris) Clozapine (Clozaril) Lurasidone (Latuda) Olanzapine (Zyprexa) Paliperidone (Invega) Quetiapine (Seroquel) Thiothixene (Navane) Trazodone (Oleptro) Trifluoperazine (Stelazine) Ziprasidone (Geodon)	Aripiprazole (Abilify) Chlorpromazine (Thorazine) Fluphenazine (Prolixin) Iloperidone (Fanapt) Perphenazine (Trilafon) Pimozide (Orap) Tetrabenazine (Xenazine)	Haloperidol (Haldol) Risperidone (Risperdal) Thioridazine (Mellaril)
Antispasmodics for Overactive Bladder	Fesoterodine (Toviaz) Mirabegron (Myrbetriq) Oxybutynin (Ditropan) Solifenacin (Vesicare) Trospium (Sanctura)	Darifenacin (Enablex) Tolterodine (Detrol)	
Benzodiazepines	Alprazolam (Xanax) Clonazepam (Klonopin) Diazepam (Valium) Lorazepam (Ativan) Oxazepam (Serax)	Clobazam (Onfi)	
Beta Blockers	Labetalol (Normodyne, Trandate) Nebivolol (Bystolic) Propranolol (Inderal)	Carvedilol (Coreg) Timolol (Timoptic)	Metoprolol (Lopressor)
Fibromyalgia Agents	Milnacipran (Savella)		
Immunomodulators	Apremilast (Otezla)	Leflunomide (Arava)	
Immunosupressants		Tacrolimus (Prograf)	

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Category	Standard Precautions	Use With Caution	Consider Alternatives
Muscle Relaxants	Carisoprodol (Soma) Cyclobenzaprine (Flexeril, Amrix) Metaxalone (Skelaxin) Methocarbamol (Robaxin) 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) Hydromorphone (Dilaudid, Exalgo) Levorphanol (Levo Dromoran) Meperidine (Demerol) Morphine (MS Contin) Oxymorphone (Opana, Numorphan) Sufentanil (Sufenta) Tapentadol (Nucynta)	Fentanyl (Actiq) Hydrocodone (Vicodin) Methadone (Dolophine) Oxycodone (Percocet, Oxycontin)	Codeine (Codeine; Fioricet with Codeine) Tramadol (Ultram)
Phosphodiesterase Inhibitors for Erectile Dysfunction	Avanafil (Stendra) Sildenafil (Viagra) Tadalafil (Cialis) Vardenafil (Levitra)		
Proton Pump Inhibitors	Dexlansoprazole (Dexilant, Kapidex) Esomeprazole (Nexium) Lansoprazole (Prevacid) Omeprazole (Prilosec) Pantoprazole (Protonix) Rabeprazole (Aciphex)		
Statins	Fluvastatin (Lescol) Lovastatin (Mevacor)	Atorvastatin (Lipitor) Pitavastatin (Livalo) Pravastatin (Pravachol) Rosuvastatin (Crestor)	Simvastatin (Zocor)
Sulfonylureas	Glimepiride (Amaryl) Glipizide (Glucotrol) Glyburide (Micronase) Tolbutamide (Orinase)		

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Dosing Guidance for: Johnny Doe

Amitriptyline (Elavil) Evidence Level: **Actionable**

Moderate Sensitivity to Amitriptyline (CYP2C19 *2/*17 Intermediate Metabolizer)

Amitriptyline should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Amitriptyline (Elavil) Evidence Level: **Actionable**

Increased Sensitivity to Amitriptyline (CYP2D6 *4/*5 Poor Metabolizer)

Select an alternative drug, or consider prescribing amitriptyline at a reduced dose (50% reduction) with monitoring of plasma concentrations of amitriptyline and nortriptyline.

Amoxapine (Amoxapine) Evidence Level: **Informative**

Possible Sensitivity to Amoxapine (CYP2D6 *4/*5 Poor Metabolizer)

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 therefore, therapy must be initiated cautiously and adjusted according to the patient's response.

Aripiprazole (Abilify) Evidence Level: **Actionable**

Increased Sensitivity to Aripiprazole (CYP2D6 *4/*5 Poor Metabolizer)

Poor metabolizers have a significantly reduced capacity to metabolize aripiprazole and its active metabolite, and should receive lower doses. Careful titration is recommended until a favorable response is achieved.

Daily dosing (oral or intramuscular): aripiprazole dose should initially be reduced to one-half (**50%**) of the usual dose, then adjusted to achieve a favorable clinical response. Reduce the **maximum dose to 10 mg/day** (67% of the maximum recommended daily dose). The dose of aripiprazole for poor metabolizers who are administered a strong CYP3A4 inhibitor should be reduced to one-quarter (25%) of the usual dose.

