Health Care Practitioner's Reference Report

Name	Female	Report Date	2020-07-01
Surname	Case Study	Date of Sample Collection	2017-05-31
Ref Number	00001118	Date Sample Received	2016-05-19
Sample Type	Buccal Swab	Referring Practitioner	Female Case Study
Gender	Female	Estimated Weight	80
Age	29	Estimated Height	1.6
Race	White/Caucasian	Estimated Waist	80
Date of Birth	1990-01-01	Blood Pressure	High

GENE-Rx™

WELCOME & INTRODUCTION

Dear Female,

Welcome to your personalised GENE-Rx™ report!

The GENE-Rx™ test from GENEWAY™ is a comprehensive pharmacogenomics test (also referred to as the medication response test), which gives you an indication of how you may respond to hundreds of medications and compounds. Genetics account for much of the variability in an individual's response to drug therapies.

Cytochrome P450 (CYP450) enzymes, largely present in the liver, regulate the metabolism of most prescription drugs. Genetic testing detects DNA variations in the CYP450 and other biological systems, that affect the way a drug is metabolized by the body. These variations influence the therapeutic effect of the medications and the risk of adverse events.

The benefits of knowing your unique pharmacogenetic profile, include the selection of better, safer medications the first time, more accurate determination of appropriate dosages, reducing the risk of side-effects that encourage better medication adherence and the potential for decreased overall cost of health care.

The information included in the report and how to interpret it:

1. Explanation of pharmacogenomics.
2. A summation of your medical history as per the online Lifestyle Questionnaire you submitted.
3. Summary of the medications you have currently been prescribed, as per the online Lifestyle Questionnaire you submitted, and the impact thereof based on your genetic risk profile.
4. Dosing guidance and detailed gene-drug interaction description of the medications you have currently been prescribed.
5. Summary of your genetic results, giving you a bird's eye view of your phenotypic risk.
6. Interpretation of the overall risk management for selected conditions.
7. A gene-drug interaction table of substrates according to your genotypes.
8. Gene-drug interaction tables of inhibitors and inducers.
9. A table showing commonly prescribed drugs that are not primary substrates for CYP P450 enzymes.
10. Dosing guidance and detailed gene-drug interaction for other medications, and the effects thereof based on your genetic risk profile.
11. Additional information with links to resources.
12. A cutout of your GeneRx™ Test results.

Your referring Healthcare Practitioner can use the science-based recommendations to assist in personalising and refining your medication prescription, to optimise your response and minimize potential side-effects you may experience.

Best Regards,
The GENEWAY™ Team

UNDERSTANDING THE RESULTS

Pharmacogenetics is the study of inherited genetic differences in drug metabolic pathways which can affect an individual's response to certain drugs, in terms of their therapeutic effectiveness and adverse side effects. The way people respond to the same drug and dose varies greatly. Knowing a patient's pharmacogenetics offer the following advantages:

- Improve treatment efficacy
- Reduce risk for side-effects
- Improve compliance
- Guide dosage requirements
- Less hospitalisations

Pharmacodynamics and Pharmacokinetics

Pharmacodynamics is the study of what the drug does to the body. Pharmacodynamics is relevant in terms of therapeutic effects of the drug and includes the pharmacological response, its duration and magnitude observed, relative to the medicine's concentration at an active site as well as the mechanisms of action.

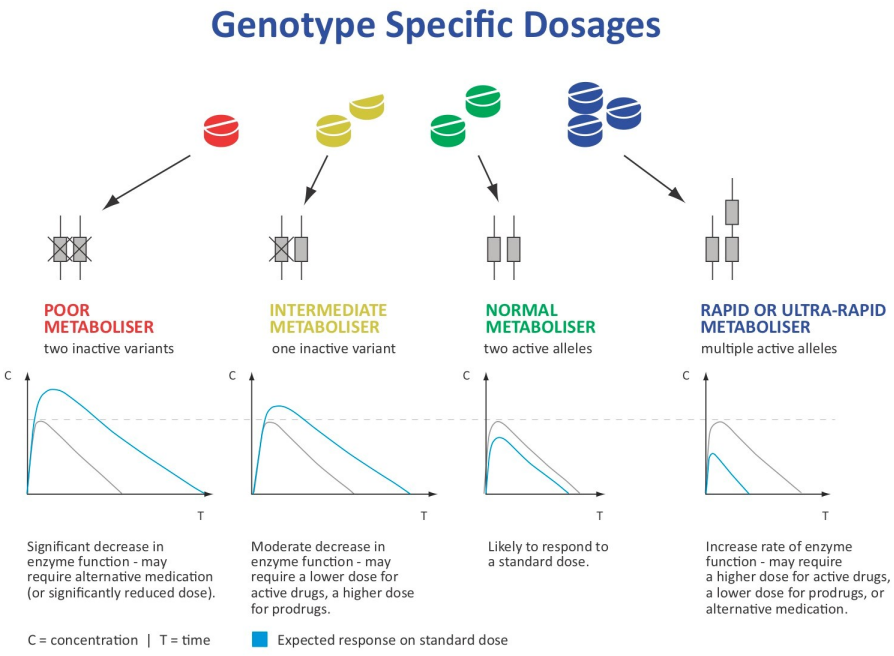
Pharmacokinetics is the study of what the body does to the drug. Pharmacokinetics informs us of the way in which drugs move through the body during absorption, distribution, metabolism and excretion. Pharmacokinetics influences the decided route of administration for the specific medication, the amount and frequency of each dose and its closing intervals. The pharmacokinetic term 'half-life' refers to the time taken to half the initial dose of medicine administered to be eliminated from the body.

Substrates, Inhibitors and Inducers

- Substrates are the medicines or compounds that are metabolised by the (gene) enzymes.
- Inhibitors are compounds that can inhibit the metabolism of the substrates and may lead to an increased plasma concentration of the substrate and increased risk of side-effects.
- Inducers have the capacity to increase the activity of the designated enzyme and therefore reduce the plasma concentrations of the listed substrates and may cause loss of efficacy.

Classification and genotype-specific dosage guidelines

The phenotype presentation of SNPs in these key drug metabolising genes can be used to distinguish whether an individual is a poor, intermediate, normal, rapid or ultra-rapid metaboliser of certain drugs. This can guide the physician whether a standard dosage will be effective or if a dosage adjustment is required.



Current Status

Personal History

- Cognitive
- Diabetes
- Fatty Liver
- Thyroid
- Overweight
- PCOS
- Pregnancy Loss
- Sleep
- Allergy: Fish

Family History

- Cognitive
- Inflammatory
- Hypertension
- Fatty Liver
- PCOS
- Pregnancy Loss
- Sleep
- Anaemias
- Bone density
- Insulin Resistance

Diet

- Fat Intake - High
- Fibre & Magnesium Intake - Moderate
- Folate Intake - Moderate

Physical Activity

- Physical Activity Level: Casual

Lifestyle

- Alcohol Consumption - Low
- Body Mass Index
- Non-Smoker

Pharmaceutical

- Vitamin B-complex
- Protein or other Shake
- Cortisone cream
- Anti-ageing/firming cream
- Methylphenidate
- Paroxetine
- Rosuvastatin
- Omeprazole
- Ethinylestradiol, Drospirenone
- Timolol

Gene-drug interactions for medications of interest

This summary is generated from the medications entered on the Lifestyle Questionnaire. Additional information about each of the medications listed below may be found on the following pages of this report.

NORMAL RESPONSE EXPECTED

MEDICATION	IMPACT
Rosuvastatin	Normal response
Methylphenidate	Normal response

PROCEED WITH CAUTION

MEDICATION	IMPACT

DECREASED RESPONSE

MEDICATION	IMPACT

POSSIBLE ALTERED RESPONSE

MEDICATION	IMPACT

Dosing & Pharmacogenetic Guidance

Based on the genetic results detected, drug prescribing and dosing suggestions using an evidence-based approach are indicated in the table below.

Actionable recommendations

Recommendations based upon publications by international pharmacogenetic expert groups or regulatory bodies (e.g. CPIC). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as new knowledge arises.

Informative recommendations

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.

Current Medication(s)

The pharmacogenetic guidance that follows is based on the patient's results and the list generated from the drugs the patient is currently taking, which were entered during completion of the lifestyle questionnaire.

COMT - Normal Metaboliser		
Methylphenidate	Informative	Normal response
Methylphenidate is thought to exert its therapeutic effects by increasing synaptic levels of dopamine and noradrenaline through the inhibition of dopamine and noradrenaline transporters. The genotype is predictive of a optimal response. Methylphenidate should be administered at the label-recommended and lowest effective dose. E.g. Ritalin, Concerta		
SLCO1B1 - Normal Metaboliser		
Rosuvastatin	Informative	Normal response
Medication can be prescribed according to standard regimens.		

Summary of the Genotype & Phenotype Results

Pharmacokinetics (PK) is the study of the rate and extent of drug absorption, distribution, metabolism and excretion. These processes determine the fate of a drug in the body. Genetic polymorphisms have been identified for cytochrome P450 enzymes giving rise to distinct phenotypes affecting your metabolism capabilities as shown in the table below.

Pharmacodynamics (PD) is the study of the pharmacologic effect resulting from the interaction between the drug and the biological system. Pharmacodynamics places particular emphasis on dose-response relationships - that is the relationships between drug concentration and effect.

Test Results

Genotype	Results	Risk	Phenotype & Clinical Consequences
CYP2D6	*1/*2x2		The activity score for the CYP2D6 genotype detected is 3. This is consistent with a Rapid Metaboliser phenotype. This patient may be at risk for an adverse or poor response to medications that are metabolized by CYP2D6. To avoid an unwanted drug response, dose adjustments may be necessary for medications metabolized by CYP2D6. Unlike most other CYP450 enzymes, CYP2D6 is not very susceptible to enzyme induction. Therefore, genetics, rather than drug therapy, accounts for most rapid CYP2D6 metabolisers.
CYP2C9	*1/*1		Normal (extensive) metaboliser. Drugs are metabolised at a normal rate. Typical (normal) risk of side effects and efficacy at standard recommended dosages are expected.
CYP2C19	*1/*2		Intermediate metaboliser. At risk for an adverse or poor response to medications that are metabolized by CYP2C19.
CYP1A2	*1A/*1F		Normal (extensive) metaboliser, increased inducibility. This genotype is classified as a normal metaboliser, but results in a rapid metaboliser phenotype in the presence of inducers. Drugs can be prescribed at standard-label recommendations, however, if inducers or inhibitors are co-prescribed, an increased risk for an adverse or poor response to medications is likely. Some of the more potent CYP1A2 inducers include beta-naptholflavone, insulin, methylcholanthrene, modafinil, nafcillin, omeprazole, tobacco, broccoli and Brussel sprouts.
CYP2B6	*1/*5		Intermediate metaboliser. At risk for an adverse or poor response to medications that are metabolized by CYP2B6. In general, lower substrate dosages are required in intermediate metabolisers and/or if inhibitors are co-administered with a substrate.
CYP3A4	*3/*22		Poor metaboliser. At significant risk for an adverse or poor response to medications that are metabolized by CYP3A4. The *22 (allele has significantly lower activity. One copy of the *22 allele has a clearance of CYP3A4-metabolised drugs reduced by 30 to 40%. The *22 frequency is only 3% of the world population. It is more common in Caucasians, with an allele frequency between 5 and 7%. Approximately 1 in every 17 Caucasians has one copy (*22).
CYP3A5	*3A/*3A		Poor metaboliser. At significant risk for an adverse or poor response to medications that are metabolized by CYP3A5. CYP3A5 poor metabolisers represent 50% of Asians and 90% of Caucasians. Clinically the most important drugs that are affected by CYP3A5 are: atazanavir, cyclosporine, felodipine, fentanyl, ifosfamide, lidocaine, midazolam, nifedipine, rivaroxaban, sildenafil, tacrolimus, triazolam, vardenafil, verapamil, vincristine.
Factor II	G/G		A normal (typical) risk of thrombosis (excess blood clotting) is associated with the Factor II (prothrombin) result. There are, however, other genetic and clinical factors that also contribute to the risk of thrombosis.
Factor V	G/G		The Factor V Leiden mutation is not detected and is consistent with a normal (typical) risk of thrombosis (excess blood clotting). There are, however, other genetic and clinical factors that also contribute to the risk of thrombosis.
MTHFR 1298	A/C		An increased risk of hyperhomocysteinemia and mood disorders such as anxiety and depression, is associated with the MTHFR 1298 result only in the presence of mutations in the MTHFR 677 gene. There are, however, other genetic and clinical factors that also contribute to the risk of these conditions.
MTHFR 677	C/C		A normal (typical) risk of hyperhomocysteinemia and mood disorders such as anxiety and depression, is associated with the MTHFR 677 result. There are, however, other genetic and clinical factors that also contribute to the risk of these conditions.

