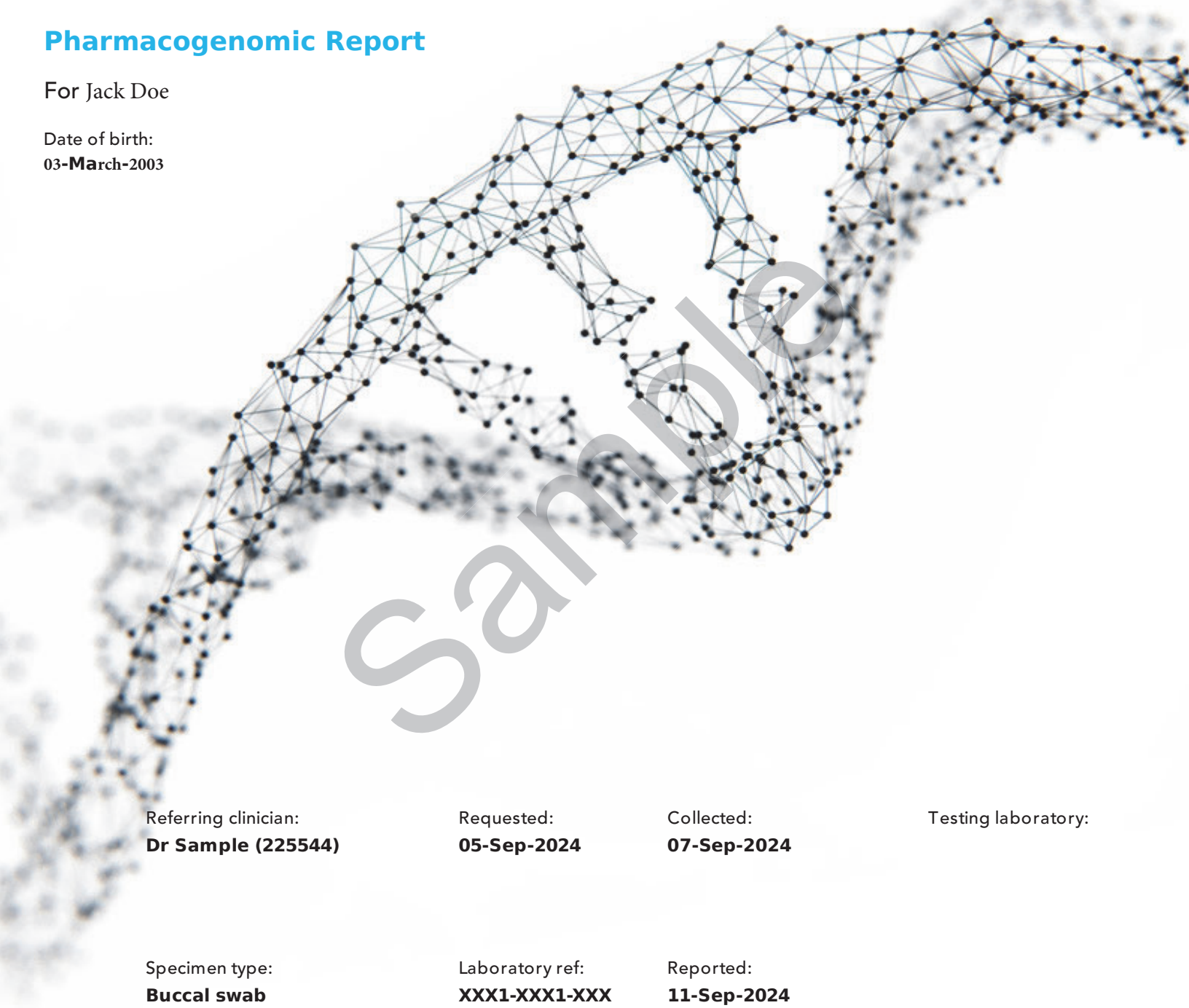
PERSONALIZED MEDICATION

Pharmacogenomic Report

For Jack Doe

Date of birth:
03-March-2003



Referring clinician:	Requested:	Collected:	Testing laboratory:
Dr Sample (225544)	**05-Sep-2024**	**07-Sep-2024**	

Specimen type:	Laboratory ref:	Reported:
Buccal swab	**XXX1-XXX1-XXX**	**11-Sep-2024**

ABOUT THIS REPORT

This report provides clinically relevant information on what the patient's genetic results predict about their response to a number of medications covered by this report.

