IntelligeneCG, LLC
17745 Metcalf Ave
Stilwell, KS 66085
Phone: (913) 258 2300
info@intelligene-cg.com

Pharmacogenetic Test
Comprehensive Panel

Name:	**Patient ID:**
Sex:	**Sample ID:**
DOB:	**Sample Received Date:**
Ordering Provider:	**Report Date:**

Test Indication: Drug Metabolism Response

Quick Summary

ADHD

AMPHETAMINE (ADDERALL®) ATOMOXETINE (STRATTERA®) CLONIDINE (KAPVAY®) DEXMETHYLPHENIDATE (FOCALIN®) DEXTROAMPHETAMINE (DEXEDRINE®) GUANFACINE (INTUIV) LISDEXAMFETAMINE (VYVANSE®) METHAMPHETAMINE (DESOXYN) METHYLPHENIDATE (RITALIN®, CONCERTA®) RISPERIDONE (RISPERDAL®)	Consider label recommended dosage if no Contraindication

ANALGESIC - NON-OPIOID

ACETAMINOPHEN (TYLENOL) CELECOXIB (CELEBREX) DICLOFENAC (VOLTAREM, CATAFLAM) FLURBIPROFEN (ANSAID) IBUPROFEN (ADVIL, MOTRIM) KETOROLAC (TORADOL) MELOXICAM (MOBIC) NAPROXEN (ALEVE, NAPROSYN) PIROXICAM (FELDENE)	Consider label recommended dosage if no Contraindication

ANALGESIC - OPIOID

ALFENTANIL (ALFENTA) CODEINE FENTANYL (DURAGESIC) HYDROCODONE (VICODIN, NORCO, LORCET) HYDROMORPHONE (DILAUDID) MEPERDINE (DEMEROL) METHADONE (DOLOPHINE, METHADOSE) MORPHINE (MS CONTIN, KADIAN) OXYCODONE (OXYCONTIN) OXYMORPHONE (OPANA) TAPENTADOL (NUCYNTA) TRAMADOL (ULTRAM)	Consider label recommended dosage if no Contraindication

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ANTICOAGULANTS

ACENOCOUMAROL WARFARIN (COUMADIN®)	✔	Consider label recommended dosage if no contraindication

GENERAL ANESTHETICS

DESFLURANE (SUPRANE®) ISOFLURANE (FORANE®) NITROUS OXIDE (NITRONOX®) SEVOFLURANE (ULTANE®, SOJOURN®) SUCCINYLCHOLINE (ANECTINE®, QUELICIN®)	✔	Consider label recommended dosage if no contraindication

ANTIDEPRESSANTS

BUPROPION (WELLBUTRIN) DESVENLAFAXINE (PRISTIQ) DULOXETINE (CYMBALTA®) ESKETAMINE (SPRAVATO) LEVOMILNACIPRAN (FETZIMA) MOCLOBEMIDE (AMIRA, AURORIX) NEFAZODONE TRAZODONE (DESYREL, OLEPTRO) VENLAFAXINE (EFFEXOR®) VILAZODONE (VIIBRYD) VORTIOXETINE (TRINTELLIX)	✔	Consider label recommended dosage if no Contraindication.
AMITRIPTYLINE (ELAVIL®) CITALOPRAM (CELEXA®) ESCITALOPRAM (LEXAPRO®)	⊘	Consider alternative drug not metabolized by CYP2C19.
FLUOXETINE (PROZAC, SARAFEM) FLUVOXAMINE (LUVOX) PAROXETINE (PAXIL®, PEXEVA®)	⚠	Risk of decreased response
MIRTAZAPINE (REMERON)	⚠	Decreased, but not absent, risk of side effects
SERTRALINE (ZOLOFT®)	⚠	Risk of an increased response

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ANTICONVULSANTS/MOOD STABILIZERS

CARBAMAZEPINE (EQUETRO, TEGRETOL) GABAPENTIN (NEUROTIN) LAMOTRIGINE (LAMICTAL) LITHIUM (LITHOBID, ESKALITH) MEPHENYTOIN (MESANTOIN®) OXCARBAMAZEPINE (TRILEPTAL, OXTELLAR) PHENYTOIN (DILANTIN®) ANTIEPILEPTICS PREGABALIN (LYRICA) TOPIRAMATE (TOPAMAX) VALPROIC ACID (DEPAKOTE®, STAVZOR®)	Consider label recommended dosage if no Contraindication.