SLCO1B1	*1/*1		This result is consistent with normal SLCO1B1 transporter function and a normal (typical) risk of statin-induced myopathy.
VKORC1	*2/*2		Significantly reduced activity of the VKORC1 enzyme is associated with this result. A substantial decrease in warfarin dose may be required.
COMT	G/G		The result is consistent with normal COMT activity.
APOE	E2/E4		The E4 result is consistent with an increased risk for cardiovascular disease (e.g. hypercholesterolemia). The rare E2 variant is associated with type III hyperlipoproteinemia. Insufficient evidence is available demonstrating the clinical impact on cardiovascular risk based on the combination of the E2/E4 genotype.

Legend

	Significantly increased risk		Moderately increased risk		Typical (Normal) risk		No known impact

Major genotype-drug interaction identified that significantly affects the metabolism of the medication and/or indicates an elevated risk of adverse reaction or loss of efficacy.

Moderate genotype-drug interaction identified that affects the metabolism of the medication and/or indicates an elevated risk of adverse reaction or loss of efficacy.

Minimal (typical) genotype-drug interaction identified. Low risk of adverse reaction(s) and high likelihood of therapeutic efficacy.

None known or limited genetic impact.

Risk Management

Hyperlipidemia

At least one mutation was detected in the apolipoprotein E (APOE) gene and is associated with the increased risk of abnormal blood lipid metabolism. Defects in APOE can result in dyslipidemia, which is an important risk factor in the development of cardiovascular disease and atherosclerosis. Measurement of low-density lipoprotein (LDL), triglycerides (TG), very low-density lipoproteins (VLDL) and high-density lipoprotein (HDL) is recommended.

Thrombophilia

The genetic mutations associated with thrombophilia were not detected. Thrombophilia is an abnormal tendency to develop blood clots. The GeneRx test does not screen for all of the genes for abnormal blood clotting, thus other factors may affect the blood clotting risk assessment.

Hyperhomocysteinemia

The MTHFR 677 gene is involved in the DNA synthesis pathway and is essential for the remethylation of homocysteine to methionine. No mutations were detected which lowers the risk of high homocysteine levels. Hyperhomocysteinemia is multifactorial, involving a combination of other genetic and environmental factors .

Statin-induced myopathy

This result is associated with normal SLCO1B1 transporter function. The risk of statin-induced myopathy is not increased and typical statin metabolism is expected. In the absence of other risk factors and risk genes, standard doses of statins can be prescribed.

Dopamine Balance

The MTHFR and COMT genes play a vital role in mental health. The MTHFR gene is key to enable the brain to synthesize folate- dependent neurotransmitters like dopamine and serotonin, which are involved in a person's emotional well-being. The COMT gene breaks down said neurotransmitters. A gene mutation was detected and an impaired folate status is expected. This is associated with an increased risk for mood disorders e.g. anxiety, depression and possibly treatment-resistant depression (TRD). Methylfolate supplementation is recommended. In patients taking anti-depressants, a higher dose of methylfolate might be required to reduce the risk for TRD.

Warfarin Dosage

Variants in the CYP2C9 and/or VKORC1 genes were detected and can account for 40% of the variability in warfarin dosage requirements. The reduced enzyme activity leads to an increased level of the active S-warfarin. The patient may take longer to achieve a steady state and may require reduced maintenance doses of warfarin. Furthermore, carriers of APOE-E4 alleles may need a higher dose of warfarin in the treatment phase. Prevalence of gene variations differs with ethnicity. CYP2C9*2: Caucasian 13%, African 3%, Asian <1%. VKORC1*2: Caucasian 39%, African 11%, Asian 91%. www.WarfarinDosing.org

SUMMARY OF YOUR GENE-DRUG INTERACTION

Below is your personalised gene-drug interaction table classified according to your phenotype, indicating substrates, inhibitors and inducers of the genetic variations detected.

The substrates are the medications metabolised by the respective enzymes. Inhibitors slow the metabolism of the substrates and may lead to an increased concentration of the substrate, increasing the risk of side-effects. Inducers increase the activity of the enzyme, resulting in a reduction the substrate's concentration and may cause loss of therapeutic efficacy.

- In general, substrates can be prescribed at standard label recommended-dosages in normal metabolisers.
- In general, lower substrate dosages are required in intermediate metabolisers and/or if inhibitors are co-administered with a substrate.
- In general, higher substrate dosages are required in rapid or ultra-rapid metabolisers and/or if inducers are co-administered with a substrate.
- In general, substrates should be avoided in poor metabolisers.
- In general, indeterminate metabolisers have rare results for which no or limited research is available. Monitor patients closely if substrates are prescribed for indeterminate metabolisers.

Legend of Metaboliser Type

- Poor metaboliser / activity
- Intermediate metaboliser / activity
- Normal metaboliser / activity
- Rapid or Ultra-Rapid metaboliser / activity
- Indeterminate

●	Primary Substrate	○	Secondary Substrate	⇧	Prodrug
■	Primary Inducer	□	Secondary Inducer		
▲	Primary Inhibitor	△	Secondary Inhibitor		

GENE-DRUG INTERACTIONS (SUBSTRATES)

● Primary Substrate ○ Secondary Substrate ⇧ Prodrug

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Allergy																
Antihistamines																
Chlorphenamine	Allergex					●										
Loratadine	Alavert						●									
Olopatadine	Patanol						●									
Promethazine	Phenergan					●										
Glucocorticoid																
Betamethasone	Celestamine						●									
Ciclesonide	Zetonna						●									
Anaesthetics																
Anaesthetics (General)																
Bupivacaine	Exparel						●									
Ketamine	Ketacine						●									
Propofol	Diprivan		●													
Sevoflurane	Sevosol		○				○									
Anaesthetics (Local)																
Levobupivacaine	Chirocaine	○					○									
Mexiletine	Mexitil	●				●										
Ropivacaine	Naropin	●														
Anaesthetics (Topical)																
Thiopental	Pentothal			●												
Anti/Coagulants & Antiplatelets																
Anticoagulants																
Rivaroxaban	Xarelto						●	●								
Warfarin	Coumadin			●												
Antiplatelets																
Clopidogrel	Plavix				●											
Anti-addictives																
Alcohol dependence																
Disulfiram	Antabuse						●					○			●	●
Heroin Dependence																
Methadone	Physeptone						●									

●	Primary Substrate	○	Secondary Substrate	⇧	Prodrug

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Nicotine Dependence																
Bupropion	Wellbutrin		●			○										
Antihypertensives																
ACE Inhibitors																
Enalapril	Enap						●		●							
Angiotensin II Receptor Antagonists																
Irbesartan	Approvel			●												
Losartan	Cozaar			●			●	●								
Losartan	Zartan			●			●	●								
Antihypertensives (other)																
Clonidine	Catapres					●										
Diltiazem	Cardizem						●	●								
Indapamide	Prexum Plus						●									
Reserpine	Unipres								○							
Verapamil	Ravamil						●	●	○							
Beta-blockers																
Bisoprolol	Bilocor						○									
Carvedilol	Carloc					●										
Metoprolol	Lopressor					●										
Propranolol	Pur-Bloka	●			●	●										
Timolol	Timoptol					●										
Atenolol	Bio-atenolol					●										
Calcium channel blockers																
Amlodipine	Amloc						●	●								
Felodipine	Plendil						●	●								
Nifedipine	Fedaloc						●	●	○							
Antiobesity																
Serotonin receptor																
Dexfenfluramine	Redux					●										
Cardiology																
Antiarrhythmics																
Amiodarone	Pacerone						●									
Flecainide	Tambocor					●										
Diuretics																

●	Primary Substrate	○	Secondary Substrate	⇧	Prodrug

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Torasemide	Unat			○												
Fibrates																
Bezafibrate	Bezalip						●									
Fenofibrate	Lipanthyl						○									
Other Lipid Modifying Agents																
Ezetimibe	Zetia								○							
Statin (HMG CoA reductase inhibitors)																
Atorvastatin	Aspavor						●	●	●							
Pravastatin	Prava							○	●							
Simvastatin	Zocor						●	●	●							
Dermalogical																
Immunomodulators																
Pimecrolimus	Elidel						○									
Dietary																
Other																
Caffeine	Caffeine	●														
Polyphenols																
Nonflavonoids	Resveratrol (Antioxidant)	○														
Vitamins																
Alpha-Tocopherol acetate	Vitamin E						○									
Calcitriol	Vitamin D3						○									
Cholecalciferol	Vitamin D3		○				○									
Ergocalciferol	Vitamin D2						○									
Tocopherol	Vitamin E						○									
Endocrinology																
Androgen deficiency																
Testosterone propionate	Andronate						●									
Androgens																
Testosterone	Androxon		○	○			●	○								
Diabetes (Sulfonylureas)																
Glicazide	Diaglucide MR			●												
Glimepiride	Amaryl			●												
Glipizide	Minidiab			●												
Diabetes (Thiazolidinediones)																

●	Primary Substrate	○	Secondary Substrate	⇧	Prodrug

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Pioglitazone	Actos			○			○		○							
Emergency contraceptives																
Levonorgestrel	Plan B One-Step						○									
Estren derivatives																
Norethisterone	Primolut-Nor						○	○								
Estrogens																
Estradiol	Estrofem	●					●		○			○				
Ethinylestradiol, Drospirenone	Yasmin / Yaz						●									
Progesterone																
Progesterone	Progest			○	○		●		○							
Progestogen																
Dienogest	Visanne						○									
Dienogest, Estradiol valerate	Qlaira						●									
Gastroenterology																
Antiemetics																
Ondansetron	Zofer	●			●	●	●	●								
Antipropulsives																
Loperamide	Imodium					○	○									
Heartburn (Propulsives)																
Domperidone	Equidone					●										
Proton Pump Inhibitors																
Esomeprazole	Nexium				●											
Lansoprazole	Lancap				●											
Omeprazole	Altosec				●											
Pantoprazole	Topzole				●				○							
Rabeprazole	Pariet				●		●	●								
Immunosuppression																
Immunomodulators																
Cyclosporine	Cequa						●	●	○							
Infectious																
Antibiotics																
Amoxicillin	Augmentin SR				○											
Antibiotics (Macrolides)																
Clarithromycin	Biaxin						●	○								