Monthly dosing (intramuscular): the starting and maintenance monthly recommended dose is lower than the usually recommended dose, and should be **300 mg**. Some patients may benefit from a reduction to 200 mg. Reduce the monthly dose to 200 mg if a CYP3A4 inhibitor is prescribed to CYP2D6 poor metabolizers receiving 300 mg of aripiprazole.

Atomoxetine (Strattera) Evidence Level: **Actionable**

Increased Sensitivity to Atomoxetine (CYP2D6 *4/*5 Poor Metabolizer)

When given a standard atomoxetine dose, CYP2D6 poor metabolizers are likely to have higher plasma levels of the drug, which may lead to a higher rate of adverse events. **Careful titration and dosing adjustment are recommended with monitoring for toxicity until a favorable response is achieved**. In children and adolescents up to 70 kg body weight, atomoxetine should be initiated at standard dosing of 0.5 mg/kg/day, and only increased to the usual target dose of 1.2 mg/kg/day if symptoms fail to improve after 4 weeks and the initial dose is well tolerated. In children and adolescents over 70 kg body weight and adults, atomoxetine should be initiated at standard dosing of 40 mg/day, and only increased to the usual target dose of 80 mg/day if symptoms fail to improve after 4 weeks and the initial dose is well tolerated.

Atorvastatin (Lipitor) Evidence Level: **Informative**

Increased Myopathy Risk (SLCO1B1 521T>C CC Low Transporter Function)

The reduced SLCO1B1 function may result in elevated atorvastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high atorvastatin doses in this patient should be avoided. If atorvastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Carvedilol (Coreg) Evidence Level: **Actionable**

Moderate Sensitivity to Carvedilol (CYP2D6 *4/*5 Poor Metabolizer)

Carvedilol can be prescribed at standard label-recommended dosage and administration. CYP2D6 poor metabolizers may experience dizziness during up-titration. Careful titration is recommended with monitoring until a favorable response is achieved.

Chlorpromazine (Thorazine) Evidence Level: **Informative**

Increased Sensitivity to Chlorpromazine (CYP2D6 *4/*5 Poor Metabolizer)

Chlorpromazine is metabolized by CYP2D6, CYP3A4 and flavin-containing monooxygenases. Decreased CYP2D6 activity results in higher chlorpromazine concentrations potentially leading to higher adverse events. Consider prescribing chlorpromazine at a lower starting dose and then adjust dosage to achieve a favorable clinical response.

Citalopram (Celexa) Evidence Level: **Informative**

Delayed Response to Citalopram (SLC6A4 S/La Decreased Serotonin Transporter Expression)

The genotype predicts a decreased serotonin transporter levels. A longer titration period may be required to achieve maximal antidepressant response. The patient may respond to citalopram more slowly (up to 12 weeks).

Clobazam (Onfi) Evidence Level: **Actionable**

Possible Sensitivity to Clobazam (CYP2C19 *2/*17 Intermediate Metabolizer)

In CYP2C19 intermediate metabolizers, plasma levels of the active metabolite N-desmethylclobazam were 2-fold higher than those found in CYP2C19 normal metabolizers. The dose adjustment for intermediate metabolizers is not well established, and therefore the recommendation for poor metabolizers is proposed. The starting dose should be 5 mg/day, and dose titration should proceed slowly according to weight. Patients should be titrated initially to 10 mg /day (≤30 kg body weight) or 20 mg/day (>30 kg body weight). If necessary and based upon clinical response, an additional titration to the maximum doses 20 mg/day (≤30 kg body weight) or 40 mg/day (>30 kg body weight) may be started on day 21.

Clomipramine (Anafranil) Evidence Level: **Actionable**

Moderate Sensitivity to Clomipramine (CYP2C19 *2/*17 Intermediate Metabolizer)

Clomipramine should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Clomipramine (Anafranil) Evidence Level: **Actionable**

Increased Sensitivity to Clomipramine (CYP2D6 *4/*5 Poor Metabolizer)

Consider an alternative drug, or prescribe clomipramine at 50% of the recommended standard starting dose. Monitor plasma concentrations of clomipramine and desmethylclomipramine, and titrate accordingly until a favorable response is achieved.

Clopidogrel (Plavix) Evidence Level: **Actionable**

Reduced Response to Clopidogrel (CYP2C19 *2/*17 Intermediate Metabolizer)

Consider alternative therapy. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole.

Codeine (Codeine; Fioricet with Codeine) Evidence Level: **Actionable**

Non-Response to Codeine (CYP2D6 *4/*5 Poor Metabolizer)

Greatly reduced morphine levels are expected, and the patient may not experience adequate pain relief when taking codeine. Avoid prescribing codeine, and consider alternative opioids other than tramadol, 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.