ANTIARRHYTHMICS

DIGOXIN (LANOXIN®, DIGITEK®) FLECAINIDE (TAMBOCOR™) PROPAFENONE (RYTHMOL SR®)	Consider label recommended dosage if no Contraindication.

ANTIHYPERTENSIVES

ATENOLOL (TENORMIN®) BENAZEPRIL (LOTENSIN®) ENALAPRIL (VASOTEC®, EPANED™) IMIDAPRIL (TANATRIL®) IRBESARTAN (AVAPRO®) LOSARTAN (COZAAR®, HYZAAR®) METOPROLOL (LOPRESSOR®, TOPROL XL®) TIMOLOL (TIMOPTIC®, ISTALOL®, BETIMOL®) VERAPAMIL (COVERA®, CALAN®, VERELAN®)	Consider label recommended dosage if no contraindication.

.ANTIDIABETICS

REPAGLINIDE (PRANDIN®) TOLBUTAMIDE (ORINASE®)	Consider label recommended dosage if no contraindication

ANTIPSYCHOTICS

ARIPIPRAZOLE (ABILIFY®) ASENAPINE (SAPHRIS) BEXPIPRAZOLE (REXULTI) CARIPRAZINE (VRAYLAR)	Consider label recommended dosage if no contraindication

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ILOPERIDONE (FANAPT) LURASIDONE (LATUDE) OLANZAPINE (ZYPREXA®) PALIPERIDONE (INVEGA) PIMAVANSERIN (NUPLAZID) QUETIAPINE (SEROQUEL) RISPERIDONE (RISPERDAL®) ZIPRASIDONE (GEODON)		
CLOZAPINE (CLOZARIL®, FAZACLO®)	⚠	Increased risk for weight gain

BENZODIAZEPINES

DIAZEPAM (VALIUM®)	✔	Consider label recommended dosage if no contraindication

CFTR

IVACAFTOR (KALYDECO®)	✔	Consider label recommended dosage if no contraindication

CHEMOTHERAPEUTICS

CISPLATIN (PLATINOL) LEUCOVORIN (FUSILEV®) MERCAPTOPURINE (PURINETHOL®) METHOTREXATE (TREXALL®) OXALIPLATIN (ELOXATIN®) PACLITAXEL (ABRAXANE®, TAXOL®, ONXOL®) TAMOXIFEN (NOLVADEX®, SOLTAMOX®) THIOGUANINE (TABLOID®)	✔	Consider label recommended dosage if no contraindication
CAPECITABINE (XELODA®) CYCLOPHOSPHAMIDE (CYTOXAN®) FLUOROURACIL (EFUDEX®) TEGAFUR	⚠	Unable to determine full genotyping results for this drug.

CORTICOSTEROIDS

PREDNISONE (DELTASONE®, STERAPRED®)	✔	Consider label recommended dosage if no Contraindication

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HEPATITIS, ANTIVIRALS

PEGINTERFERON-ALFA (PEGASYS®, PEGINTRON®) RIBAVIRIN (COPEGUS®, REBETOL®)	⚠	Increased risk for depression

HIV/AIDS

EFAVIRENZ (SUSTIVA®) NEVIRAPINE (VIRAMUNE®)	✔	Consider label recommended dosage if no contraindication.
NELFINAVIR (VIRACEPT®)	⚠	Risk of decreased metabolism and increased concentrations of nelfinavir