●	Primary Substrate	○	Secondary Substrate	⇧	Prodrug

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Erythromycin	Theramycin						●		○							
Telithromycin	Ketek						●	●	○							
Antibiotics (TB)																
Rifampicin	IsonaRif						●		○							
Antifungals																
Terbinafine	Lamisil	●		●	●		●									
Antimalarials																
Atovaquone, Proguanil (prodrug)	Malanil				●											
Antimalarials (Aminoquinolines)																
Chloroquine	Aralen						●	●								
Antimalarials (Biguanides)																
Proguanil (prodrug)	Paludrine				●											
Anti-parasites																
Albendazole	Zentel				●											
Mebendazole	Vermox						●									
Praziquantel	Equimax						●									
Antiretroviral																
Efavirenz	Stocrin		●				○									
Nevirapine	Viramune		●				●	●								
Antivirals																
Acyclovir	Lidovir	○														
Famciclovir	Famvir						●									
Protease Inh (HIV)																
Nelfinavir	Viracept				●				○							
Saquinavir	Fortovase						●	●								
Neurology																
Anti-ADHD Agents																
Atomoxetine	Strattera					●						●				
Clonidine	Menograine					●										
Anti-epileptics																
Carbamazepine	Tegretol						●	●								
Clobazam	Urbanol				●											
Ethosuximide	Zarontin						●									
Phenytoin	Epanutin			●												

●	Primary Substrate	○	Secondary Substrate	⇧	Prodrug

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Anti-migraine																
Zolmitriptan	Zomig	○														
Dementia, Alzheimers, Parkinsons																
Donepezil	Aricept					●	●									
Ropinirole	Requip	○					○									
Rasagiline	Azilect	●														
Oncology																
Aromatase inhibitors																
Exemestane	Aromasin						●									
Letrozole	Femara						○									
Chemotherapy																
Fluorouracil	Fluoroplex	○													○	○
Methotrexate	Abitrexate						○		○						●	●
Vinblastine	Velban						○		○							
Vincristine	Vincasar						●	●	○							
Tamoxifen	Kessar		○	○	○	⇧	○	○					○	○		
Other																
Neurotransmitters																
Dopamine, Nor/Epinephrine					○							○				
Pain Management																
Analgesic																
Acetaminophen (Paracetamol)	Panado, Tylenol	○				○	○									
Anesthetics - topical																
Lidocaine	Xylocaine	●	●	○		●	●	●								
Anti-inflammatory (Corticosteroids)																
Clobetasol propionate	Dovate						○									
Fludrocortisone	Florinef						○									
Fluticasone	Foxair						●		○							
Hydrocortisone	Cortaid						●	○								
Methylprednisolone	Advantan						○									
Anti-inflammatory (Glucocorticoid)																
Prednisolone (prodrug)	Aspelone (0201)						○									
Prednisone	Be-tabs prednisone						○									
Anti-inflammatory (NSAIDs)																

●	Primary Substrate	○	Secondary Substrate	⇧	Prodrug

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Acetylsalicylic acid (Aspirin)	Ecotrin			○												
Celecoxib	Celebrex			●												
Diclofenac	Voltaren			●			●		○							
Diclofenac sodium	Panamor			●			●									
Etoricoxib	Arcoxia						●									
Flurbiprofen	Transact			●												
Ibuprofen	Nurofen			●	●											
Ibuprofen, Acetaminophen (Paracetamol), Code	Mybulen	○		●	●	○	○	○								
Indomethacin	Tivorbex								○							
Meloxicam	Mobic			●												
Naproxen	Vimovo			●												
Piroxicam	Xycam			●												
Muscle Pain & Muscle Relaxants																
Cyclobenzaprine	Myprocam	●				●	●									
Pentoxifylline	Pentoxil	○														
Opioids																
Acetaminophen (Paracetamol), Caffeine, Codein	Adco-Dol	○		○		○	○	○								
Acetaminophen (Paracetamol), Codeine	Genpayne	○		○		○	○	○								
Buprenorphine	Suboxone						●	○								
Dihydrocodeine	DF118 Forte					●										
Fentanyl	Durogesic						○	●								
Meperidine	Pethidine		●													
Methadone	Physeptone	○	●	●	●	○	●	○								
Morphine	MST					○	○					●				
Tramadone	Tramacet					●										
Sedatives & Hypnotics																
Acetaminophen (Paracetamol), Caffeine, Codein	Stilpane	○		○	○	○	○	○								
Psychotropic																
Antidepressants (NaSSA)																
Mirtazapine	Remeron	●				●	●									
Antidepressants (Other)																
Bupropion	Wellbutrin		●			○	○									
Nefazodone	Serzone					●	○									
Venlafaxine	Venlor					●										

●	Primary Substrate	○	Secondary Substrate	⇧	Prodrug

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Vortioxetine	Brintellix					●										
Antidepressants (SNRI)																
Desvenlafaxine	Exsira				○		○									
Duloxetine	Cymgen	●				●										
Antidepressants (SSRI)																
Citalopram	Cilift				●											
Escitalopram	Lexamil				●											
Fluoxetine	Prozac			●		○										
Fluvoxamine	Luvox	●				●										
Paroxetine	Aropax					●										
Sertraline	Serdep				●											
Antidepressants (TCA)																
Amitriptyline	Trepiline				●	●										
Clomipramine	Clomidep				●	●										
Imipramine	Tofranil				●	●										
Antipsychotics																
Aripiprazole	Abilify					●	●									
Chlorpromazine	Largactil					●										
Haloperidol	Serenace					●										
Prochlorperazine	Compro					○	○									
Quetiapine	Dopaquel					○	●									
Risperidone	Risperdal					●	○									
Trifluorperazine	Stelazine	○														
Ziprasidone	Geodon	●					●	●								
Anxiolytics																
Buspirone	Buspar						●	●								
Chlordiazepoxide	Librax	○					○									
Benzodiazepines																
Alprazolam	Xanor						●	●								
Clonazepam	Rivotril						●									
Clozapine	Leponex	○			●	●										
Sedatives & Hypnotics																
Melatonin	Restone	●														
Meprobamate	Synaleve				○											

●	Primary Substrate	○	Secondary Substrate	⇧	Prodrug

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Modafinil	Provigil						●									
Zolpidem	Stilnox MR						●	●								
Zopiclone	Zopivane			○			○									
Sedatives (Benzodiazepine)																
Midazolam	Dormicum						●	●								
Temazepam	Normison		●													
Triazolam	Halcion						●	●								
Respiratory																
Antimuscarinic																
Ipratropium bromide	Duolin Respules					○	○									
Asthma / COPD																
Aformoterol	Brovana					●										
Aminophylline	Norstan	○					○									
Dextromethorphan	Uni-Tris			●		●										
Salmeterol	Foxair						●	●								
Theophylline	Alcophyllex	○														
Vilanterol	Relvar						●									
Rheumatology																
Anti-hyperuricemics / Anti-gout Agents																
Colchicine	Colcrys						●									
Immunomodulators																
Leflunomide	Arava				●											
Transplantation																
Immunosuppression																
Azathioprine	Azapress	○													○	○
Tacrolimus	Protopic						●	●	○							
Urology																
5-Alpha Reductase Inhibitors																
Dutasteride	Duodart						●									
Finasteride	Propecia						●	●								
Alpha-Blockers for Benign Prostatic Hyperplasia																
Doxazosin	Cardura				○	○										
Silodosin	Silodyx						●									
Tamsulosin	Uromax					●	●	●								

●	Primary Substrate	○	Secondary Substrate	⇧	Prodrug

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Antispasmodics for Overactive Bladder																
Darifenacin	Enablex						●									
Oxybutynin	Ditropan						●	●								
Erectile Dysfunction																
Sildenafil	Viagra			●			○	●	○							
Tadalafil	Cialis						●	○								
Vardenafil	Levitra			●			○	●								

Inducer: a drug or nutrient which increases the activity of the enzymes (genes) resulting in a decrease in the effect of the substrates (drugs).
An increase in the dose of the affected substrates (drugs) may be necessary.

GENE-DRUG INTERACTIONS (INDUCERS)

■ Primary Inducer ☐ Secondary Inducer

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Anti-addictives																
Nicotine Dependence																
Bupropion	Wellbutrin		☐													
Nicotine	Nicorette	■														
Antihypertensives																
Antihypertensives (other)																
Reserpine	Unipres							☐								
Calcium channel blockers																
Nifedipine	Fedaloc			☐												
Dietary																
Botanicals																
Echinacea purpurea (Immunostimulant)	Echinacea						☐									
Foods																
Cruciferous vegetables	Broccoli, Brussels Sprouts	☐														
Herbal																
Ginkgo Biloba	Ginkgo Biloba						☐									
Hypericum perforatum (Antidepressant)	St John's Wort			☐	☐		☐									
Vitamins																
Calcitriol	Vitamin D3						☐									
Endocrinology																
Diabetes (Thiazolidinediones)																
Pioglitazone	Actos						■									
Estren derivatives																
Norethisterone	Primolut-Nor				☐											
Estrogens																
Estradiol	Estrofem						☐									
Progesterone																
Progesterone	Progest				☐											
Immunosuppression																
Immunomodulators																

■ Primary Inducer ☐ Secondary Inducer

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Cyclosporine	Cequa							☐								
Infectious																
Antibiotics (TB)																
Rifampicin	IsonaRif	■			■	■	■									
Rifampin	Rimactazid						■									
Antifungals																
Griseofulvin	Fulvicin U/F	☐				☐										
Terbinafine	Lamisil						☐									
Antiretroviral																
Efavirenz	Stocrin						■	■								
Nevirapine	Viramune		☐				■									
Neurology																
Anti-epileptics																
Carbamazepine	Tegretol	■			■		■	☐								
Phenobarbital	Sedabarb			■			■	■								
Phenytoin	Epanutin					■	■									
Primidone	Mysoline	■				■	■									
Topiramate	Topamax						■									
Pain Management																
Analgesic																
Acetaminophen (Paracetamol)	Panado, Tylenol						☐									
Anti-inflammatory (Glucocorticoid)																
Prednisone	Be-tabs prednisone				■											
Anti-inflammatory (NSAIDs)																
Acetylsalicylic acid (Aspirin)	Ecotrin				☐											
Ibuprofen, Acetaminophen (Paracetamol), Code	Mybulen						☐									
Opioids																
Acetaminophen (Paracetamol), Caffeine, Codein	Adco-Dol						☐									
Acetaminophen (Paracetamol), Codeine	Genpayne						☐									
Sedatives & Hypnotics																
Acetaminophen (Paracetamol), Caffeine, Codein	Stilpane						☐									
Psychotropic																
Antidepressants (Other)																
Bupropion	Wellbutrin		☐													

■	Primary Inducer	☐	Secondary Inducer

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Sedatives & Hypnotics																
Modafinil	Provigil	☐					☐	☐								
Respiratory																
Asthma / COPD																
Montelukast	Singulair	■														

Inhibitor: a drug or nutrient which decreases the activity of the enzymes (genes) resulting in an increase in the effect of the substrates (drugs).
A decrease in the dose of the affected substrates (drugs) may be necessary.

