4U Health

PATIENT INFORMATION		SPECIMEN DETAILS		PROVIDER INFORMATION
NAME:	**Demo Patient**	**SPECIMEN TYPE:**	Buccal Swab	DEMO PHYSICIAN
ACC #:	DEMO	**COLLECTION DATE:**	8/20/2020	
DOB:	1/1/1900	**RECEIVED DATE:**	8/15/2020	
SEX:		**REPORT DATE:**	8/20/2020	

Pain & Rheumatology Pharmacogenetic Report

Report Comment: VL BATCH 08202020-1 CO

Potentially Impacted Medications

CATEGORY	DRUG CLASS	STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVES
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®) Oxymorphone (Opana®, Numorphan®) Sufentanil (Sufenta®) Tapentadol (Nucynta®)	Benzhydrocodone (Apadaz®) Codeine (Codeine; Fioricet® with Codeine) Hydrocodone (Vicodin®) Methadone (Dolophine®) Morphine (MS Contin®) Oxycodone (Percocet®, Oxycontin®) Tramadol (Ultram®)	
Rheumatology	Anti-Hyperuricemics and Anti-Gout Agents	Colchicine (Mitigare®) Febuxostat (Uloric®)		
	Immunomodulators	Apremilast (Otezla®) Leflunomide (Arava®) Tofacitinib (Xeljanz®)		

PATIENT INFORMATION

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Dosing Guidance

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).

Carisoprodol
Soma®

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

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

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).

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).

Methadone
Dolophine®

Increased Methadone Exposure (CYP2B6: Intermediate Metabolizer) — **INFORMATIVE**

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

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

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

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.

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).

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.

Alfentanil
Alfenta®

Normal Response to Alfentanil — INFORMATIVE

Pharmacogenetic guidance: alfentanil is primarily metabolized by CYP3A4 and CYP3A5. Studies in healthy subjects showed that CYP3A5 genotype had no effect on the systemic or apparent oral clearances, or pharmacodynamics of alfentanil. **Polypharmacy guidance:** Alfentanil should be used with caution when prescribed to patients taking CYP3A4 inhibitors or inducers.

Apremilast
Otezla®

Normal Response to Apremilast — ACTIONABLE

Pharmacogenetic guidance: Apremilast is primarily eliminated via both hydrolysis and cytochrome P450-mediated oxidative metabolism (with subsequent glucuronidation). Cytochrome P450-metabolism is mediated by CYP3A4, with minor contributions from CYP1A2 and CYP2A6. Genetic polymorphisms of these enzymes are not expected to affect the efficacy or safety profiles of apremilast. **Polypharmacy guidance:** The use of metabolizing enzyme inducers (e.g. rifampin, phenobarbital, carbamazepine, phenytoin) with apremilast is not recommended.

Buprenorphine
Butrans®, Buprenex®

Normal Response to Buprenorphine — INFORMATIVE

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. Buprenorphine is primarily metabolized by CYP3A4 to norbuprenorphine and by UGT enzymes (mainly UGT1A1 and 2B7). The effects of genetic variants in these enzymes on its response have not been studied. **Polypharmacy guidance:** The concomitant use of buprenorphine with all CYP3A4 inhibitors may result in an increase in the drug levels, which could increase or prolong adverse drug effects. Monitor patients receiving buprenorphine with a CYP3A4 inhibitor. CYP and UGT inducers may decrease buprenorphine levels.

Celecoxib
Celebrex®

Normal Celecoxib Exposure (CYP2C9: Normal Metabolizer) — ACTIONABLE

Celecoxib therapy can be initiated at standard label-recommended dosage and administration.

Consider initiating treatment at the lowest end of the dosing range in geriatric patients. A dosage adjustment may be warranted when celecoxib is administered with CYP2C9 inhibitors or inducers.

Osteoarthritis, Rheumatoid Arthritis, Ankylosing Spondylitis, Acute Pain, Primary Dysmenorrhea: Consider using the lowest effective dosage for the shortest duration consistent with the patient treatment goals.

Acute Migraine: Consider using for the fewest number of days per month, as needed.

Osteoarthritis and Hypertension (co-formulation with amlodipine): Consider using the lowest effective dosage for the shortest duration consistent with the patient treatment goals.