MISCELLANEOUS

BACLOFEN (LIORESAL) BUPRENORPHINE (BUTRANS) CARISOPRODOL (SOMA) CYCLOBENZAPRINE (FLEXERIL) DEUTETRABENZINE (AUSTEDO) DEXTROMETHORPHAN/QUINIDINE (NUEDEXTA) METAXALONE (SKELAXIN) METHOCARBAMOL (ROBAXIN) NALTREXONE (REVIA, VIVITROL) TIZANIDINE (ZANAFLEX) VALBENAZINE (INGREZZA)	✔	Consider label recommended dosage if no Contraindication

PLATELET AGGREGATION INHIBITORS

CLOPIDOGREL (PLAVIX®) TICGRELOR (BRILINTA)	✔	Consider label recommended dosage if no contraindication
PRASUGREL (EFFIENT)	⚠	Risk of a lower rate of high on-treatment platelet reactivity at 1 month of treatment.

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PROTON PUMP INHIBITORS

LANSOPRAZOLE (PREVACID®) OMEPRAZOLE (PRILOSEC®) PANTOPRAZOLE (PROTONIX®)	⚠ Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.

STATINS

ATORVASTATIN (LIPITOR®) FLUVASTATIN (LESCOL®) LOVASTATIN (ALTOPREV®, MEVACOR®) PRAVASTATIN (PRAVACHOL®) ROSUVASTATIN (CRESTOR®) SIMVASTATIN (ZOCOR®, SIMCOR®)	✔ Consider label recommended dosage if no contraindication

THROMBOPHILIA

Thrombophilia	✔ Patient is negative for the Factor V Leiden and Factor II Prothrombin variants.

IMMUNOSUPPRESSANTS

AZATHIOPRINE (IMURAN®) CYCLOSPORINE (SANDIMMUNE®) MERCAPTOPURINE (PURINETHOL®) SIROLIMUS (RAPAMUNE®) TACROLIMUS (PROGRAF®)	✔ Consider label recommended dosage if no contraindication

IMPORTANT

This Quick Summary provides a brief overview of the predicted response of the patient. This information is based solely on the genotype information and is not based on a complete patient profile. Detection or absence of variants does not replace the need for therapeutic monitoring. Physicians should consider the information contained in the Details section, as well as consider current prescriptions, family history, presenting symptoms, and other factors before making any clinical or therapeutic decisions.

✔ No negative assertions based on genotype. Prescribe as directed.
⚠ Genotype may present increased risk or decreased effectiveness; prescribe with caution.
⊘ Genotype may present increased risk or decreased effectiveness; select alternative drug.

Gene Summary

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GENE	GENOTYPE	PHENOTYPE
CYP2D6	*1/*1	Extensive (Normal) Metabolizer
CYP2C19	*1/*17	Rapid Metabolizer
CYP2C9	*1/*1	Extensive (Normal) Metabolizer
CYP3A4	*1/*1	Extensive (Normal) Metabolizer
CYP3A5	*1/*1	Extensive (Normal) Metabolizer
CYP1A2	*1A/*1A	Extensive (Normal) Metabolizer
CYP2B6	*1/*2	Extensive (Normal) Metabolizer
CYP2E1	Uncertain Allele	Unknown Metabolizer
DPYD	Uncertain Allele	Unknown Metabolizer
HLA-A	*31:01	Not Detected
HLA-B	*15:02	Not Detected
SLC6A4	S/S	Low Activity
SLCO1B1	*1A/*20	Indeterminate Metabolizer
TPMT	*1/*1	Extensive (Normal) Metabolizer
UGT1A1	*1/*1	Extensive (Normal) Metabolizer
UGT1A4	*1A/*1A	Extensive (Normal) Metabolizer
UGT2B15	*1/*1	Extensive (Normal) Metabolizer

Detailed Information

KEY FOR VARIANT-DRUG COMBINATION EVIDENCE

★★★ Replicated in multiple studies with statistical significance and strong effect size.
★★ Replicated in multiple studies with and without statistical significance and effect size may be minimal.
★ Not yet replicated or replicated but lacking clear evidence of an association.