GENE-DRUG INTERACTIONS (INHIBITORS)

▲ Primary Inhibitor △ Secondary Inhibitor

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Allergy																
Antihistamines																
Chlorphenamine	Allergex					△										
Desloratadine	Clarinex				△	△										
Hydroxyzine	Atarax					△										
Anaesthetics																
Anaesthetics (General)																
Isoflurane	Forane		▲													
Ketamine	Ketacine		▲													
Propofol	Diprivan						△									
Anaesthetics (Local)																
Levobupivacaine	Chirocaine						△									
Anaesthetics (Topical)																
Thiopental	Pentothal						△									
Antidotes																
Naloxone	Narcan						▲									
Anti/Coagulants & Antiplatelets																
Anticoagulants																
Warfarin	Coumadin									△						
Anti-addictives																
Alcohol dependence																
Disulfiram	Antabuse	△														
Heroin Dependence																
Methadone	Physeptone					▲	△									
Nicotine Dependence																
Bupropion	Wellbutrin					▲										
Antihypertensives																
Angiotensin II Receptor Antagonists																
Irbesartan	Approvel						△									
Telmisartan	Co-Pritor				△											
Losartan	Cozaar				△		△									

▲	Primary Inhibitor	△	Secondary Inhibitor

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Losartan	Zartan				△		△									
Antihypertensives (other)																
Diltiazem	Cardizem						△	△								
Reserpine	Unipres								△							
Verapamil	Ravamil					△	△	△	△							
Beta-blockers																
Metoprolol	Lopressor					△										
Propranolol	Pur-Bloka					△										
Calcium channel blockers																
Amlodipine	Amloc		△	△		△										
Felodipine	Plendil			△		△	△									
Nifedipine	Fedaloc						△		△							
Antiobesity																
Serotonin receptor																
Dexfenfluramine	Redux					△										
Fenfluramine	Pondimin					△										
Cardiology																
Antiarrhythmics																
Amiodarone	Pacerone						△	△								
Fibrates																
Fenofibrate	Lipanthyl			△												
Other Lipid Modifying Agents																
Ezetimibe	Zetia						△									
Statin (HMG CoA reductase inhibitors)																
Atorvastatin	Aspavor								△							
Pravastatin	Prava								△							
Simvastatin	Zocor						△		△							
Dermalogical																
Immunomodulators																
Pimecrolimus	Elidel						△									
Dietary																
Botanicals																
Echinacea purpurea (Immunostimulant)	Echinacea	△					△									
Hydrastis canadensis (Respiratory /Colds)	Goldenseal					△	△	△								

▲	Primary Inhibitor	△	Secondary Inhibitor

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Foods																
Naringin, naringenin	Grapefruit (juice)						△	△								
Herbal																
Ginkgo Biloba	Ginkgo Biloba		△	△												
Polyphenols																
Curcuma longa	Curcumin	△	△	△		△	△									
Flavonoids	Quercetin, Kaempferol, Galang						△									
Nonflavonoids	Resveratrol (Antioxidant)	△					△									
Nonflavonoids	Tannins (tea), Lignans (fibre)						△									
Phenolic acids (Hydroxycinnamic)	Caffeic acid						△									
Vitamins																
Cholecalciferol	Vitamin D3					△										
Niacin	Vitamin B3					△										
Endocrinology																
Androgen deficiency																
Testosterone propionate	Andronate											△				
Diabetes (Thiazolidinediones)																
Pioglitazone	Actos								△							
Progesterone																
Progesterone	Progest						△		△							
Selective estrogen receptor modulators																
Raloxifene	Evista						△									
Gastroenterology																
Antiemetics																
Metoclopramide	Clopamon					▲										
Antipropulsives																
Loperamide	Imodium		△				▲									
H2 receptor antagonists																
Cimetidine	Tagamet			△	△	△	△	△								
Ranitidine	Zantac					▲										
Proton Pump Inhibitors																
Esomeprazole	Nexium				△											
Lansoprazole	Lancap				▲											
Omeprazole	Altosec				△											

▲	Primary Inhibitor	△	Secondary Inhibitor

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Pantoprazole	Topzole				△				△							
Immunosuppression																
Immunomodulators																
Cyclosporine	Cequa							△	△							
Infectious																
Antibiotics																
Clindamycin	Duac						▲									
Metronidazole	Flagyl			△			△									
Nystatin	Mycostatin						△		△							
Tetracycline	Pylera						△									
Antibiotics (Fluoroquinolones)																
Ciprofloxacin	Ciprodex	▲														
Levofloxacin	Tavanic	△					△									
Moxifloxacin	Moxeza	△														
Norfloxacin	Noroxin						△	△								
Antibiotics (Macrolides)																
Clarithromycin	Biaxin						▲	▲								
Erythromycin	Theramycin		△				△	△	△							
Telithromycin	Ketek						▲	△	△							
Antibiotics (TB)																
Rifampicin	IsonaRif								△							
Antifungals																
Clotrimazole	Lotrisone						▲									
Fluconazole	Diflucan			▲	▲											
Terbinafine	Lamisil					▲										
Antimicrobial (Sulfonamides)																
Sulfamethoxazole	Purbac DS			▲			△									
Antiretroviral																
Efavirenz	Stocrin						▲									
Lopinavir	Aluvia						▲									
Nevirapine	Viramune					▲										
Protease Inh (HIV)																
Nelfinavir	Viracept						▲	▲	△							
Ritonavir	Aluvia					▲	▲									

▲	Primary Inhibitor	△	Secondary Inhibitor

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Saquinavir	Fortovase						▲	△								
Neurology																
Anti-ADHD Agents																
Atomoxetine	Strattera					△	△									
Anti-epileptics																
Acetazolamide	Diamox						△									
Topiramate	Topamax				▲											
Dementia, Alzheimers, Parkinsons																
Biperiden	Akineton					△										
Entacapone	Comtan					△						△				
Memantine	Ebixa		△		△											
Ropinirole	Requip					△										
Tolcapone	Tasmar			△								△				
Oncology																
Aromatase inhibitors																
Anastrozole	Arimidex			△			△									
Chemotherapy																
Fluorouracil	Fluoroplex					△										
Vinblastine	Velban					△	△		△							
Vincristine	Vincasar						△		△							
Tamoxifen	Kessar			△		△	△									
Protein Kinase Inhibitors																
Acalabrutinib	Calquence						△	△								
Pain Management																
Analgesic																
Acetaminophen (Paracetamol)	Panado, Tylenol						△									
Anesthetics - topical																
Lidocaine	Xylocaine	△	△			△										
Anti-inflammatory (Corticosteroids)																
Fluticasone	Foxair						△		△							
Anti-inflammatory (NSAIDs)																
Celecoxib	Celebrex					▲										
Diclofenac	Voltaren								△							
Ibuprofen, Acetaminophen (Paracetamol), Code	Mybulen						△									

▲	Primary Inhibitor	△	Secondary Inhibitor

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Indomethacin	Tivorbex				△				△							
Opioids																
Acetaminophen (Paracetamol), Caffeine, Codein	Adco-Dol	△					△									
Acetaminophen (Paracetamol), Codeine	Genpayne						△									
Buprenorphine	Suboxone						△									
Methadone	Physeptone					△	△									
Sedatives & Hypnotics																
Acetaminophen (Paracetamol), Caffeine, Codein	Stilpane	△					△									
Psychotropic																
Antidepressants (NaSSA)																
Mirtazapine	Remeron						△									
Antidepressants (Other)																
Bupropion	Wellbutrin					▲										
Nefazodone	Serzone					△	▲	▲								
Tranylcypromine	Parnate			△	△	△	△									
Venlafaxine	Venlor					▲										
Antidepressants (SNRI)																
Desvenlafaxine	Exsira						△									
Duloxetine	Cymgen					△										
Antidepressants (SSRI)																
Citalopram	Cilift				△	△										
Escitalopram	Lexamil					△										
Fluoxetine	Prozac				▲	▲										
Fluvoxamine	Luvox	▲		▲	▲	△										
Paroxetine	Aropax					▲										
Sertraline	Serdep			△		▲										
Antidepressants (TCA)																
Amitriptyline	Trepiline				▲											
Clomipramine	Clomidep				▲	△										
Imipramine	Tofranil				▲											
Antipsychotics																
Chlorpromazine	Largactil					△										
Haloperidol	Serenace					△										
Risperidone	Risperdal					△										

▲	Primary Inhibitor	△	Secondary Inhibitor

ACTIVE INGREDIENT / MEDICATION	TRADE NAME	CYP1A2	CYP2B6	CYP2C9	CYP2C19	CYP2D6	CYP3A4	CYP3A5	SLCO1B1	VKORC1	APOE	COMT	FACTOR2	FACTOR5	MTHFR1298	MTHFR677
Ziprasidone	Geodon						▲									
Anxiolytics																
Hydroxyzine	Atarax					▲										
Benzodiazepines																
Clozapine	Leponex				△	△										
Sedatives & Hypnotics																
Modafinil	Provigil				△											
Sedatives (Benzodiazepine)																
Midazolam	Dormicum						△									
Respiratory																
Asthma / COPD																
Salbutamol	Duolin Respules						△									
Rheumatology																
Anti-hyperuricemics / Anti-gout Agents																
Colchicine	Colcrys						△									
Probenecid	Benemid				△											
Transplantation																
Immunosuppression																
Tacrolimus	Protopic								△							
Urology																
Antispasmodics for Overactive Bladder																
Oxybutynin	Ditropan					△	△									
Erectile Dysfunction																
Sildenafil	Viagra								△							

Commonly prescribed drugs that are NOT primary substrates for CYP P450 enzymes

Allergy	Endocrinology	Oncology
Phenylephrine	Exenatide	Afatinib*
Desloratadine	Ibandronate	Afutuzumab*
Analgesic/Anesthesiology	Levothyroxine	Alemtuzumab*
Dexmedetomidine	Metformin	Asparaginase
Hydromorphone	Propylthiouracil	Bevacizumab*
Morphine	Raloxifene	Carboplatin
Naloxone	Vasopressin	Cetuximab*
Propofol**	Haematology	Ibritumomab*
Anti-inflammatory	Azacitidine	Lenalidomide
Beclomethasone	Darbepoetin alfa	Obinutuzumab
Anticoagulant/Antiplatelet	Decitabine	Ofatumumab*
Dalteparin	Epoetin alfa	Oxaliplatin
Enoxaparin	Infectious Disease	Panitumumab*
Heparin	Abacavir	Pemetrexed
Prasugrel**	Atazanavir	Pertuzumab*
Cardiovascular	Ceftriaxone	Rituximab*
Atenolol**	Flucytosine	Temozolomide
Chlorthalidone	Levofloxacin	Thalidomide
Colesevelam	Meropenem	Trastuzumab*
Digoxin**	Moxifloxacin	Vorinostat
Enalapril ** (SLCO1B1 gene)	Piperacillin	Bleomycin
Ezetimibe ** (SLCO1B1 gene)	Vancomycin	Chlorambucil
Fenofibric acid	Zanamivir	Fulvestrant
Furosemide	Neurology	Opthalmology
Hydralazine	Gabapentin	Verteporfin
Hydrochlorothiazide	Lamotragine	Pulmonary
Lisinopril	Levetiracetam	Montelukast
Nitroglycerin	Oxcarbazepine	Rheumatology
Telmisartan	Pramipexole	Allopurinol
Fosinopril	Rivastigmine	Etanercept
Sotalol	Vigabatrin	Belimumab
Gastroenterology	Psychiatry	Other
Certolizumab Pegol	Lorazepam	Carglumic acid
Immunosuppressives	Varenicline	Risedronate
Mycophenolate	Sedatives	
	Zaleplon	

This is not an exhaustive list for all of the alternate drugs in the pharmacopeia but focuses on commonly used drugs.

* Additional genetic or tumor testing maybe needed to establish the indication for use of this drug.