Darifenacin (Enablex) Evidence Level: **Actionable**

Possible Sensitivity to Darifenacin (CYP2D6 *4/*5 Poor Metabolizer)

Darifenacin exposure is increased 30% in CYP2D6 poor metabolizers. Although dose adjustment may not be needed in these patients, monitor patients for increased side effects when darifenacin is prescribed at standard label-recommended dosage and administration.

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Desipramine (Norpramin) Evidence Level: **Actionable**

Increased Sensitivity to Desipramine (CYP2D6 *4/*5 Poor Metabolizer)

Consider an alternative drug, or prescribe desipramine at 50% of recommended standard starting dose. Monitor plasma concentrations of desipramine and metabolites and titrate accordingly until a favorable response is achieved.

Dexmethylphenidate (Focalin) Evidence Level: **Informative**

Decreased Response to Dexmethylphenidate (COMT Val158Met AG Intermediate COMT Activity)

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.

Dexmethylphenidate (Focalin) Evidence Level: **Informative**

Unfavorable Response to Dexmethylphenidate (ADRA2A C-1291G C/C Homozygous for C Allele)

The patient carries two C alleles of the ADRA2A –1291 C>G polymorphism. Preliminary studies suggest that this genotype may be associated with an unfavorable response to dexmethylphenidate in children and adolescents with the attention-deficit and hyperactivity disorder of inattentive type.

Donepezil (Aricept) Evidence Level: **Informative**

Possible Altered Response to Donepezil (CYP2D6 *4/*5 Poor Metabolizer)

When compared to a normal metabolizer, a poor metabolizer has a 30% decrease in donepezil clearance. The clinical significance of this decrease is not well documented. Consider using a standard dosing regimen, be alert for adverse events, and adjust dosage in response to clinical response and tolerability.

Doxepin (Silenor) Evidence Level: **Actionable**

Moderate Sensitivity to Doxepin (CYP2C19 *2/*17 Intermediate Metabolizer)

Doxepin should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Doxepin (Silenor) Evidence Level: **Actionable**

Increased Sensitivity to Doxepin (CYP2D6 *4/*5 Poor Metabolizer)

Consider an alternative drug or reduce doxepin starting dose by 50%. Adjust maintenance dose according to nordoxepin plasma concentrations.

Duloxetine (Cymbalta) Evidence Level: **Informative**

Possible Sensitivity to Duloxetine (CYP2D6 *4/*5 Poor Metabolizer)

Limited data suggest that duloxetine plasma concentrations might be increased in CYP2D6 poor metabolizers. Therefore, duloxetine can be prescribed at standard label-recommended dosage, and careful titration is recommended until a favorable response is achieved.

Escitalopram (Lexapro) Evidence Level: **Informative**

Delayed Response to Escitalopram (SLC6A4 S/La Decreased Serotonin Transporter Expression)

The genotype predicts a decreased serotonin transporter levels. A longer titration period may be required to achieve maximal antidepressant response. The patient may respond to escitalopram more slowly (up to 12 weeks).

Fentanyl (Actiq) Evidence Level: **Informative**

Altered Response to Fentanyl (OPRM1 A118G AG Altered OPRM1 Function)

The patient carries one copy of the OPRM1 118A>G mutation. Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia at standard fentanyl doses. Therefore, the patient may require higher doses of this drug. Because fentanyl has a narrow therapeutic window, it is advised to carefully titrate this drug to a tolerable dose that provides adequate analgesia with minimal side effects.

Flecainide (Tambocor) Evidence Level: **Actionable**

Significantly Increased Sensitivity to Flecainide (CYP2D6 *4/*5 Poor Metabolizer)

Consider prescribing a lower flecainide dose. When compared to a CYP2D6 normal metabolizer, a poor metabolizer may require a 50% dose reduction. Careful titration with ECG recording and monitoring of flecainide plasma concentrations are recommended until a favorable clinical response is achieved.

Fluphenazine (Prolixin) Evidence Level: **Informative**

Increased Sensitivity to Fluphenazine (CYP2D6 *4/*5 Poor Metabolizer)

Fluphenazine is metabolized by CYP2D6, CYP1A2 and other enzymes. **Decreased CYP2D6 activity may result in higher fluphenazine concentrations potentially leading to higher adverse events such as extrapyramidal symptoms**. There are no established dosing adjustments for patients lacking CYP2D6 function therefore, therapy must be initiated cautiously with oral or parenteral fluphenazine hydrochloride. When the pharmacological effects and an appropriate dosage are apparent, an equivalent dose of fluphenazine decanoate (IM or SC) may be administered and subsequent dosage adjustments may be necessary.