AMITRIPTYLINE	CYP2C19 *1/*17 Rapid Metabolizer Increased metabolism of tertiary amines compared to normal metabolizers. Greater conversion of tertiary amines to secondary amines may affect response or side effects. Avoid tertiary amine use due to potential for sub-optimal response. Consider alternative drug not metabolized by CYP2C19. TCAs without major CYP2C19 metabolism include the secondary amines nortriptyline and desipramine. If a tertiary amine is warranted, utilize therapeutic drug monitoring to guide dose adjustments.	Evidence ★★
CITALOPRAM	CYP2C19 *1/*17 Rapid Metabolizer Increased metabolism when compared to extensive metabolizers. Lower plasma concentrations will increase probability of pharmacotherapy failure. Consider an alternative drug not predominantly metabolized by CYP2C19.	Evidence ★★

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CLOZAPINE	DRD2 rs6277 A/G Patients with the AG genotype may have an increased risk for weight gain when treated with clozapine or olanzepine as compared to patients with the AA genotype. Other genetic and clinical factors may also influence a patient's risk of side-effects.	Evidence ★
ESCITALOPRAM	CYP2C19 *1/*17 Rapid Metabolizer Increased metabolism when compared to extensive metabolizers. Lower plasma concentrations will increase probability of pharmacotherapy failure. Consider an alternative drug not predominantly metabolized by CYP2C19	Evidence ★★
FLUOXETINE	SLC6A4 S/S Low Activity Patients with the SLC6A4 HTTLPR short form (S allele)/SLC6A4 HTTLPR short form (S allele) genotype who are treated with fluoxetine may have decreased response and increased risk for side effects as compared to patients with the SLC6A4 HTTLPR long form (L allele)/HTTLPR long form (L allele) genotype. However, contradictory findings exist reporting no association with the genotype and fluoxetine response. Other genetic and clinical factors may also influence a patient's response to fluoxetine.	Evidence ★
FLUVOXAMINE	SLC6A4 S/S Low Activity Patients with the SLC6A4 HTTLPR short form (S allele)/HTTLPR short form (S allele) genotype who are treated with fluvoxamine may have decreased response or decreased improvement based on HAMD score reduction as compared to patients with the SLC6A4 HTTLPR long form (L allele)/HTTLPR long form (L allele) genotype. However, contradictory findings exist reporting either no association of the genotype with fluvoxamine response or the opposite effect with an association of the SLC6A4 HTTLPR long form (L allele)/HTTLPR long form (L allele) genotype and increased response. Other genetic and clinical factors may also influence a patient's response to fluvoxamine.	Evidence ★
LANSOPRAZOLE	CYP2C19 *1/*17 Rapid Metabolizer Decreased plasma concentrations of PPIs compared to CYP2C19 NMs; increased risk of therapeutic failure. Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.	Evidence ★★
MIRTAZAPINE	SLC6A4 S/S Low Activity Patients with the HTTLPR short form (S allele)/SLC6A4 HTTLPR short form (S allele) genotype who are treated with mirtazapine	Evidence ★