** Although a CYP gene is involved in the metabolism of this drug, the CYP genetic variation within the gene may have minimal impact on metabolism.

Recommendations & Comments

Additional information

Visit http://www.geneway.co.za/generx+resources or click here for:

* An extensive list of substrates, inhibitors and inducers per gene
* Gene monographs
* Educational tools
* References
* Additional resources

Once the recommended drugs are selected, check potential drug-drug and nutritional interactions here:

MedScape
https://reference.medscape.com/drug-interactionchecker

Drugs.Com
https://www.drugs.com/interaction/list/

RxRisk
https://rxisk.org/tools/drug-interaction-checker/

DrugBank
https://www.drugbank.ca/interax/multi_search

The Drug Gene Database
http://www.dgidb.org/search_interactions

Clinical Pharmacogenetics Implementation Consortium (CPIC®)
https://cpicpgx.org/

Additional Comments

Medical Scientist / Geneticist

Comments:

Dietitian

Comments:

Medical Laboratory Scientist

Comments:

Other Medication(s)

CYP2B6 - Intermediate Metaboliser

Methadone	Informative	Increased sensitivity
Increased S-methadone plasma concentrations with associated-cardiotoxicity may occur. Consider a lower initial dose, and adjust dosing based on the clinical response. CYP2B6 intermediate 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. Other drugs known to inhibit methadone metabolism include ketoconazole, nelfinavir, paroxetine and sertraline. Concomitant use of any of these drugs with methadone may lead to increased methadone concentrations.		
Efavirenz	Informative	Increased sensitivity
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. Other drugs known to inhibit methadone metabolism include ketoconazole, nelfinavir, paroxetine and sertraline. Concomitant use of any of these drugs with methadone may lead to increased methadone concentrations.		
Nevirapine	Informative	Increased sensitivity
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. Other drugs known to inhibit methadone metabolism include ketoconazole, nelfinavir, paroxetine and sertraline. Concomitant use of any of these drugs with methadone may lead to increased methadone concentrations.		
Lidocaine	Informative	Increased risk of an adverse reaction
Limited evidence exists regarding the clinical impact on the drug in intermediate CYP2B6 metabolizers. Inhibitors or inducers of the CYP2B6 enzyme may modify its activity. Inhibitors include: clopidogrel, darunavir, prasugrel, ticlopidine, voriconazole, ritonavir and thiotepa. Inducers include: artemether, carbamazepine, dabrafenib, efavirenz, metamizole, nevirapine, phenobarbital, phenytoin, rifampin, ritonavir and St. John's Wort.		
Methadone	Informative	Increased risk of an adverse reaction
Based on currently available evidence, S-methadone plasma concentrations may increase, resulting in higher risk of cardiac arrhythmias and QTc prolongation. Consider lower starting doses of methadone, and adjust dosing based on the clinical response.		
Bupropion	Informative	Decreased response
Intermediate metabolisers may or may not have lower blood levels of hydroxybupropion (the active metabolite) which may or may not result in a reduced response to bupropion treatment. Bupropion can be prescribed at standard label-recommended dosage with careful monitoring of the patient's response. Therapeutic monitoring of hydroxybupropion levels may be considered to guide dosing adjustment. Bupropion is further metabolized by CYP2C19. Note that co-administration of bupropion alongside a drug that is a CYP2D6 substrate could result in harmful drug-drug interactions due to varied circulating drug levels which may cause unexpected toxicities.		
Temazepam	Informative	Increased sensitivity
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. Other drugs known to inhibit methadone metabolism include ketoconazole, nelfinavir, paroxetine and sertraline. Concomitant use of any of these drugs with methadone may lead to increased methadone concentrations.		
Artemisinin	Informative	Possible increased sensitivity
Artemisinin is an extract obtained from the Chinese herb Artemisia annua and is utilized as an antimalarial agent, though poor bioavailability limits its efficacy. The metabolism of artemisinin is mediated primarily by CYP2B6 in the liver with some contribution from CYP3A4. While there is currently no literature available regarding the impact of CYP2B6 pharmacogenetics on artemisinin disposition, it is reasonable to anticipate that Intermediate metabolisers of CYP2B6 may experience decreased metabolism and clearance of the drug and potentially increased toxicities. In addition, CYP2B6 inhibitors reduce clearance further. CYP2B6 inhibitors include clopidogrel, darunavir, prasugrel, ticlopidine, voriconazole, ritonavir and thiotepa.		

Cyclophosphamide (prodrug)	Informative	Possible Normal response
Cyclophosphamide is an oxazaphosphorine prodrug with a very narrow therapeutic indicex, requiring bioactivation by CYP2B6. CYP2B6 activates cyclophosphamide to 4-hydroxycyclophosphamide. The patient has a intermediate metaboliser genotype and reduce the drug's activation. Use with caution and review the MTHFR results for additional information. PMID: 27709010		
Diazepam	Informative	Possible increased sensitivity
Diazepam is primarily metabolised by CYP2B6 and CYP2C19, with a minor contribution of CYP3A4.intermediate CYP2B6 metaboliser demonstrate slower clearance and an increased elimination half-life of diazepam. Consider reducing the dosage and review CYP2C19 results.		
Ifosfamide	Informative	Possible Normal response
Ifosfamide is a prodrug used for treating different types of solid tumors and hematologic malignancies. The bioactivation is catalyzed by CYP2B6 and CYP3A4/5 which contribute roughly equivalently. The patient has an intermediate metaboliser genotype for CYP2B6 and decreased ifosfamide dosages may be required. Review the CYP3A5 phenotype.		
Ketamine	Informative	Possible adverse events
Ketamine has multiple clinical uses including analgesia and moderate stimulation of the cardiovascular system. Ketamine is primarily metabolised by CYP2B6 with contrIbutions from 3A4/5 and 2D6. Based on the CYP2B6 result, consider a reduction in the dosage of ketamine due to decreased drug clearance. It has been demonstrated that co-administration of ketamine with diazepam, a substrate of CYP2C19 and CYP3A4, or secobarbital, a CYP2B6 inhibitor, significantly increased the plasma half-life of ketamine.		
Meperidine	Informative	Possible increased sensitivity
No genetically guided drug selection or dosing recommendations are available. Meperidine is metabolised to normeperidine by CYP2B6, CYP3A4 and CYP2C19 accounting for 57%, 28%, and 15% of its total intrinsic clearance, respectively. The effects of genetic variants in these enzymes have not been studied. In patients taking strong CYP2B6 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, therefore, this combination should be avoided if possible.		
CYP2C19 - Intermediate Metaboliser		
Fexofenadine	Informative	Possible altered response
Patients who are intermediate metabolizers may require lower than usual doses to achieve optimal response. In addition, the absorption of fexofenadine decreases by 40% with 200ml or more of grapefruit, orange, apple juice or green tea. Eating these fruit does not seem to affect the absorption.		
Clopidogrel	Actionable	Increased risk of an adverse reaction
Consider alternative agents. Examples of alternative drugs: prasugrel (contraindicated in TIA/Stroke patients), ticagrelor, aspirin, aspirin plus dipyridamole. Reduced platelet inhibition, increased residual platelet aggregation and an increased risk for adverse cardiovascular events are associated with this genotype. Clopidogrel is a prodrug. A prodrug is a medication or compound that, after administration, is metabolized into a pharmacologically active drug.		
Propranolol	Informative	Increased risk of an adverse reaction
Prescribe the lowest typically effective dose, or consider an alternative drug. Inhibitors or inducers of CYP2C19 enzyme may modify its activity and change the patient’s metabolizer status. Some inducers include: carbamazepine, rifampin and prednisone. Some inhibitors include: cimetidine, fluoxetine, fluvoxamine, modafinil and topiramate. Propranolol is metabolized by CYP2C19, CYP2D6 and CYP1A2 enzymes. Caution needed in co-administration of drugs that are inhibitors of these enzymes which may increase the plasma levels of propranolol.		
Esomeprazole	Informative	Normal response
Esomeprazole can be prescribed at standard label recommended-dosage and administration. A positive clinical effect is expected in intermediate metabolizers.		
Lansoprazole	Informative	Normal response
Lansoprazole can be prescribed at standard label recommended-dosage and administration. A positive clinical effect is expected.		
Pantoprazole	Informative	Normal response
Pantoprazole can be prescribed at standard label recommended-dosage and administration. A positive clinical effect is expected.		

Rabeprazole	Informative	Normal response
Rabeprazole can be prescribed at standard label recommended-dosage and administration. A positive clinical effect is expected in intermediate metabolisers.		
Atovaquone, Proguanil (prodrug)	Informative	Possible altered response
No dosing recommendations related to CYP2C19 phenotypes have been published but consideration should be given to avoiding atovaquone / proguanil in intermediate metabolisers because of possible reduced efficacy. In general, prodrugs should be avoided in intermediate CYP2C19 metabolisers.		
Clobazam	Actionable	Possible increased sensitivity
In CYP2C19 intermediate metabolisers, plasma levels of the active metabolite N-desmethylclobazam are 2-fold higher than those found in CYP2C19 normal metabolisers. The dose adjustment for intermediate metabolizers is not well established, therefore, the recommendation for poor metabolisers is proposed. Starting dose: 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.		
Phenobarbital	Informative	Possible increased sensitivity
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. Therefore, phenobarbital can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.		
Primidone	Informative	Normal response
CYP2C19 is partly involved in the metabolism of primidone, and although CYP2C19 intermediate metabolizers have a lower clearance of the 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.		
Citalopram	Informative	Increased risk of an adverse reaction
Increased risk of an adverse reaction due to elevated citalopram plasma concentrations. Consider a 15% reduction of the recommended starting dose and titrate to response or select alternative drug not predominantly metabolized by CYP2C19 such as vilazodone (Viibryd) or paroxetine (Paxil). CYP3A4 and CYP2D6 are also involved in the metabolism of citalopram.		
Escitalopram	Informative	Modest increased risk of an adverse reaction
Consider a 15% reduction of the recommended starting dose and titrate to response. Alaternatively, select a drug not predominantly metabolized by CYP2C19 such as fluoxetine (CYP2D6). Escitalopram is the pharmacologically active S-enantiomer of citalopram and one of the most commonly prescribed SSRIs.		
Fluoxetine	Informative	Altered response
Increased risk of an adverse reaction due to elevated plasma concentrations. Consider a 30% reduction of the recommended starting dose and titrate to response or select alternative drug not predominantly metabolized by CYP2C19. Fluoxetine is metabolized to its active metabolite norfluoxetine by other enzymes also including CYP2D6, CYP2C9 and CYP3A4.		
Sertraline	Informative	Normal response
Medication can be prescribed according to standard regimens.		
Amitriptyline	Actionable	Altered response
Decrease the dose by 25%. 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.		
Clomipramine	Informative	Moderate sensitivity
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.		