The information concerns drug metabolism and plasma concentrations (drug exposure), as well as the potential for altered clinical effects.

Based on the available information found in the published literature, each medication has been assigned a category according to the likely clinical significance of each gene-drug interaction.
The three categories are:

MAJOR PRESCRIBING CONSIDERATIONS

A potentially significant effect on drug response is predicted. There may be guidelines or a drug label recommending consideration be given to a change in the dose, the medication type, or further monitoring in order to minimize the risk of the potential clinical issue noted.
Of note, "Major" prescribing considerations do not always preclude the use of a specific medication or necessitate a dosage change if the drug is currently effective and well tolerated, this will be dependent on the individual gene-drug interaction and the clinical circumstances.

MINOR PRESCRIBING CONSIDERATIONS

Altered drug response is possible, but either the clinical significance is thought to be minor or there is currently limited evidence available. Consider monitoring for any potential clinical effects annotated in this report. There are generally no specific recommendations to alter dosage or medication according to current guidelines.

USUAL PRESCRIBING CONSIDERATIONS

Genetic results are not predicted to have a significant effect on drug response, based on the literature currently available, and there are no additional prescribing considerations. Other factors may still influence drug response and therefore usual monitoring for adverse effects and efficacy still applies.

Medications which have a prescribing consideration to use an alternative medication will be annotated with this symbol ⚠. Consult the personalized prescribing considerations section of the report for the detailed recommendations.

PHARMACOGENOMIC GUIDELINES

For many medications covered in this report, evidence-based guidelines and drug label information are available and where relevant are referenced in this report.
Key practice guidelines include:

1. Clinical Pharmacogenetics Implementation Consortium (CPIC)
2. The Royal Dutch Pharmacists Association – Pharmacogenetics Working Group (DPWG).
3. The FDA Table of Pharmacogenetic Associations and drug label information

REPORT BREAKDOWN

The report consists of the following 6 sections:

1. Medications of Interest (if provided)- presents summarized and detailed prescribing considerations for medications of interest based on the pharmacogenomic test results.
2. Personalized Medication Guide - provides a list of all medications covered by the test categorized as having major, minor or usual prescribing considerations.
3. Genetic test results summary – presents the patients genotypes for the genes relevant to the medications covered by this report.
4. Medication tables arranged according to the three categories of MAJOR, MINOR or USUAL prescribing considerations.
5. Details of genetic test results – provides an explanation of genotype results and the predicted effect on drug exposure and drug response.
6. References – list of key peer-reviewed literature that has been used to produce the report.