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	may have decreased, but not absent, risk of side effects as compared to patients with the SLC6A4 HTTLPR long form (L allele)/HTTLPR long form (L allele) genotype. Other genetic and clinical factors may also influence a patient's response to mirtazapine.	
NELFINAVIR	CYP2C19 rs4244285 A/G Patients with the AG genotype and pancreatic cancer or HIV may have decreased metabolism and increased concentrations of nelfinavir as compared to patients with the GG genotype. Other genetic and clinical factors may also influence metabolism and concentration of nelfinavir.	Evidence ★
OMEPRAZOLE	SLC6A4 S/S Low Activity Decreased plasma concentrations of PPIs compared to CYP2C19 NMs; increased risk of therapeutic failure. Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.	Evidence ★★
PANTOPRAZOLE	SLC6A4 S/S Low Activity Decreased plasma concentrations of PPIs compared to CYP2C19 NMs; increased risk of therapeutic failure. Initiate standard starting daily dose. Consider increasing dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis. Daily dose may be given in divided doses. Monitor for efficacy.	Evidence ★★
PAROXETINE	SLC6A4 S/S Low Activity Patients with the SLC6A4 HTTLPR short form (S allele)/HTTLPR short form (S allele) genotype who are treated with paroxetine may have an decreased response as compared to patients with the SLC6A4 HTTLPR long form (L allele)/HTTLPR long form (L allele) genotype. However, a number of contradictory findings exist showing an increased response for the HTTLPR short form (S allele)/HTTLPR short form (S allele) genotype. Further, studies exist reporting no association with the genotype and paroxetine response. Other genetic and clinical factors may also influence a patient's response to paroxetine.	Evidence ★
PEGINTERFERON-ALFA	SLC6A4 S/S Low Activity Patients with the HTTLPR short form (S allele)/HTTLPR short form (S allele) genotype and chronic hepatitis C may have an increased risk for depression when treated with peginterferon alfa-2b and ribavirin as compared to patients with the HTTLPR L allele/L allele	Evidence ★

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	genotype. Other genetic and clinical factors may also influence risk for depression in patients receiving peginterferon alfa-2b and ribavirin.	
PRASUGREL	CYP2C19 rs4244285 A/G Patients with the GG genotype who are treated with prasugrel may have a lower rate of high on-treatment platelet reactivity at 1 month of treatment as compared to patients with the AG or AA genotype. However, contradictory findings are reported. Other genetic and clinical factors may also influence a patient's response to prasugrel.	Evidence ★
RIBAVIRIN	SLC6A4 S/S Low Activity Patients with the HTTLPR short form (S allele)/HTTLPR short form (S allele) genotype and chronic hepatitis C may have an increased risk for depression when treated with peginterferon alfa-2b and ribavirin as compared to patients with the HTTLPR L allele/L allele genotype. Other genetic and clinical factors may also influence risk for depression in patients receiving peginterferon alfa-2b and ribavirin.	Evidence ★
SERTRALINE	SLC6A4 S/S Low Activity Patients with the SLC6A4 HTTLPR short form (S allele)/SLC6A4 HTTLPR short form (S allele) genotype who are treated with sertraline may have increased response as compared to patients with the SLC6A4 HTTLPR long form (L allele)/HTTLPR long form (L allele) genotype or the SLC6A4 HTTLPR short form (S allele)/HTTLPR long form (L allele) genotype. However, a study has also found no association between this genotype and response to sertraline. Other genetic and clinical factors may also influence a patient's response to sertraline.	Evidence ★

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Pharmacodynamic and Pharmacokinetics Gene Variations