Fluvoxamine (Luvox) Evidence Level: **Informative**

Delayed Response to Fluvoxamine (SLC6A4 S/La Decreased Serotonin Transporter Expression)

The genotype predicts a decreased serotonin transporter levels. A longer titration period may be required to achieve maximal antidepressant response. The patient may respond to fluvoxamine more slowly (up to 12 weeks).

Fluvoxamine (Luvox) Evidence Level: **Informative**

Increased Sensitivity to Fluvoxamine (CYP2D6 *4/*5 Poor Metabolizer)

At standard label-recommended dosage, fluvoxamine levels are expected to be high and adverse events may occur. Consider a 25-50% reduction of recommended starting dose to help prevent concentration-dependent adverse events and titrate based on the clinical response and tolerability. An alternative medication may also be considered.

Galantamine (Razadyne) Evidence Level: **Informative**

Possible Sensitivity to Galantamine (CYP2D6 *4/*5 Poor Metabolizer)

A CYP2D6 poor metabolizer has a drug exposure that is approximately 50% higher than the exposure in a normal metabolizer. Although dosage adjustment is not necessary in a patient identified as a CYP2D6 poor metabolizer as the dose of drug is individually titrated to tolerability, a slower titration can be considered as it may improve tolerability.

Haloperidol (Haldol) Evidence Level: **Actionable**

Increased Sensitivity to Haloperidol (CYP2D6 *4/*5 Poor Metabolizer)

Haloperidol is metabolized by CYP2D6, CYP3A4, and other enzymes. **Decreased CYP2D6 activity results in higher haloperidol concentrations, potentially leading to more adverse events.** Consider an alternative drug, or prescribe haloperidol at 50% of the usual starting dose, then adjust dosage to achieve a favorable clinical response.

Hydrocodone (Vicodin) Evidence Level: **Informative**

Possible Altered Response to Hydrocodone (CYP2D6 *4/*5 Poor Metabolizer)

Decreased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 poor metabolizers. However, there is insufficient evidence whether poor metabolizers 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).

Hydrocodone (Vicodin) Evidence Level: **Informative**

Altered Response to Hydrocodone (OPRM1 A118G AG Altered OPRM1 Function)

Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia and increased opioid side effects at standard or high hydrocodone doses. If the patient fails to respond to increased hydrocodone doses, an alternative opioid may be considered.

Iloperidone (Fanapt) Evidence Level: **Actionable**

Increased Sensitivity to Iloperidone (CYP2D6 *4/*5 Poor Metabolizer)

Iloperidone **dose should be reduced by one-half and titrated slowly to avoid orthostatic hypotension**. Because iloperidone is associated with QTc prolongation, caution is warranted when prescribing the drug in patients with reduced CYP2D6 activity. 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.

Imipramine (Tofranil) Evidence Level: **Actionable**

Moderate Sensitivity to Imipramine (CYP2C19 *2/*17 Intermediate Metabolizer)

Imipramine should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Imipramine (Tofranil) Evidence Level: **Actionable**

Increased Sensitivity to Imipramine (CYP2D6 *4/*5 Poor Metabolizer)

Consider an alternative drug, or consider a 50% reduction of the imipramine recommended starting dose, then titrate in response to imipramine and desipramine plasma concentrations.

Leflunomide (Arava) Evidence Level: **Informative**

Increased Sensitivity to Leflunomide (CYP2C19 *2/*17 Intermediate Metabolizer)

Leflunomide is metabolized by CYP2C19 and CYP1A2 to its active metabolite teriflunomide. Preliminary studies indicate that patients with decreased CYP2C19 activity have a higher risk of developing gastrointestinal side effects and hepatotoxicity. There is insufficient data to calculate dose adjustment. If leflunomide is prescribed at standard dosing, monitor closely the patient's response and be alert to increased side effects. Full blood cell count (CBC) and liver function parameters should be checked no more than 6 months before beginning treatment, and every month for the initial 6 months of therapy. Blood pressure should be checked before beginning treatment and periodically thereafter.

Maprotiline (Ludiomil) Evidence Level: **Informative**

Increased Sensitivity to Maprotiline (CYP2D6 *4/*5 Poor Metabolizer)

Like other tricyclic and tetracyclic antidepressants, maprotiline is metabolized by CYP2D6 as well as CYP1A2. Compared to CYP2D6 normal metabolizers, CYP2D6 poor metabolizers have higher exposure to maprotiline at therapeutic doses which may increase the risk of concentration-dependent toxicities. There are no established dosing adjustments for patients with decreased CYP2D6 function however, it is recommended to initiate maprotiline therapy at a low dosage and gradually adjust the dosing according to the patient's response. The lowest effective dosage should always be considered during maintenance therapy.