Colchicine
Mitigare®

Normal Response to Colchicine — INFORMATIVE

Pharmacogenetic guidance: Colchicine in eliminated both by renal excretion and metabolism. While 50% of the absorbed dose in eliminated unchanged in urine, less than 20% is metabolized by CYP3A4. Glucuronidation is also a metabolic pathway for colchicine. Colchicine is a substrate of P-glycoprotein (encoded by ABCB1 gene) and its efflux by this transporter is important in its disposition. Colchicine has a narrow therapeutic index. Preliminary and limited studies indicate a lack of an effect of CYP3A4 or ABCB1 genetic polymorphisms on clinical response to colchicine in individuals with familial Mediterranean fever (FMF). There are no available genetically-guided drug selection or dosing recommendations. **Polypharmacy guidance:** Because colchicine is a substrate for both the CYP3A4 metabolizing enzyme and the P-glycoprotein efflux transporter, inhibition of either of these pathways may lead to colchicine-related toxicity. Inhibition of both CYP3A4 and P-gp by dual inhibitors such as clarithromycin has been reported to produce life-threatening or fatal colchicine toxicity due to significant increases in systemic colchicine levels. Therefore, concomitant use of colchicine and inhibitors of CYP3A4 or P-glycoprotein should be avoided.

Cyclobenzaprine
Flexeril®, Amrix®

Normal Response to Cyclobenzaprine
INFORMATIVE

Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available. Cyclobenzaprine is excreted primarily as a glucuronide via the kidneys, and as an N-demethylated metabolite by CYP3A4, CYP1A2, and to a lesser extent CYP2D6. Due to the minor involvement of CYP2D6 in the metabolism of cyclobenzaprine, the polymorphism of this enzyme is not of concern in its the clinical use.

Diclofenac
Voltaren®

Normal Diclofenac Exposure
INFORMATIVE

Pharmacogenetic guidance: Diclofenac is extensively metabolized by hydroxylation and direct glucuronidation. About 50% of diclofenac is eliminated as a 4-hydroxymetabolite, a reaction mediated by CYP2C9. Other CYP enzymes including CYP2C8, CYP2C19 and CYP3A4 are also involved in the formation of a 5-hydroxymetabolite. A substantial portion of the drug is also directly glucuronidated by UGT2B7 and UGT2B4. Genetic polymorphisms of CYP2C9 have not been found to affect the response to diclofenac. No dosing recommendations or genetically guided drug selection are recommended. **Polypharmacy guidance**: Co-administration of diclofenac with CYP2C9 inhibitors may enhance the drug exposure and toxicity of whereas co-administration with CYP2C9 inducers may lead to compromised efficacy of diclofenac. A dosage adjustment may be warranted when diclofenac is administered with CYP2C9 inhibitors or inducers.

Dihydrocodeine
Synalgos-DC®

Normal Response to Dihydrocodeine (CYP2D6: Intermediate Metabolizer)
INFORMATIVE

Decreased conversion of dihydrocodeine to the more active metabolite dihydromorphine is possible in CYP2D6 intermediate metabolizers. However, there is insufficient evidence whether these patients have decreased analgesia when taking dihydrocodeine. Adequate pain relief can be achieved by increasing the dose in response to pain symptoms.

Febuxostat
Uloric®

Normal Response to Febuxostat
INFORMATIVE

Pharmacogenetic guidance: Febuxostat is eliminated by both hepatic metabolism and renal excretion. The drug is metabolized both by glucuronidation (40%) and oxidative pathways (35%). The oxidative metabolism involves several cytochrome P450 enzymes (CYPs): CYP1A2, CYP2C8 and CYP2C9 as well as other non-CYP enzymes. Febuxostat is also glucuronidated primarily by UGT1A1 and UGT1A3. Preliminary studies indicate that febuxostat clearance is increased in subjects with UGT1A1*28 allele-UGT1A3*2a allele and decreased in those with the UGT1A1*6 allele. The clinical relevance of these changes is not known. Although serious skin and hypersensitivity reactions have been reported in patients taking febuxostat, there are no genetic biomarkers for predicting such reactions; no genotype-based recommendations are available. **Polypharmacy guidance:** Concomitant administration of febuxostat, a xanthine oxidase inhibitor, with substrate drugs such as theophylline, azathioprine or mercaptopurine could increase plasma concentrations of these drugs resulting in severe toxicity.