Gene Result	Therapeutic Implications	Clinical Impact
ABCB1 [Normal activity]	ABCB1 encodes transporter and channel proteins that function as efflux pumps. • **This genotype confers normal activity**	No known significant clinical impact
ABCG2 [Normal activity]	ABCG2 gene encodes the breast cancer resistance protein (BCRP), which plays an important role in drug response and disposition. • **This genotype confers normal activity**	No known significant clinical impact
ADRA2A [Normal activity]	Alpha-2A Adrenergic Receptor (ADRA2A) is a receptor which plays an important role in norepinephrine signaling • **This genotype confers normal activity**	No known significant clinical impact
BDNF [Normal activity]	Brain-derived Neurotrophic Factor (BDNF) is a protein involved in neuronal development and neural plasticity • **This genotype confers normal activity**	No known significant clinical impact
CES1 [Normal activity]	This gene encodes a member of the carboxylesterase large family. They may participate in fatty acyl and cholesterol ester metabolism and may play a role in the blood-brain barrier system. • **This genotype confers normal activity**	No known significant clinical impact
COMT [Normal activity]	COMT have been linked to psychiatric disorders, including schizophrenia, opioid receptor-mediated pain perception, and breast cancer. The association of COMT polymorphisms with neuropsychiatric diseases is thought to be related to the metabolism of catecholamine neurotransmitters. • **This genotype confers normal activity**	Normal metabolism is expected (other factors may influence metabolism)
CYP2D6 IM *1/*1 [Normal Activity]	**Extensive (Normal) Metabolizer:** Variations in the CYP2D6 liver enzyme can result in altered drug metabolism and unexpected drug serum levels. • **This genotype confers normal activity**	Normal metabolism is expected (other factors may influence metabolism)

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CYP2C19 EM *1/*17 [Normal Activity]	**Rapid Metabolizer** Variations in the CYP2C19 liver enzyme can result in altered drug metabolism and unexpected drug serum levels • **A dose adjustment or alternate therapy may be considered**	**Be advised that there may be altered exposure to medications metabolized by CYP2C19**
CYP2C9 EM *1/*1 [Normal Activity]	**Extensive (Normal) Metabolizer:** Variations in the CYP2C9 liver enzyme can result in altered drug metabolism and unexpected drug serum levels • **This genotype confers normal activity**	Normal metabolism is expected (other factors may influence metabolism)
CYP3A4 EM *1/*1 [Normal Activity]	**Extensive (Normal) Metabolizer:** Variations in the CYP3A4/5 liver enzymes can result in altered drug metabolism and unexpected drug serum levels • 3A5 non-expresser • CYP3A activity is determined by the sum activity of the CYP3A family of genes; in adults the most influential are 3A4 and 3A5 • **This genotype confers normal activity**	Normal metabolism is expected (other factors may influence metabolism)
CYP3A5 EM *1/*1 [Normal Activity]	**Extensive (Normal) Metabolizer:** Variations in the CYP3A4/5 liver enzymes can result in altered drug metabolism and unexpected drug serum levels • **This genotype confers normal activity**	Normal metabolism is expected (other factors may influence metabolism
CYP2B6 EM *1/*2 [Normal Activity]	**Extensive (Normal) Metabolizer:** Variations in the CYP2B6 liver enzyme can result in altered drug metabolism and unexpected drug serum levels • **This genotype confers normal activity**	Normal metabolism is expected (other factors may influence metabolism)
CYP1A2 EM *1A/*1A [Normal activity]	Variations in the CYP1A2 liver enzyme can result in altered drug metabolism and unexpected drug serum levels. • **This genotype confers normal activity**	Normal metabolism is expected (other factors may influence metabolism)
CYP2E1 EM Uncertain Allele	CYP2E1 is a member of the cytochrome P450 family of drug metabolizing enzymes. It is constitutively expressed in the liver but makes up less than 1% of the total hepatic P450 isoforms. • **Unknown Metabolizer**	Unable to determine full genotyping results for this drug.