Methadone (Dolophine) Evidence Level: **Informative**

Increased Sensitivity to Methadone (CYP2B6 *6/*6 Poor Metabolizer)

Increased S-methadone plasma concentrations with associated-cardiotoxicity may occur. Consider a lower initial dose, and adjust dosing based on the clinical response. CYP2B6 poor metabolizers require lower maintenance doses than normal metabolizers. Consider an alternative medication in patients with other arrhythmias or a family history of long QT syndrome.

Methotrexate (Trexall) Evidence Level: **Informative**

Increased risk for methotrexate toxicity (MTHFR 677C>T CT Reduced MTHFR Activity)

The patient carries the MTHFR 677 T allele 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. Consider at least a 25% reduction in methotrexate starting dose, followed by titration based on toxicity. 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 the MTHFR 677 T allele 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 (Ritalin) Evidence Level: **Informative**

Decreased Response to Methylphenidate (COMT Val158Met AG Intermediate COMT Activity)

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.

Methylphenidate (Ritalin) Evidence Level: **Informative**

Unfavorable Response to Methylphenidate (ADRA2A C-1291G C/C Homozygous for C Allele)

The patient carries two C alleles of the ADRA2A –1291 C>G polymorphism. Preliminary studies suggest that this genotype may be associated with an unfavorable response to methylphenidate in children and adolescents with the attention-deficit and hyperactivity disorder of inattentive type.

Metoclopramide (Reglan) Evidence Level: **Informative**

Increased Sensitivity to Metoclopramide (CYP2D6 *4/*5 Poor Metabolizer)

Metoclopramide is metabolized at a slower rate in CYP2D6 poor metabolizers which results in significantly higher serum concentrations of the drug. Considering the CNS and extrapyramidal adverse effects of metoclopramide, close monitoring for toxicity and eventually a dose decrease are recommended. Patients with renal disease at increased risk.

Metoprolol (Lopressor) Evidence Level: **Actionable**

Significantly Increased Sensitivity to Metoprolol (CYP2D6 *4/*5 Poor Metabolizer)

Based on the genotype result, this patient is at risk of excessive beta-blockade when taking metoprolol at standard dosage. Heart Failure: Consider alternative beta-blockers such as bisoprolol or carvedilol, or prescribe metoprolol at a lower dose. When compared to a normal metabolizer, a poor metabolizer may require a 75% dose reduction. Other indications: Consider alternative beta-blockers such as bisoprolol or atenolol, or prescribe metoprolol at a lower dose. When compared to a normal metabolizer, a poor metabolizer may require a 75% dose reduction. If metoprolol is prescribed, be alert to adverse events (e.g., bradycardia or cold extremities).

Mexiletine (Mexitil) Evidence Level: **Actionable**

Significantly Increased Sensitivity to Mexiletine (CYP2D6 *4/*5 Poor Metabolizer)

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.

Nefazodone (Serzone) Evidence Level: **Informative**

Possible Sensitivity to Nefazodone (CYP2D6 *4/*5 Poor Metabolizer)

Nefazodone is metabolized by CYP3A4 to its active metabolite m-chlorophenylpiperazine and other metabolites. The m-chlorophenylpiperazine metabolite which may contribute to adverse events, is further metabolized by CYP2D6. Individuals lacking CYP2D6 activity have higher levels of m-chlorophenylpiperazine metabolite and may experience more moderate and transient side effects when starting therapy. Consider prescribing nefazodone at a lower dose and adjust dose according to the patient's tolerability and clinical response.

Nortriptyline (Pamelor) Evidence Level: **Actionable**

Increased Sensitivity to Nortriptyline (CYP2D6 *4/*5 Poor Metabolizer)

Select an alternative drug, or consider prescribing nortriptyline at a reduced dose (50% reduction) with monitoring of plasma concentrations of nortriptyline and metabolites.

Oxycodone (Percocet, Oxycontin) Evidence Level: **Actionable**

Possible Altered Response to Oxycodone (CYP2D6 *4/*5 Poor Metabolizer)

Decreased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 poor metabolizers. However, there is insufficient evidence whether poor metabolizers 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).

Paclitaxel (Taxol, Abraxane) Evidence Level: **Informative**

Increased risk for peripheral neuropathy (CYP2C8 *1A/*2 Intermediate Metabolizer)

Paroxetine (Paxil, Brisdelle) Evidence Level: **Informative**

Increased Sensitivity to Paroxetine (CYP2D6 *4/*5 Poor Metabolizer)

At standard label-recommended dosage, paroxetine levels are expected to be high, and adverse events may occur. Consider an alternative medication. If paroxetine is warranted, consider a 50% decrease of the initial dose and titrate based on the clinical response and tolerability. Some studies show that compared to normal metabolizers, poor metabolizers may experience more sexual dysfunction.