Fentanyl
Actiq®

Good Response to Fentanyl (OPRM1: Normal OPRM1 Function)
INFORMATIVE

The patient does not carry the OPRM1 118A>G variant. Acute postoperative and cancer pain: the patient is expected to experience good analgesia at standard fentanyl doses. 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.

Flurbiprofen
Ansaid®

Normal Flurbiprofen Exposure (CYP2C9: Normal Metabolizer)
ACTIONABLE

Rheumatoid Arthritis and Osteoarthritis: Flurbiprofen therapy can be initiated at standard label-recommended dosage and administration. Consider using the lowest effective dosage for the shortest duration consistent with the patient treatment goals.

Consider initiating treatment at the lowest end of the dosing range in geriatric patients. A dosage adjustment may be warranted when flurbiprofen is administered with CYP2C9 inhibitors or inducers.

Hydromorphone
Dilaudid®, Exalgo®

Normal Response to Hydromorphone — INFORMATIVE

No genetically guided drug selection or dosing recommendations are available. Hydromorphone is not metabolized by CYPs, and genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Hydromorphone can be prescribed at standard label-recommended dosage and administration.

Ibuprofen
Advil®, Motrin®

Normal Ibuprofen Exposure (CYP2C9: Normal Metabolizer) — ACTIONABLE

Pain, Dysmenorrhea, Rheumatoid Arthritis, Osteoarthritis, Fever and Other Anti-Inflammatory Uses: Ibuprofen therapy can be initiated at standard label-recommended dosage and administration. Consider using the lowest effective dosage for the shortest duration consistent with the patient treatment goals.

Consider initiating treatment at the lowest end of the dosing range in geriatric patients. A dosage adjustment may be warranted when ibuprofen is administered with CYP2C9 inhibitors or inducers.

Indomethacin
Indocin®

Normal Indomethacin Exposure — INFORMATIVE

Pharmacogenetic guidance: Indomethacin is metabolized mainly by O-demethylation to its inactive metabolite O-desmethyl indomethacin, a reaction catalyzed by CYP2C9. Genetic polymorphisms of CYP2C9 have not been found to affect the response to indomethacin. No genetically guided drug selection or dosing recommendations are available.

Ketoprofen
Orudis®

Normal Response to Ketoprofen — INFORMATIVE

Pharmacogenetic guidance: Ketoprofen is primarily eliminated by glucuronidation (by UGT1A3, UGT1A9 and UGT2B7) and no major implication of CYP2C9 in the metabolism of this drug has been demonstrated. No genetically guided drug selection or dosing recommendations are available.

Ketorolac
Toradol®

Normal Response to Ketorolac — INFORMATIVE

Pharmacogenetic guidance: Ketorolac is metabolized by glucuronidation (UGT enzymes) and oxidation but the enzymes catalyzing the oxidation are not well characterized. No genetically guided drug selection or dosing recommendations are available.

Leflunomide
Arava®

Normal Exposure to Leflunomide (CYP2C19: Ultra-Rapid Metabolizer) — INFORMATIVE

Leflunomide can be prescribed according to standard label-recommended dosage and administration.

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.

Levorphanol
Levo Dromoran®

Normal Response to Levorphanol — INFORMATIVE

Pharmacogenetic guidance: Levorphanol is metabolized by glucuronidation which is mediated by UGT2B7. There are no studies documenting the impact of genetic polymorphisms of this metabolizing enzyme on levorphanol response. And no genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** Enzyme inducing drugs are expected to increase levorphanol clearance significantly.

Meloxicam
Mobic®

Normal Meloxicam Exposure (CYP2C9: Normal Metabolizer) — ACTIONABLE

Pain, Rheumatoid Arthritis and Osteoarthritis: Meloxicam therapy can be initiated at standard label-recommended dosage and administration. Consider using the lowest effective dosage for the shortest duration consistent with the patient treatment goals.

Consider initiating treatment at the lowest end of the dosing range in geriatric patients. A dosage adjustment may be warranted when meloxicam is administered with CYP2C9 inhibitors or inducers.