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DRD2 rs6277 A/G [Altered activity]	Dopamine Receptor D2 (DRD2) is a receptor activated by dopamine in the brain • **risk for weight gain**	**Be advised that there may be altered exposure to medications metabolized by DRD2**
DRD1 [Normal activity]	This gene encodes the D1 subtype of the dopamine receptor. The D1 subtype is the most abundant dopamine receptor in the central nervous system. • **This genotype confers normal activity**	No known significant clinical impact
DRD3 [Normal activity]	This gene encodes the D3 subtype of the five (D1-D5) dopamine receptors. • **This genotype confers normal activity**	No known significant clinical impact
DRD4 [Normal activity]	This gene encodes the D4 subtype of the dopamine receptor. It is a target for drugs which treat schizophrenia and Parkinson disease. • **This genotype confers normal activity**	No known significant clinical impact
DPYD EM Uncertain Allele	Dihydropyrimidine dehydrogenase is an essential gene in the pyrimidine metabolic pathway and involved in pharmacogenomics of fluoropyrimidine drugs. • **Unknown Metabolizer**	Unable to determine full genotyping results for this drug.
F2 [Normal activity]	Coagulation factor II is proteolytically cleaved to form thrombin in the first step of the coagulation cascade which ultimately results in the stemming of blood loss. F2 also plays a role in maintaining vascular integrity during development and postnatal life. • **This genotype confers normal activity**	No known significant clinical impact
F5 [Normal activity]	Factor V is an essential coagulation cofactor that enhances thrombin activation by factor Xa. Genetic variant of F5 (Factor V Leiden (FVL) polymorphism) has been associated with risk of venous thromboembolism (VTE). • **This genotype confers normal activity**	No known significant clinical impact
GRIK1 [Normal activity]	Glutamate Receptor Kainate 1 (GRIK1) is an excitatory neurotransmitter receptor. • **This genotype confers normal activity**	No known significant clinical impact

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GRIK4 [Normal activity]	This gene encodes a protein that belongs to the glutamate-gated ionic channel family. • **This genotype confers normal activity**	No known significant clinical impact
HLA-A *31:01 Not Detected [Normal]	Major histocompatibility complex, class I, A (HLA-A) is part of a cluster of genes known as the Human Leukocyte Antigen Complex Certain variants greatly increase risk of drug induced skin reactions. • **This genotype is associated with normal risk of skin reactions with carbamazepine**	**Normal risk of skin reactions with carbamazepine, oxcarbazepine**
HLA-B *15:02 Not Detected [Normal]	Major histocompatibility complex, class I, B (HLA-B) is part of a cluster of genes known as the Human Leukocyte Antigen Complex Certain variants greatly increase risk of drug induced skin reactions. • **This genotype is associated with normal risk of skin reactions with carbamazepine, oxcarbazepine, phenytoin and fosphenytoin**	**Normal risk of skin reactions with carbamazepine, oxcarbazepine, phenytoin/fosphenytoin**
MC4R [Normal activity]	Melanocortin 4 Receptor (MC4R) is a receptor that plays a central role in the control. • **This genotype confers normal activity**	No known significant clinical impact
MTHFR [Normal activity]	Methylenetetrahydrofolate Reductase (MTHFR) is an enzyme responsible for the conversion of folic acid to methylfolate which is a cofactor needed for serotonin, norepinephrine, and dopamine synthesis. • **This genotype confers normal activity**	No known significant clinical impact
OPRM1 [Normal activity]	opioid receptor mu 1 is an opioid receptor which is affected by endogenous and exogenous opioids OPRM1 is involved in response to opioids • **This genotype confers normal activity**	No known significant clinical impact
RYR1 [Normal activity]	RYR1 encodes the ryanodine receptor isoform 1, a calcium channel. It plays a critical role in calcium release and muscle contraction in skeletal muscle and is the primary locus for malignant hyperthermia susceptibility, a pharmacogenetic condition. • **This genotype confers normal activity**	No known significant clinical impact

IntelligeneCG, LLC
17745 Metcalf Ave
Stilwell, KS 66085
Phone: (913) 258 2300
info@intelligene-cg.com