Imipramine	Informative	Moderate sensitivity
Consider a lower starting dose and increase dosing over several days until an optimal response is achieved. Imipramine is metabolized primarily via the CYP2C19 and CYP2D6 enzymes.		
Meprobamate	Informative	Possible altered response
Patients who are intermediate metabolizers may require lower than usual doses to achieve optimal response.		
Tamoxifen	Informative	Possible altered response
Consider an alternative drug. Prodrugs, such as tamoxifen, should be avoided in intermediate CYP2C19 metabolizers.		
CBD (Cannabidiol)	Informative	Normal response
CBD (Cannabidiol) is the "non-addictive" cannabinoid within the Cannabis plant. CBD has shown promise as an analgesic, anticonvulsant, muscle relaxant and anxiolytic and has shown neuroprotective, anti-inflammatory and antioxidant activity. Label-recommended dosages are recommended with this result; however, CBD is a potent inhibitor of 2C19 with oral doses >5mg/kg/day. Caution should be applied when combining high dose CBD with 2C19 substrates and a dose adjustment is likely to be necessary. High dose CBD may potentially cause 2 to 5-fold increases in exposure to sensitive substrates. Co-administration with a moderate or strong inhibitor of 2C19 will increase CBD plasma concentrations, which may result in a greater risk of adverse reactions. Strong 2C19 inhibitors: chloramphenicol, cimetidine, clopidogrel, delavirdine, efavirenz, esomeprazole, felbamate, fluconazole, fluoxetine, fluvoxamine, isoniazid, modafinil, omeprazole, oxcarbazepine, ticlopidine, and voriconazole. CPD is further metabolised by CYP3A4.		
Aspirin	Informative	Possible Normal response
The clinical evidence is not sufficient to recommend dosage adjustments. Concomitant use of alcohol and aspirin may increase the risk of gastrointestinal injury and bleeding and should be undertaken with caution. Chronic or heavy alcohol consumption will increase this risk significantly.		
Carisoprodol	Informative	Normal response
This patient's genotype is associated with intermediate CYP2C19 activity and possibly .nrmal plasma concentrations of carisoprodol at standard doses. Carisoprodol can be prescribed at standard label-recommended dosage or alternatives to consider include acetaminophen, NSAID, morphine but avoid opioids. Oral contraceptives containing ethinylestradiol, desogestrel, gestodene or 3-ketodesogestrel inhibit the CYP2C19 enzyme and caution should be exercised when prescribing carisoprodol to patients taking oral contraceptives.		
Diazepam	Informative	Possible increased sensitivity to Diazepam (Valium)
CYP2C19 Intermediate metabolisers have a lower capacity to metabolise diazepam and its active metabolite nordiazepam. Therefore, they may experience more concentration dependent side-effects such as increased or prolonged sedation, if treated with standard doses of diazepam. Diazepam should be used with caution in these patients and a reduced dose or longer dosing interval may be needed. Consider CYP2B6 results also.		
Doxepin	Actionable	Moderate sensitivity
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 is also metabolised by CYP2D6 and the activity of this enzyme should also be considered when establishing a starting dose. Consult the dosing guidance provided for the patient's CYP2D6 status in addition to this recommendation when establishing or adjusting the dose of doxepin. While taking doxepin, patients should be counseled on the signs and symptoms of parasomnia. Patients should be urged against sudden discontinuation of treatment and concurrent alcohol and/or CNS depressant use. Sleeping patterns, suicidal ideation and unusual changes in behavioUr should be monitored during treatment.		
Prasugrel	Actionable	Normal response
Prasugrel is a prodrug is hydrolyzed in the intestine to a thiolactone, which is then converted to the active metabolite primarily by CYP3A4 and CYP2B6 and to a lesser extent by CYP2C9 and CYP2C19. Prasugrel active metabolite exposure and platelet reactivity are not affected by CYP2C19 metaboliser status.		
Protriptyline	Informative	Possible increased sensitivity to Diazepam (Valium)
Consider reducing the protriptyline starting dose by 25% and adjust maintenance dose according to plasma concentrations. Review results from CYP2D6 due to protriptyline being a substrate of the enzyme. Higher plasma concentrations of active drug will increase the probability of side effects.		

Trimipramine	Informative	Possible Normal response
Intermediate metabolisers have a decreased conversion of tertiary amines to secondary amines and may affect response or side effects. Consider a 25% reduction of the recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments. Trimipramine is also metabolised by CYP2D6 and CYP1A2 and the activities of theze enzymes should also be considered when establishing a starting dose.		
Brivaracetam	Informative	Normal response
Brivaracetam is primarily metabolised by hydrolysis and to a minor extent by hydroxylation, which is mediated by CYP2C19. In CYP2C19 intermediate metabolisers, the plasma concentration of brivaracetam is increased by 22%, but this change is not clinically significant. Brivaracetam can be prescribed at the standard label recommended dosage.		
Dexlansoprazole	Actionable	Normal response
Dexlansoprazole is the R-enantiomer of lansoprazole. Dexlansoprazole is the major circulating component in plasma regardless of CYP2C19 metaboliser status. Dexlansoprazole can be prescribed at standard label recommended-dosage and administration - a positive clinical effect is expected in intermediate metabolisers. Oxidation to the sulfone metabolite is mainly by CYP3A4.		
Flibanserin	Informative	Normal response
For treating premenopausal women with acquired, generalized hypoactive sexual desire disorder (HSDD): Flibanserin is primarily metabolised by CYP3A4 and, to a lesser extent, by CYP2C19. The genotype results predict that the patient is expected to have a normal clearance and a typical exposure to flibanserin. Use label-recommended dosage and follow standard precautions.		
Labetalol	Informative	Normal response
Labetalol can be prescribed at standard label recommended-dosage and administration. Standard precautions apply. Polypharmacy guidance: Cimetidine increases the bioavailability of labetalol and clinical monitoring is advised when both drugs are coadministered.		
Lacosamide	Actionable	Normal response
CYP2C19 is partly involved in the metabolism of lacosamide along with CYP2C9 and CYP3A. CYP2C19 reduced activity, seen in intermediate metabolisers, does not affect the pharmacokinetics of lacosamide but results in lower plasma levels of its O-desmethyl metabolite (pharmacologically inactive). This change is not expected to affect the clinical outcome of this drug. Therefore, lacosamide can be prescribed at standard label-recommended dosage and administration.		
Leflunomide	Informative	Increased sensitivity
Leflunomide is metabolised 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.		
Voriconazole	Actionable	Moderate sensitivity
Approximately 18-45% of patients are intermediate metabolisers. Intermediate metabolisers have higher dose-adjusted trough concentrations of voriconazole compared to normal metabolisers. A trough level is the lowest concentration reached by a drug before the next dose is administered. Initiate therapy with recommended standard of care dosing. Monitor closely voriconazole plasma concentrations and adjust the dose accordingly.		
CYP3A4 - Poor Metaboliser		
Loratadine	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient’s phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Olopatadine	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient’s phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		

Betamethasone	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Ciclesonide	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Rivaroxaban	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Indapamide	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Amiodarone	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Atorvastatin	Informative	Altered response
Patients with poor CYP3A4 functionality, may achieve an optimal lipid control goal with lower atorvastatin dose requirements. The drug should be used with caution when prescribed with CYP3A4 inhibitors and inducers. Higher doses may be needed when the drug is coadministered inducers. Lower doses may be needed when the drug is coadministered with inhibitors. Medication can be prescribed according to standard regimens. CYP3A metabolism is highly sensitive to inhibition and induction when a patient is taking multiple drugs. This drug should be used with caution when prescribed with CYP3A4 inhibitors and inducers. Higher doses may be needed when the drug is coadministered inducers. Lower doses may be needed when the drug is coadministered with inhibitors. Higher risk of myopathy/rabdomyolysis with CYP3A4 inhibitors , colchicine , cyclosporine, and fibric acid derivatives. Concurrent use with cyclosporine , gemfibrozil , tipranavir/ritoavir and telaprever is contraindicated. Concurrent use with some other CYP3A4 inhibitors requires lower dose. Grapefruit juice increases the drug levels.		
Estradiol	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Progesterone	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Dienogest	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Ondansetron	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		

Cyclosporine	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Carbamazepine	Informative	Increased risk of an adverse reaction
This genotype is associated with decreased metabolism and increased plasma concentration of carbamazepine. This patient may require lower doses of carbamazepine to achieve therapeutic effects. Consider starting at a lower dose or switch to an alternative therapy. Carbamazepine also autoinduces its own metabolism, and this activity should be considered when establishing a starting dose. While taking carbamazepine, patients should be counseled on the signs and symptoms of myelosuppression and cutaneous toxicity. CBC (with platelets and differential), LFTs, suicidal ideation and ophthalmic function should be monitored during treatment.		
Ethosuximide	Informative	Increased risk of an adverse reaction
No genetically guided drug selection or dosing recommendations are available. Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. Ethosuximide is extensively metabolized by CYP3A4, therefore this drug should be used with caution when prescribed with CYP3A4 inhibitors. Inducers of CYP3A4 increase ethosuximide clearance and higher doses may be needed when the drug is coadministered with enzyme-inducing drugs.		
Fluticasone	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Cyclobenzaprine	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Buprenorphine	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. CYP3A metabolism is highly sensitive to inhibitors and inducers.		
Meperidine	Informative	Normal response
Meperidine is metabolized to normeperidine by multiple enzymes including CYP2B6, CYP3A4 and CYP2C19. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: In patients taking strong CYP inducers, meperidine metabolism is increased resulting in higher levels of its neurotoxic metabolite, normeperidine. Avoid coadministration with ritonavir. In the 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.		
Methadone	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. Careful monitoring is recommended. CYP3A metabolism is highly sensitive to inhibition and induction when a patient is taking multiple drugs. Some known strong CYP3A inhibitors include: ketoconazole, itraconazole, ritonavir and grapefruit juice (high dose). CYP3A4 inducers include: carbamazepine, efavirenz, nevirapine, phenobarbital, rifampicin and St John's Wort. Other enzymes involved in methadone's metabolism 2B6,2D6,3A5 and COMT.		
Desvenlafaxine	Informative	Normal response
Medication can be prescribed according to standard regimens. Desvenlafaxine is primarily metabolized by conjugation (mediated by UGT enzymes) and, to a minor extent, through oxidative metabolism (mediated by CYP3A4). The CYP2D6 enzyme is not involved in its metabolism.		
Aripiprazole	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		

Quetiapine	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. Careful monitoring is recommended. Dose adjustment of quetiapine will be necessary if it is coadministered with phenytoin or ketoconazole. Alternatives: olanzapine (Zyprexa®), asenapine, paliperidone, risperidone (2D6); aripiprazole (2D6), haloperidol (2D6), Stelazine (1A2), Geodon (1A2).		
Buspirone	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. Careful monitoring is recommended. CYP3A metabolism is highly sensitive to inhibition and induction when a patient is taking multiple drugs. Some known strong CYP3A inhibitors include: ketoconazole, itraconazole, ritonavir and grapefruit juice (high dose). CYP3A4 inducers include: carbamazepine, efavirenz, nevirapine, phenobarbital, rifampicin and St John's Wort.		
Alprazolam	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. Careful monitoring is recommended. CYP3A metabolism is highly sensitive to inhibition and induction when a patient is taking multiple drugs. Some known strong CYP3A inhibitors include: ketoconazole, itraconazole, ritonavir and grapefruit juice (high dose). CYP3A4 inducers include: carbamazepine, efavirenz, nevirapine, phenobarbital, rifampicin and St John's Wort.		
Clonazepam	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. Careful monitoring is recommended. No genetically guided drug selection or dosing recommendations are available. Clonazepam is extensively metabolized by CYP3A4 to an amino metabolite that is further acetylated by N-acethyltransferases. This drug should be used with caution when prescribed with CYP3A4 inhibitors or inducers.		
Midazolam	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. Careful monitoring is recommended. No genetically guided drug selection or dosing recommendations are available. Midazolam is extensively metabolized by CYP3A4 to an amino metabolite that is further acetylated by N-acethyltransferases. This drug should be used with caution when prescribed with CYP3A4 inhibitors or inducers.		
Modafinil	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. Careful monitoring is recommended. CYP3A metabolism is highly sensitive to inhibition and induction when a patient is taking multiple drugs. Some known strong CYP3A inhibitors include: ketoconazole, itraconazole, ritonavir and grapefruit juice (high dose). CYP3A4 inducers include: carbamazepine, efavirenz, nevirapine, phenobarbital, rifampicin and St John's Wort.		
Zolpidem	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. Careful monitoring is recommended. CYP3A metabolism is highly sensitive to inhibition and induction when a patient is taking multiple drugs. Some known strong CYP3A inhibitors include: ketoconazole, itraconazole, ritonavir and grapefruit juice (high dose). CYP3A4 inducers include: carbamazepine, efavirenz, nevirapine, phenobarbital, rifampicin and St John's Wort. Zolpidem is further metabolized by CYP3A5, CYP1A2 and CYP2D6.		
Zopiclone	Informative	Increased risk of an adverse reaction
If the drug is warranted, consider prescribing a decreased dose. Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. Careful monitoring is recommended. CYP3A metabolism is highly sensitive to inhibition and induction when a patient is taking multiple drugs. Some known strong CYP3A inhibitors include: ketoconazole, itraconazole, ritonavir and grapefruit juice (high dose). CYP3A4 inducers include: carbamazepine, efavirenz, nevirapine, phenobarbital, rifampicin and St John's Wort.		
Exemestane	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		