Meperidine
Demerol®

Normal Response to Meperidine
INFORMATIVE

Pharmacogenetic guidance: no genetically guided drug selection or dosing recommendations are available. Meperidine is metabolized to normeperidine by multiple CYPs, including CYP2B6, CYP3A4, and CYP2C19. The effects of genetic variants in these enzymes have not been studied. **Polypharmacy guidance:** In patients taking **strong CYP inducers**, meperidine metabolism is increased resulting in higher levels of its neurotoxic metabolite normeperidine. In presence of ritonavir, meperidine's exposure is significantly reduced while normeperidine concentrations are increased. Based on these findings, the risk of narcotic-related adverse effects from this combination appears to be minimal. However, increased concentrations of normeperidine suggest a potential for toxicity with increased dosages or long-term therapy. This combination should be avoided is possible.

Metaxalone
Skelaxin®

Normal Response to Metaxalone
INFORMATIVE

Pharmacogenetic guidance: Metaxalone is extensively metabolized by multiple CYP enzymes, including CYP1A2, CYP2D6, CYP2E1, and CYP3A4. Genetic polymorphisms of these enzymes are unlikely to affect its exposure to a significant extent. no genetically guided drug selection or dosing recommendations are available.

Methocarbamol
Robaxin®

Normal Response to Methocarbamol
INFORMATIVE

Pharmacogenetic guidance: Methocarbamol is metabolized via dealkylation and hydroxylation. The enzymes responsible for the metabolism of this drug have not been characterized. No genetically guided drug selection or dosing recommendations are available.

Milnacipran
Savella®

Normal Response to Milnacipran
INFORMATIVE

Pharmacogenetic guidance: milnacipran is minimally metabolized by UGT enzymes and primarily excreted unchanged in urine. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy guidance:** coadministration of drugs that inhibit or induce CYP or UGT enzymes are unlikely to affect the exposure of milnacipran.

Nabumetone
Relafen®

Normal Response to Nabumetone
INFORMATIVE

Pharmacogenetic guidance: Nabumetone is a prodrug, which is converted by CYP1A2 to an active metabolite (6-MNA) that is further metabolized by CYP2C9 to an inactive metabolite. Theoretically, individuals with reduced CYP2C9 activity (i.e CYP2C9 poor metabolizers) may have higher levels of the active metabolite, but it is unknown whether this results in an altered drug response. No genetically guided drug selection or dosing recommendations are available. **Polypharmacy Guidance:** CYP1A2 inhibitors may inhibit the activation of nabumetone to its active metabolite resulting in a reduction in the therapeutic effects of this drug. On the other hand, CYP1A2 inducers (i.e smoking) may result in higher levels of nabumetone active metabolite, which may affect the response to this drug.

Naproxen
Aleve®

Normal Sensitivity to Naproxen
INFORMATIVE

Pharmacogenetic guidance: UGT2B7 is responsible for hepatic naproxen acyl glucuronidation, which is the primary elimination pathway for this drug (60% of total clearance). CYP2C9 and CYP1A2 are responsible for the formation of O-desmethylnaproxen but this pathway is not the primary pathway for the elimination for naproxen. Genetic polymorphism of CYP2C9 has not been found to affect the response to naproxen. No genetically guided drug selection or dosing recommendations are available.

Oxymorphone
Opana®, Numorphan®

Normal Response to Oxymorphone
INFORMATIVE

No genetically guided drug selection or dosing recommendations are available. Oxymorphone is not metabolized by CYPs, and genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Oxymorphone can be prescribed at standard label-recommended dosage and administration.

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Piroxicam
Feldene®

Normal Piroxicam Exposure (CYP2C9: Normal Metabolizer) — **ACTIONABLE**

Rheumatoid Arthritis and Osteoarthritis: Piroxicam therapy can be initiated at standard label-recommended dosage and administration. Consider using the lowest effective dosage for the shortest duration consistent with the patient treatment goals.

Consider initiating treatment at the lowest end of the dosing range in geriatric patients. A dosage adjustment may be warranted when piroxicam is administered with CYP2C9 inhibitors or inducers.

Sufentanil
Sufenta®

Normal Response to Sufentanil — **INFORMATIVE**

Pharmacogenetic guidance: No genetically guided drug selection or dosing recommendations are available.
Polypharmacy guidance: Sufentanil is primarily metabolized by CYP3A4 and so should be used with caution when prescribed with CYP3A4 inhibitors or inducers.