Pharmacogenetic Test
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SLC6A2 [Normal activity]	This gene encodes a protein that responsible for reuptake of norepinephrine into presynaptic nerve terminals and is a regulator of norepinephrine homeostasis. • **This genotype confers normal activity**	No known significant clinical impact
SLC6A3 [Normal activity]	This gene encodes a dopamine transporter which is a member of the sodium- and chloride-dependent neurotransmitter transporter family. • **This genotype confers normal activity**	No known significant clinical impact
SLC6A4 S/S [Low activity]	Serotonin Transporter (SLC6A4) is a synaptic transporter protein responsible for serotonin reuptake **A dose adjustment or alternate therapy may be considered**	**Be advised that there may be altered exposure to medications metabolized by SLC6A4**
TPMT EM *1/*1 [Normal Activity]	TPMT encodes thiopurine S-methyltransferase which catalyzes the S-methylation of thiopurine drugs (such as 6-mercaptopurine (6-MP) and azathioprine) and aromatic and heterocyclic sulfhydryl compounds. • **This genotype confers normal activity**	Normal metabolism is expected (other factors may influence metabolism)
UGT1A1 EM *1/*1 [Normal activity]	Variations in the UGT1A1 liver enzyme can result in altered drug metabolism and unexpected drug serum levels. • **This genotype confers normal activity**	Normal metabolism is expected (other factors may influence metabolism)
UGT1A4 EM *1A/*1A [Normal activity]	Variations in the UGT1A4 liver enzyme can result in altered drug metabolism and unexpected drug serum levels. • **This genotype confers normal activity**	Normal metabolism is expected (other factors may influence metabolism)
UGT2B15 EM *1/*1 [Normal activity]	Variations in the UGT2B15 liver enzyme can result in altered drug metabolism and unexpected drug serum levels. **This genotype confers normal activity**	Normal metabolism is expected (other factors may influence metabolism)
5HT2C [Normal activity]	Serotonin Receptor 2C (5HT2C) is a receptor involved in the regulation of satiety. • **This genotype confers normal activity**	No known significant clinical impact

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VKORC1 [Normal activity]	The VKORC1 gene encodes the Vitamin K epoxide reductase, a key enzyme in the Vitamin K cycle and the pharmacological target of warfarin. Genetic variants of VKORC1 have been shown to be important genetic factors for warfarin dose and response. • **This genotype confers normal activity**	No known significant clinical impact

Disclaimer

- This test does not detect the presence of structural rearrangements of genes, such as copy number variation and large gene duplications, as this is a limitation of the next-generation sequencing method.
- The information presented on this report is provided as supplementary health information. The results presented are intended to be use by a physician, pharmacist or other healthcare professional in conjunction to the patient's clinical presentation, to advise a patient on the use of prescribed medications.
- This test is not a 510k cleared test but managed by CMS and FDA under the Clinical Laboratory Improvement Amendment (CLIA) as an LDT. The ordering physician is responsible for the diagnosis and management of disease and decisions based on the data provided. Results are dependent on adequate specimen collection and processing.

METHODOLOGY

***Genes Analyzed**: ABCB1, ABCG2, ADRA2A, BDNF, CES1, COMT, CYP1A2, CYP2B6, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP2E1, DPYD, DRD1, DRD2, DRD3, DRD4, F2, F5, GRIK1, GRIK4, HLA-A, HLA-B, HTR2A, MC4R, MTHFR, OPRM1, RYR1, SLC6A2, SLC6A3, SLC6A4, SLCO1B1, TPMT, UGT1A1, UGT2B15, UGT1A4, VKORC1 and HTR2C.*

- Genomic DNA was extracted from the submitted specimen and enriched for the genes analyzed (above). Next-generation automated sequencing was performed on the Illumina MiSeq platform.
- The alignment of the sequences generated was performed on the respective reference coding sequences deposited in the GenBank NCBI coding sequence and its flanking regions containing splice sites. Variant calls are generated using the Burrows-Wheeler Aligner (bwa) followed by GATK analysis. The same regions were also evaluated to find large deletions and/or insertions. This test detects 100% of substitution variants (95%CI=82-100) and 95% of small insertions and deletions (95%CI=98.5-100).
- This test was developed by IntelligeneCG. Performance and accuracy of this test were validated by CLIA (CLIA#17D2097343). This test has not been cleared or approved by the U.S Food and Drug Administration (FDA).

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