Salmeterol	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Vilanterol	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. CYP3A4 metabolism is highly sensitive to inhibition and induction when a patient is taking multiple drugs.		
Colchicine	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. CYP3A4 metabolism is highly sensitive to inhibition and induction when a patient is taking multiple drugs.		
Dutasteride	Informative	Increased risk of an adverse reaction
Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of dutasteride. If dutasteride is warranted, consider prescribing a decreased dose. CYP3A4 metabolism is highly sensitive to inhibition and induction when a patient is taking multiple drugs.		
Finasteride	Informative	Increased risk of an adverse reaction
Finasteride is extensively metabolized in humans by CYP3A4. Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of dutasteride. Consider prescribing a decreased dose. CYP3A4 metabolism is highly sensitive to inhibition and induction when a patient is taking multiple drugs.		
Oxybutynin	Informative	Increased risk of an adverse reaction
Oxybutynin is extensively metabolized in humans by CYP3A4. Poor CYP3A4 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose.		
Tadalafil	Informative	Possibly altered response
Consider prescribing a decreased dose. Tadalafil is extensively metabolized by CYP3A4. Taking concomitant potent inhibitors of CYP3A4, such as ketoconazole or ritonavir, increases the plasma levels of tadalafil. The exposure of tadalafil is reduced when coadministered with rifampin or other CYP3A4 inducers.		
Tetrahydrocannabinol (THC)	Informative	Increased risk of an adverse reactions
Tetrahydrocannabinol (THC) is the principal psychoactive constituent of cannabis. In poor CYP3A4 metabolisers, a 75% reduction in starting dose for THC is recommended. The main metabolic pathway of THC metabolism is catalyzed by CYP2C9. CYP2C9 metabolises THC to the psychoactive metabolite 11-OH-THC, which is then further metabolised to the inactive metabolite THC-COOH excreted via the kidneys. An alternative pathway utilizes CYP3A4 whereby metabolites are excreted mostly in the faeces (and are not detected by urine tests). In poor CYP3A4 metabolisers, the metabolism of THC will be slow, leading to increased psychoactive effects which are longer in duration. By inducing CYP3A4, THC metabolite levels can be reduced. Rifampin is a strong 3A4 inducer that reduce the concentration of THC by 40%.		
CBD (Cannabidiol)	Informative	Dose adjustment
In poor CYP3A4 metabolisers, a 50% reduction in CBD starting dose is recommended. CPD is also metabolised by CYP2C19. CBD (Cannabidiol) is a nonintoxicating cannabinoid found in cannabis and hemp and lacks associated reinforcement, craving, compulsive use, that would indicate a significant drug abuse liability, such as with the other well-known cannabinoid THC (Tetrahydrocannabinol). CBD may have anticonvulsant, anti-psychotic, anti-inflammatory and neuroprotective properties. At the same time, CBD is also an inhibitor of CYP3A4 and would be responsible for the extension of THC's effects, if both cannabinoids are taken simultaneously.		
Diltiazem	Informative	Increased risk of adverse events
Use caution when prescribing diltiazem to CYP3A4 Poor metabolisers due to significant increase in drug exposure and therefore clinical monitoring and dose adjustment may thus be required.		
Metaxalone	Informative	Normal response
Metaxalone is extensively metabolised by multiple CYP enzymes including CYP1A2, CYP2D6 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.		

Oxybutynin	Informative	Normal sensitivity
No genetically guided drug selection or dosing recommendations are available. Oxybutynin is extensively metabolised in humans by CYP3A4 and coadminstration of a CYP3A4 strong inhibitor (itraconazole) increases oxybutynin serum concentrations. Therefore, use caution when prescribing this drug to patients taking CYP3A4 enzyme inhibitors.		
Pimozide	Informative	Increased sensitivity
Consider a lower dose of pimozide. Pimozide metabolism is catalyzed mainly by the CYP3A4 and to a lesser extent, by CYP1A2 and CYP2D6. Drugs that inhibit CYP3A4 activity can increase the plasma concentrations of Pimozide, leading to adverse events. Some drugs, such as clarithromycin, itraconazole, ketoconazole, nefazo done, nelfinavir and ritonavir, are particularly potent inhibitors of CYP3A4.		
Tamsulosin	Informative	Possible Normal response
Tamsulosin may be metabolised at a slower rate in CYP3A4 poor Metabolisers, potentially resulting in increased serum concentrations of tamsulosin. However, there is insufficient data related to the clinical impact of this potential change. Therefore, tamsulosin can be prescribed at standard label recommended-dosage and administratio but it should not be used in combination with strong inhibitors of CYP3A4 (e.g. ketoconazole). Tamsulosin is also metabolised by CYP2D6.		
Alfuzosin	Informative	Possible altered response
No genetically guided drug selection or dosing recommendations are available. Alfuzosin is extensively metabolised by CYP3A4 to pharmacologically inactive metabolites. Alfuzosin is contraindicated with strong CYP3A4 inhibitors as the risk for QTc prolongation induced by this drug is increased at higher concentrations. Caution when this drug is prescribed with CYP3A4 moderate inhibitors as drug levels may increase.		
Amlodipine	Informative	Increased risk of adverse events
Use caution when prescribing amlodipine to CYP3A4 poor metabolisers due to significant increase in drug exposure and therefore clinical monitoring and dose adjustment may thus be required.		
Avanafil	Informative	Possible altered response
No genetically guided drug selection or dosing recommendations are available. Avanafil is extensively metabolised by CYP3A4, therefore Avanafil should not be used with strong CYP3A4 inhibitors such as ketoconazole, itraconazole, voriconazole, ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir and telithromycin. If taking a moderate CYP3A4 inhibitor such as erythromycin, amprenavir, aprepitant, diltiazem, fluconazole, fosamprenavir and verapamil, the dose should be no more than 50 mg in a 24-hour period. Inducers of CYP3A4 may decrease the concentrations of avanafil.		
Bisoprolol	Informative	Possible normal response
Bisoprolol is eliminated by renal and non-renal pathways with 50% of the total dose being metabolised in the liver and 50% being excreted via the kidneys unchanged. Bisoprolol is predominantly metabolised by CYP3A4 with smaller contribution from CYP2D6. Limited studies suggest that bisoprolol plasma concentrations and its beta-adrenergic inhibition are not affected by CYP2D6 genetic variability. No genetically-guided drug selection or dosing recommendations are available.		
Eszopiclone	Informative	Possible altered response
The patient's genotype result predicts poor CYP3A4 metabolic activity. Eszopiclone may need to be prescribed at lower than label-recommended dosage. Alternatives to eszopiclone include zaleplon (Sonata), ramelteon (Rozerem) and melatonin.		
Everolimus	Informative	Possible altered response
Therapy with everolimus always requires close supervision, irrespective of CYP3A4 genotype. Individuals with poor CYP3A4 activity may require a lower dose of everolimus to avoid adverse events.		
Felbamate	Informative	Possible normal response
No genetically guided drug selection or dosing recommendations are available. About 40-50% of absorbed felbamate dose appears unchanged in urine and an additional 50% is present as metabolites and conjugates. Felbamate is a substrate of CYP3A4 and CYP2E1 but these pathways are minor for the drug elimination when the drug is given as a monotherapy. This pathway is enhanced by concomitant use of enzyme-inducing antiepileptic drugs which results in 30 to 50% decrease in felbamate plasma concentrations. Felbamate should be titrated slowly and dose adjustment must be considered in presence of inducers.		
Felodipine	Informative	Increased risk of adverse events
Use caution when prescribing felodipine to CYP3A4 poor metabolisers due to significant increase in drug exposure and therefore clinical monitoring and dose adjustment may thus be required.		

Lercanidipine	Informative	Increased risk of adverse events
Use caution when prescribing lercanidipine to CYP3A4 poor metabolisers due to significant increase in drug exposure and therefore clinical monitoring and dose adjustment may thus be required.		
Tiagabine	Informative	Possible altered response
No genetically guided drug selection or dosing recommendations are available. It is expected that higher plasma concentrations of tiagabine will be present in poor metabolisers. Tiagabine is extensively metabolised by CYP3A4, therefore this drug should be used with caution when prescribed with CYP3A4 inhibitors.		
Verapamil	Informative	Increased risk of adverse events
Use caution when prescribing verapamil to CYP3A4 poor metabolisers due to significant increase in drug exposure and therefore clinical monitoring and dose adjustment may thus be required.		
Trazodone	Informative	Unknown
Pharmacogenetic guidance: Trazodone is metabolized to its active metabolite (m-chlorophenylpiperazine) by CYP3A4. This metabolite which may contribute to adverse events, is further metabolized by CYP2D6. The impact of genetic polymorphism detected on the clinical response to trazodone is not well documented. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: It is likely that CYP3A4 inhibitors may lead to substantial increases in trazodone plasma concentrations with the potential for adverse effects. If trazodone is used with a potent CYP3A4 inhibitor, the risk of cardiac arrhythmia may be increased. Therefore coadministration of trazodone with drugs that are inhibit CYP3A4 should be approached with caution.		
CYP3A5 - Poor Metaboliser		
Rivaroxaban	Informative	Increased risk of an adverse reaction
Poor CYP3A5 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended. The majority of the Caucasian population would demonstrate nonexistent or lowered CYP3A5 enzyme activity.		
Verapamil	Informative	Good response
Medication can be prescribed according to standard regimens for poor CYP3A5 metabolizers (nonexpresser). When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended. At the same time, veramipil is also a moderate inhibitor of CYP3A with 50-80% decrease in clearance.		
Felodipine	Informative	Good response
Medication can be prescribed according to standard regimens for poor CYP3A5 metabolizers (nonexpresser). When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications. Careful monitoring is recommended.		
Nifedipine	Informative	Good response
Medication can be prescribed according to standard regimens for poor CYP3A5 metabolisers, also known as nonexpresser. When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A4 and CYP3A5 since both usually metabolize the same medications.		
Cyclosporine	Informative	Good response
Medication can be prescribed according to standard regimens for poor CYP3A5 metabolizers (nonexpresser). When selecting a dose, consideration has to be given to the patient's phenotype for both CYP3A5 and CYP3A4 since both usually metabolize the same medications.		
Fentanyl	Informative	Increased risk of an adverse reaction
Fentanyl is a narrow therapeutic drug that is mainly metabolized by CYP3A. There is limited evidence suggesting that the response to this drug is altered in individuals with abnormal CYP3A activity.		