Sulindac
Clinoril®

Normal Response to Sulindac — **INFORMATIVE**

Pharmacogenetic guidance: Sulindac is primarily eliminated by glucuronidation which is catalyzed by several isoforms including UGT1A3, UGT1A9 and UGT2B7. The role of CYP2C9 in sulindac metabolism is of minor relevance. No genetically guided drug selection or dosing recommendations are available.

Tapentadol
Nucynta®

Normal Response to Tapentadol — **INFORMATIVE**

No genetically guided drug selection or dosing recommendations are available. Tapentadol is not metabolized by CYPs, and genetic variations in these metabolizing enzymes are not expected to affect its efficacy or toxicity profiles. Tapentadol can be prescribed at standard label-recommended dosage and administration.

Tofacitinib
Xeljanz®

Normal Exposure to Tofacitinib — **INFORMATIVE**

Pharmacogenetic guidance: Tofacitinib is metabolized primarily by CYP3A4 with some contribution from CYP2C19. Genetic variations in the CYP2C19 gene do not significantly influence tofacitinib exposure. Tofacitinib may be prescribed at standard dosing, but consider a dose reduction if a CYP2C19 poor metabolizer is also prescribed a CYP3A4 inhibitor such as ketoconazole, erythromycin, diltiazem, troleandomycin, nefazodone, fluconazole, verapamil or HIV protease inhibitors. **Polypharmacy guidance**: Tofacitinib dose should be reduced if a patient is taking strong CYP3A4 inhibitors (e.g., ketoconazole), or if a patient is taking a moderate CYP3A4 inhibitor (e.g., alprazolam) with a strong CYP2C19 inhibitor (e.g., fluconazole).

A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.	
Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate 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.
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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Test Details

Gene	Genotype	Phenotype	Alleles Tested
COMT	Val158Met G/G	**High/Normal COMT Activity**	Val158Met
CYP1A2	*1A/*1L	**Normal Metabolizer- Possible Inducibility**	*1C, *1D, *1F, *1K, *1L, *1V, *1W
CYP2B6	*1/*6	**Intermediate Metabolizer**	*6, *9
CYP2C19	*17/*17	**Ultra-Rapid Metabolizer**	*2, *3, *4A, *4B, *6, *7, *8, *9, *10, *17
CYP2C9	*1/*1	**Normal Metabolizer**	*2, *3, *4, *5, *6, *8, *11, *27
CYP2D6	*10/*17	**Intermediate Metabolizer**	*2, *3, *4, *4M, *6, *7, *8, *9, *10, *12, *114, *14, *17, *29, *35, *41, *5 (gene deletion), XN (gene duplication)
OPRM1	A118G A/A	**Normal OPRM1 Function**	A118G
TPMT	*1/*1	**Normal Metabolizer**	*2, *3A, *3B, *3C

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

Limitation: *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. There may be other genetic factors impacting individual patient dosing that are not included in this test.*

Disclaimer: *This test was developed and its performance characteristics determined by Vision Laboratories. It has not been cleared or approved by the US Food and Drug Administration (FDA). The FDA does not require this test to go through premarket FDA review. This test is used for clinical purposes. It should not be regarded as investigational or for research. This laboratory is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of information in this report.*

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 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.

Lab Director: Lekh Sharma, Ph.D., MT (AAB), TC (NRCC) | CLIA: 44D2080585 | 6130 Shallowford Road, 100, Chattanooga TN 37421 | visionlaboratories.com | 1.844.484.3522

Vision Laboratories

REPORT DETAILS
Name: Demo Patient
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Pharmacogenetic Test Summary

COMT	Val158Met G/G	High/Normal COMT Activity
CYP1A2	*1A/*1L	Normal Metabolizer- Possible Inducibility
CYP2B6	*1/*6	Intermediate Metabolizer
CYP2C19	*17/*17	Ultra-Rapid Metabolizer
CYP2C9	*1/*1	Normal Metabolizer
CYP2D6	*10/*17	Intermediate Metabolizer
OPRM1	A118G A/A	Normal OPRM1 Function
TPMT	*1/*1	Normal Metabolizer

For a complete report contact Vision Laboratories, LLC
visionlaboratories.com

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