Perphenazine (Trilafon) Evidence Level: **Actionable**

Increased Sensitivity to Perphenazine (CYP2D6 *4/*5 Poor Metabolizer)

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.

Phenobarbital (Luminal) Evidence Level: **Informative**

Possible Sensitivity to Phenobarbital (CYP2C19 *2/*17 Intermediate Metabolizer)

CYP2C19 is partly involved in the metabolism of phenobarbital, and although CYP2C19 intermediate metabolizers have a lower clearance of phenobarbital than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, phenobarbital can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Pimozide (Orap) Evidence Level: **Actionable**

Increased Sensitivity to Pimozide (CYP2D6 *4/*5 Poor Metabolizer)

The pimozide concentrations observed in poor CYP2D6 metabolizers are expected to be high, and the time to achieve steady-state pimozide concentrations is expected to be long (approximately 2 weeks). Consequently, CYP2D6 poor metabolizers are at an increased risk of QT prolongation at standard doses of pimozide. In CYP2D6 poor metabolizers, pimozide doses should not exceed 4 mg/day in adults or 0.05 mg/kg/day in children, and doses should not be increased earlier than 14 days.

Pitavastatin (Livalo) Evidence Level: **Informative**

Increased Myopathy Risk (SLCO1B1 521T>C CC Low Transporter Function)

The reduced SLCO1B1 function may result in elevated pitavastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pitavastatin doses in this patient should be avoided. If pitavastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Pravastatin (Pravachol) Evidence Level: **Informative**

Increased Myopathy Risk (SLCO1B1 521T>C CC Low Transporter Function)

The reduced SLCO1B1 function may result in elevated pravastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pravastatin doses in this patient should be avoided. If pravastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Primidone (Mysoline) Evidence Level: **Informative**

Possible Sensitivity to Primidone (CYP2C19 *2/*17 Intermediate Metabolizer)

CYP2C19 is partly involved in the metabolism of primidone, and although CYP2C19 intermediate metabolizers have a lower clearance of phenobarbital (active metabolite) than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, primidone can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

Propafenone (Rythmol) Evidence Level: **Actionable**

Increased Sensitivity to Propafenone (CYP2D6 *4/*5 Poor Metabolizer)

Consider reducing the propafenone dose, and monitor ECG. Compared to normal metabolizers, poor metabolizers may require a 70% dose reduction. Consider monitoring for plasma concentrations.

Protriptyline (Vivactil) Evidence Level: **Actionable**

Increased Sensitivity to Protriptyline (CYP2D6 *4/*5 Poor Metabolizer)

Consider alternative or prescribe protriptyline at 50% of recommended standard starting dose. Monitor plasma concentrations of protriptyline and metabolites and titrate accordingly until a favorable response is achieved.

Ranolazine (Ranexa) Evidence Level: **Actionable**

Increased Sensitivity to Ranolazine (CYP2D6 *4/*5 Poor Metabolizer)

Ranolazine is metabolized mainly by CYP3A4, and to a lesser extent by CYP2D6. At 500 mg twice daily, subjects lacking CYP2D6 activity (poor metabolizers) had 62% higher ranolazine exposure than subjects with normal CYP2D6 activity. The corresponding difference at 1000 mg twice daily dose was 25%.

The risk for increased exposure leading to adverse events is higher in patients lacking CYP2D6 activity (i.e., poor metabolizers). The recommended initial oral dose is 375 mg twice daily. **A slower up titration and additional monitoring is recommended in these patients.** Exposure related side effects might include nausea, vomiting, syncope, and dizziness. If a patient experiences treatment-related adverse events, down titration of the dose to 500 mg or 375 mg twice daily may be required. If symptoms do not resolve after dose reduction, treatment should be discontinued.

Ranolazine is a QTc prolonging drug. Caution should be observed when treating: 1- patients with a history of congenital or a family history of long QT syndrome, 2- patients with known acquired QT interval prolongation, and 3- patients treated with drugs affecting the QTc interval. Administration of CYP3A4 inhibitors increases the exposure of ranolazine significantly. As a consequence, the QTc prolongation by ranolazine in the presence of potent CYP3A inhibitors is significantly elevated relative to when the drug is administered alone.

Risperidone (Risperdal) Evidence Level: **Actionable**

Significantly Increased Sensitivity to Risperidone (CYP2D6 *4/*5 Poor Metabolizer)

Consider an alternative drug, OR prescribe risperidone at a reduced dose, be extra alert of adverse events, and adjust dosage in response to clinical response and tolerability.