Triazolam	Informative	Increased risk of an adverse reaction
Poor CYP3A5 metabolisers may be at increased risk for adverse effects resulting from higher plasma levels of the triazolam. Consider prescribing a decreased dose. The initial step in triazolam metabolism is catalyzed by enzymes within CYP3A family. Drugs that inhibit this metabolic pathway may have a profound effect on the clearance of triazolam. Consequently, triazolam should be avoided in patients receiving very potent inhibitors of CYP3A. With drugs inhibiting CYP3A to a lesser but still significant degree, triazolam should be used only with caution and consideration of appropriate dosage reduction. For some drugs, an interaction with triazolam has been quantified with clinical data; for other drugs, interactions are predicted from in vitro data and/or experience with similar drugs in the same pharmacologic class.		
Vincristine	Informative	Increased risk of an adverse reaction
Vincristine is preferentially metabolized by CYP3A5 and results in a much higher rate of neurotoxicity in Caucasians who have a much lower expression rate than in Africans. Poor CYP3A5 metabolizers may be at increased risk for adverse effects resulting from higher plasma levels of the drug. If the drug is warranted, consider prescribing a decreased dose.		
Tacrolimus	Informative	Increased risk of an adverse reaction.
Tacrolimus is extensively used for immunosuppression after various transplants. Its clearance is significantly affected by CYP3A5 polymorphisms. Several studies in kidney, heart and liver transplant recipients have reported homozygous poor metabolizers require a significant dose reduction. Dosing guidelines recommend initiating therapy at a normal standard dose and utilizing therapeutic drug monitoring to guide dose adjustment. Patients should be urged against extensive UV exposure and concurrent alcohol use. While taking tacrolimus, patients should be counseled on signs and symptoms of infection, hyperglycemia and hyperkalemia.		
Sildenafil	Informative	Increased risk of an adverse reaction.
Sildenafil exposure is 1.5-times higher in individuals with CYP3A5 poor metaboliser genotype compared to the normal genotype. The clinical significance of this is unknown. In patients taking strong CYP3A inhibitors, sildenafil exposure is significantly increased and it is recommended not to exceed a maximum single dose of 25 mg in a 48 hour period. Inducers of CYP3A may decrease the concentration of the drug. Sildenafil is also metabolised by CYP3A4 (major route) and CYP2C9 (minor route) enzymes.		
Vardenafil	Actionable	Increased risk of an adverse reaction and no therapeutic response.
Vardenafil exposure is 3-times higher in individuals with the poor CYP3A5 metaboliser genotype compared to normal CYP3A5 metabolisers. The clinical impact of this change is unknown. Polypharmacy guidance: The dosage of vardenafil may require adjustment in patients receiving strong CYP3A4 inhibitors such as ketoconazole, itraconazole, ritonavir, indinavir, saquinavir, atazanavir, and clarithromycin as well as in other patients receiving moderate CYP3A4 inhibitors such as erythromycin. For ritonavir, a single dose of 2.5 mg vardenafil should not be exceeded in a 72-hour period. For indinavir, saquinavir, atazanavir, ketoconazole 400 mg daily, and itraconazole 400 mg daily, and clarithromycin, a single dose of 2.5 mg vardenafil should not be exceeded in a 24-hour period. For ketoconazole 200 mg daily, itraconazole 200 mg daily, and erythromycin, a single dose of 5 mg vardenafil should not be exceeded in a 24-hour period. Inducers of CYP3A4 may decrease the concentrations of vardenafil.		
Ifosfamide	Informative	Possible altered response
Ifosfamide is a prodrug used for treating different types of solid tumors and hematologic malignancies. The bioactivation is catalyzed by CYP2B6 and CYP3A4/5 which contribute roughly equivalently. The patient has a poor Metaboliser genotype for CYP3A5 and decreased ifosfamide dosages may be required. Review the CYP2B6 phenotype.		
Alfentanil	Informative	Normal response
Alfentanil is primarily metabolised 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. Alfentanil can be prescribed at standard label recommended-dosage and administration. Alfentanil should be used with caution when prescribed to patients taking CYP3A4 inhibitors or inducers.		
MTHFR 1298 - Intermediate Metaboliser		
Carboplatin	Informative	Decreased response and increased risk of toxicity
The patient has a variation in the MTHFR gene and antineoplastic agents such as carboplatin (Paraplatin) should be prescribed with caution due to increased risk of toxicity and poor response.		
Cyclophosphamide (prodrug)	Informative	Decreased response and increased risk of toxicity
The patient has a variation in the MTHFR gene and antineoplastic agents such as cyclophosphamide should be prescribed with caution due to increased risk of toxicity and poor response.		

Leucovorin	Informative	Normal response
Leucovorin is the active form of folate and does not require MTHFR for activation. Therefore, the variation in the MTHFR gene that was detected does not influence the outcome and leucovorin (Wellcovorin) can be prescribed at standard label-recommended dosage and administration.		
Oxaliplatin	Informative	Decreased response and increased risk of toxicity
The patient has a variation in the MTHFR gene and antineoplastic agents such as oxaliplatin (Eloxatin) should be prescribed with caution due to increased risk of toxicity and poor response.		
VKORC1 - Poor Metaboliser		
Warfarin	Actionable	Increased risk of an adverse reaction
Warfarin sensitivity is affected by both the VKORC1 and CYP2C9 enzymes. Therefore, both results should be considered when making warfarin dosage recommendations. With this VKORC1 result: If the CYP2C9 result is *1/*1 (Normal Metaboliser), the recommended warfarin dose: 3-4mg/day. If the CYP2C9 result is *1/*2 (Intermediate Metaboliser), the recommended warfarin dose: 3-4mg/day. If the CYP2C9 result is *2/*2 (Poor Metaboliser), the recommended warfarin dose: 0.5-2mg/day. If the CYP2C9 result is *1/*3 (Intermediate Metaboliser), the recommended warfarin dose: 0.5-2mg/day. If the CYP2C9 result is *2/*3 (Poor Metaboliser), the recommended warfarin dose: 0.5-2mg/day. If the CYP2C9 result is *3/*3 (Very Poor Metaboliser), the recommended warfarin dose: 0.5-2mg/day.		

Additional Information

Methodology

SNP (Single nucleotide ploymorphism) detection takes place using a biomedical technology called polymerase chain reaction (PCR). During this process a few copies of a piece of DNA are amplified generating an exponential number of copies of a particular DNA sequence. Variations in the genes, called polymorphisms, are detected and feedback on the possible (disease) associations of these variations are provided in a report format.

Disclaimer

Always consult your physician or pharmacist before taking or changing medication or the dosage thereof. The information contained in this report is supplied as general educational health information. It is not intended to be a substitute for professional medical advice, diagnosis or treatment. It remains the responsibility of the health care provider to determine the best course of treatment for a patient, including any decisions made based on a patient's genotype. The pharmacogenetic report is one of multiple pieces of information that physicians should consider in guiding their therapeutic choice for each patient. Those factors typically relate, but are not limited to, age, gender, weight, familial factors, environment (e.g. smoking and diet), other medical conditions, drug interactions and are not integrated into this report. Administration of any medication, including those listed in the GENEWAY™ reports, requires careful therapeutic monitoring regardless of the phenotype or genotype-derived recommendations.

Genotype-derived classification of medications is provided as a service by GENEWAY™ and is intended solely for use by a medical professional who has reviewed and understands all sections within this report, including possible limitations of the services provided by GENEWAY™. The relationships between the drugs and pharmacogenes annotated in this report are supported by scientific literature that meets the stringent criteria for inclusion as set by GENEWAY™. The information are believed to be current, however, research data and amendments to the prescribing information of the drugs listed will change over time. As a matter of practice, GENEWAY™ will routinely update its pharmacogenomic database as new information becomes available to the scientific community. The order in which drugs are listed does not have any clinical or medical implications.

The analytical results were interpreted by GENEWAY™ to produce the pharmacogenomic interpretations and annotations described in the gene and phenotype summary. Method-specific analytical limitations or inferred haplotypes may limit the ability to produce a definitive phenotype interpretation. See the Laboratory Comments sections in the report for additional information. The associated genes listed for each medication do not imply that a specific gene-drug interaction exists, as some genes may only be informative in nature.

Methodology and Limitations
Genomic DNA was analysed using Real-Time OpenArray based assays by Thermo Fischer Scientific to detect listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%. Analytical results were produced using tests validated by GENEWAY™ Laboratory, 354 Derdepoort Road, Silverton, Pretoria. These tests have not been cleared or approved by the South African Health Products Regulatory Authority. This test is used for clinical purposes and should not be regarded as investigational or for research. The test does not detect all known and unknown variations in the genes tested, nor does absence of a detectable variant (designated as *1 for genes encoding drug metabolizing enzymes) rule out the presence of other, non-detected variants. The absence of a detectable gene mutation does not rule out the possibility that a patient has different phenotypes due to the presence of an undetected polymorphism or due to other factors such as drug-drug interactions, co-morbidities and lifestyle habits. These assays cannot differentiate between the maternal and paternal chromosomes. In cases where observed variants are associated with more than one haplotype, GENEWAY™ infers and reports the most likely diplotype based on published allele frequency and/or ethnicity data. Inferences with potential clinical impact are stated in the report and Laboratory Comments section.

Approved By

Approval Signatures:

Medical Scientist / Geneticist

Dietitian

Medical Laboratory Scientist

Gene Variations Tested

APOE (E2/E3/E4) (rs7412 & rs429358)
COMT (rs4680)
CYP1A2 *1C, *1D, *1F, *1K
CYP2B6 *5, *16, *22
CYP2C19 *2, *3, *4, *5, *6, *7, *8, *9, *10, *17
CYP2C9 *2, *3, *4, *5, *6, *11
CYP2D6 *2A, *2, *3, *4, *4J, *4M, *6, *7, *8, *9, *10, *12, *14, *29 and exon 9
CYP3A4 *1B, *2, *3, *12, *17
CYP3A5 *2, *3, *6, *7, *8, *9, *H30Y
Factor 2 (rs1799963)
Factor 5 (rs6025)
MTHFR 677 (rs1801133)
MTHFR 1298 (rs1801131)
SLCO1B1 (rs4149056)
VKORC1 (rs9923231)

Patient Information Card
Pharmacogenetic Test Summary

Gene	Results	Phenotype
CYP2D6	*1/*2x2	UND Metaboliser
CYP2C9	*1/*1	Normal Metaboliser
CYP2C19	*1/*2	Intermediate Metaboliser
CYP1A2	*1A/*1F	Normal Metaboliser
CYP2B6	*1/*5	Intermediate Metaboliser
CYP3A4	*3/*22	Poor Metaboliser
CYP3A5	*3A/*3A	Poor Metaboliser
Factor II	G/G	Normal thrombosis risk
Factor V	G/G	Normal thrombosis risk
MTHFR 1298	A/C	Reduced MTHFR 1298 activity
MTHFR 677	C/C	Normal MTHFR 677 activity
SLCO1B1	*1/*1	Normal transporter function
VKORC1	*2/*2	High warfarin sensitivity
COMT	G/G	High / Normal COMT activity
APOE	E2/E4	Increased risk of hyperlipedemia / atherosclerosis

This is a summary of your genetic results to share with healthcare providers. For a complete report contact info@geneway.co.za