Rosuvastatin (Crestor) Evidence Level: **Informative**

Increased Myopathy Risk (SLCO1B1 521T>C CC)

The reduced SLCO1B1 function may result in elevated rosuvastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high rosuvastatin doses in this patient should be avoided. If rosuvastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Simvastatin (Zocor) Evidence Level: **Actionable**

High Myopathy Risk (SLCO1B1 521T>C CC Low Transporter Function)

Simvastatin plasma concentrations are expected to be elevated. **Consider avoiding simvastatin** and prescribe an alternative statin or another hypolipidemic drug, or consider prescribing simvastatin at a lower starting dose (20 mg/day). Routine creatine kinase (CK) monitoring is also advised. **The FDA recommends against the 80 mg daily dose.** Although the association between the SLCO1B1 521C>T variant and myopathy risk is not clearly established for other statins such as atorvastatin, pitavastatin, rosuvastatin, and pravastatin, caution is advised if high doses of these statins are used in this patient. Fluvastatin plasma levels are not affected by the SLCO1B1 521C>T variant.

Tacrolimus (Prograf) Evidence Level: **Actionable**

Insufficient Response to Tacrolimus (CYP3A5 *1/*3 Intermediate Metabolizer)

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.

Tamsulosin (Flomax) Evidence Level: **Actionable**

Increased Sensitivity to Tamsulosin (CYP2D6 *4/*5 Poor Metabolizer)

Tamsulosin is metabolized at a slower rate in CYP2D6 poor metabolizers, which results in significantly higher serum concentrations of tamsulosin. Therefore, this drug should be used with caution in patients known to be CYP2D6 poor metabolizers, particularly at a daily dose higher than 0.4 mg.

Tetrabenazine (Xenazine) Evidence Level: **Actionable**

Increased Sensitivity to Tetrabenazine (CYP2D6 *4/*5 Poor Metabolizer)

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 poor metabolizers is 50 mg with a maximum single dose of 25 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.

Thioridazine (Mellaril) Evidence Level: **Actionable**

Increased Sensitivity to Thioridazine (CYP2D6 *4/*5 Poor Metabolizer)

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.

Timolol (Timoptic) Evidence Level: **Actionable**

Increased Sensitivity to Timolol (CYP2D6 *4/*5 Poor Metabolizer)

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.

Tolterodine (Detrol) Evidence Level: **Informative**

Possible Sensitivity to Tolterodine (CYP2D6 *4/*5 Poor Metabolizer)

Tolterodine is metabolized at a slower rate in CYP2D6 poor metabolizers, which results in significantly higher serum concentrations of tolterodine and negligible concentrations of its active metabolite (5-hydroxymethytolterodine). Considering the antimuscarinic potency of tolterodine and its active metabolite, and the protein binding of these compounds, tolterodine accounts for the major part of the clinical effect in poor metabolizers, and the same dosage can be applied irrespective of phenotype status.

Patients with congenital or acquired QT prolongation: the effect of tolterodine on the QT interval prolongation is greater for 8 mg/day (two times the therapeutic dose) compared to 4 mg/day, and is more pronounced in CYP2D6 poor metabolizers than normal metabolizers. This should be considered when tolterodine is prescribed to patients with a known history of QT prolongation, or patients who are taking Class IA or Class III antiarrhythmics.

Tramadol (Ultram) Evidence Level: **Actionable**

Non-Response to Tramadol (CYP2D6 *4/*5 Poor Metabolizer)

The patient will not experience adequate pain relief when taking tramadol. Avoid prescribing tramadol, and consider alternative opioids other than codeine 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.

Trimipramine (Surmontil) Evidence Level: **Actionable**

Moderate Sensitivity to Trimipramine (CYP2C19 *2/*17 Intermediate Metabolizer)

Trimipramine should be used with caution in patients with reduced CYP2C19 activity. Consider a lower starting dose, and increase dosing over several days until an optimal response is achieved.

Trimipramine (Surmontil) Evidence Level: **Actionable**

Increased Sensitivity to Trimipramine (CYP2D6 *4/*5 Poor Metabolizer)

Consider an alternative drug, or consider a 50% reduction of the trimipramine recommended starting dose, then titrate in response to trimipramine plasma concentrations.

Venlafaxine (Effexor) Evidence Level: **Actionable**

Significantly Increased Sensitivity to Venlafaxine (CYP2D6 *4/*5 Poor Metabolizer)

The patient has an increased risk of side effects when taking standard doses of venlafaxine. Consider an alternative drug, OR prescribe venlafaxine, be extra alert of adverse events, and adjust dosage in response to clinical response and tolerability. Monitor O-desmethylvenlafaxine plasma concentrations.

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Vortioxetine (Brintellix) Evidence Level: **Actionable**

Increased Sensitivity to Vortioxetine (CYP2D6 *4/*5 Poor Metabolizer)

CYP2D6 is the primary enzyme catalyzing the metabolism of vortioxetine to its major, pharmacologically inactive carboxylic acid metabolite. CYP2D6 poor metabolizers have approximately twice the vortioxetine plasma concentrations of normal metabolizers. **Vortioxetine starting dose should be reduced by one-half. The maximum recommended dose is 10 mg/day in known CYP2D6 poor metabolizers.** Consider 5 mg/day for patients who do not tolerate higher doses.

Warfarin (Coumadin) Evidence Level: **Actionable**

Normal Sensitivity to Warfarin (CYP2C9 *1/*1 VKORC1 -1639G>A G/A)

Initiation Therapy: consider using the following standard warfarin dose range as provided in the FDA-approved label: **5-7 mg/day**. OR consider using a personalized dose calculated by a pharmacogenetic algorithm. The estimated time to reach steady state is 4-5 days.

Zonisamide (Zonegran) Evidence Level: **Informative**

Possible Sensitivity to Zonisamide (CYP2C19 *2/*17 Intermediate Metabolizer)

CYP2C19 is partly involved in the metabolism of zonisamide, and although preliminary studies show that CYP2C19 intermediate metabolizers have a slightly lower (15%) zonisamide clearance than normal metabolizers, no significant change in the clinical outcome has been reported with this antiepileptic drug. Therefore, zonisamide can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

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Test Details for: Johnny Doe

Gene	Genotype	Phenotype	Alleles Tested
ABCB1	2677G>A G/G	Variant Allele Not Present	3435C>T, 2677G>A, 2677G>T
ABCB1	2677G>T G/T	Heterozygous- Variant Allele Present	3435C>T, 2677G>A, 2677G>T
ABCB1	3435C>T C/T	Heterozygous- Variant Allele Present	3435C>T, 2677G>A, 2677G>T
ADRA2A	C-1291G C/C	Homozygous for C Allele	C-1291G
ANKK1/DRD2	DRD2:Taq1A GG	Unaltered DRD2 function	DRD2:Taq1A
Apolipoprotein E	ε3/ε3	No Increased Risk of Hyperlipidemia/Atherosclerotic Vascular Disease	ε2, ε4
COMT	Val158Met AG	Intermediate COMT Activity	Val158Met, c.1-98A>G
CYP1A2	*1A/*1A	Normal Metabolizer- Possible Inducibility	*1C, *1D, *1E, *1F, *1J, *1K, *1L, *1V, *1W
CYP2B6	*6/*6	Poor Metabolizer	*2, *3, *5, *6, *9, *18, *28
CYP2C19	*2/*17	Intermediate Metabolizer	*2, *3, *4, *4B, *5, *6, *7, *8, *9, *10, *17
CYP2C9	*1/*1	Normal Metabolizer	*2, *3, *5, *6, *8, *11, *27
CYP2D6	*4/*5	Poor Metabolizer	*2, *3, *4, *4M, *6, *7, *8, *9, *10, *11, *12, *14A, *14B, *17, *29, *35, *41, *5 (gene deletion), XN (gene duplication)
CYP3A4	*1/*1	Normal Metabolizer	*2, *3, *12, *17, *22
CYP3A5	*1/*3	Intermediate Metabolizer	*1D, *2, *3, *3C, *6, *7, *8, *9
Factor II	20210G>A GG	Normal Thrombosis Risk	20210G>A
Factor V Leiden	1691G>A GG	Normal Thrombosis Risk	1691G>A
MTHFR	1298A>C AC	Reduced MTHFR Activity	1298A>C
MTHFR	677C>T CT	Reduced MTHFR Activity	677C>T
OPRK1	36G>T C/C	Homozygous for G Allele	36G>T, rs6989250
OPRK1	rs6989250 C/C	Homozygous for C Allele	36G>T, rs6989250
OPRM1	A118G AG	Altered OPRM1 Function	A118G
SLC6A4	S/La	Decreased Serotonin Transporter Expression	La, S, Lg
SLCO1B1	521T>C CC	Low Transporter Function	521T>C, 388A>G
SULT4A1	rs138060 A/C	Heterozygous for C Allele	rs138097, rs138060
SULT4A1	rs138097 A/G	Heterozygous for A Allele	rs138097, rs138060
UGT2B15	*1/*1	Normal Metabolizer	*2
VKORC1	-1639G>A G/A	Intermediate Warfarin Sensitivity	-1639G>A, 1173C>T

Disclaimer: Only a physician, pharmacist or other healthcare professional should advise a patient on the use of information in this report.

M**ethodology**: Array based assays detect 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 mutations that result in altered or inactive tested genes. Absence of a detectable gene mutation or polymorphism does not rule out the possibility that a patient has intermediate or high sensitivity phenotypes due to the presence of an undetected polymorphism or due to drug-drug interactions.

Laboratory Certification: CLIA #11D2071408