MEDICATIONS OF INTEREST

MEDICATION	INTERPRETATION	RECOMMENDATION
ATORVASTATIN	**SLCO1B1 - Decreased transporter function:** This SLCO1B1 genotype is associated with increased atorvastatin exposure compared with a normal function genotype, which may translate to increased risk of atorvastatin related myopathy.[1] Other factors that may further increase this myopathy risk include: higher doses, certain co-administered drugs, female sex, patient frailty, renal failure, hypothyroidism, advanced age, low BMI, intense physical exercise and Asian or African ancestry.	Based on this SLCO1B1 genotype, CPIC guidelines[1] provide a moderate recommendation to prescribe less than or equal to 40 mg as a starting dose and adjust doses based on disease-specific guidelines. Be aware of possible increased risk for myopathy especially for the 40 mg dose. If doses >40mg are needed for desired efficacy, consider combination therapy (i.e. atorvastatin plus non-statin guideline directed medical therapy). Based on this SLCO1B1 genotype, the risk of statin-associated musculoskeletal symptoms (SAMS)[1] is as follows: Atorvastatin 80mg - High SAMS risk If used < 1 year: Consider changing to a statin/dose combination with lower SAMS risk. If used > 1 year without SAMS: it is reasonable to continue. Atorvastatin 40mg - Moderate SAMS risk If used < 4 weeks: Consider changing to a statin/dose combination with lower SAMS risk. If used > 4 weeks without SAMS: it is reasonable to continue. Atorvastatin 10-20mg - Low SAMS risk.
CODEINE	**CYP2D6 - Intermediate metabolizer** **OPRM1 - Normal mu opioid receptor expression :** Reduced metabolism of codeine by CYP2D6 into its active metabolite morphine is predicted. This could lead to a reduction in analgesic response to codeine. Whilst this OPRM1 genotype has been associated with increased sensitivity to morphine and by extrapolation, to codeine as well, there is insufficient evidence for its clinical significance. Codeine is contraindicated in children under 12 years of age.[2]	Based on the CYP2D6 genotype CPIC[3] provides a moderate recommendation to prescribe codeine according to usual label recommended age or weight specific dosing. Monitor for a reduced clinical response. If response is inadequate and opioid use is warranted, consider a non-tramadol opioid. DPWG [4] provides a recommendation to be alert to possible reduced analgesic effects. In the case of reduced effectiveness, increase the dose or choose a non-tramadol alternative. There is no additional genotype-guided dosing recommendation based on the OPRM1 result.
ESOMEPRAZOLE	**CYP2C19 - Normal metabolizer:** Typical metabolism of esomeprazole by CYP2C19 is predicted. Note that this genotype has a lesser effect with esomeprazole and rabeprazole compared to other PPIs.	Standard dosing and prescribing measures apply. If response is inadequate, consider a trial of rabeprazole as an alternative.
PRASUGREL	**CYP2C19 - Normal metabolizer:** DPWG[5] states that there is no gene-drug interaction for CYP2C19 and prasugrel.	No genotype-guided dosing recommendation available for this genotype. Standard dosing and prescribing measures apply.

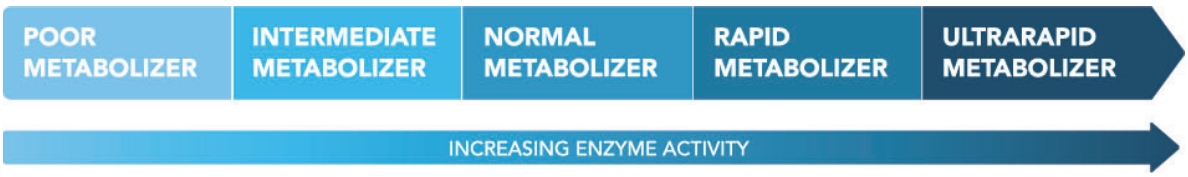
MEDICATIONS WITH NO PRESCRIBING CONSIDERATIONS BASED ON myDNA TEST

CANDESARTAN, METFORMIN, PARACETAMOL

PHARMACOGENOMIC TEST RESULTS SUMMARY

GENE	GENOTYPE	PREDICTED PHENOTYPE
ABCG2 (rs2231142)	CC	**Normal transporter function**
COMT	GG	**Normal to high COMT enzyme activity**
CYP1A2	*1A/*1F	**Normal metabolizer**
CYP2B6	*1/*6	**Intermediate metabolizer**
CYP2C19	*1/*1	**Normal metabolizer**
CYP2C9	*1/*1	**Normal metabolizer**
CYP2D6	*4/*41	**Intermediate metabolizer**
CYP3A4	*1/*1	**Normal metabolizer**
CYP3A5	*3/*3	**Poor metabolizer**
F2 (rs1799963)	GG	**No prothrombin G20210A variant detected**
F5 (rs6025)	GG	**No Factor V Leiden variant detected**
HLA A*31:01 (rs1061235)	AA	**Normal risk of certain hypersensitivity reactions**
HLA B*15:02 (rs144012689)	TT	**Normal risk of certain hypersensitivity reactions**
MTHFR (rs1801133)	CC	**Normal MTHFR enzyme activity**
OPRM1	AA	**Normal mu opioid receptor expression**
SLCO1B1	*1/*5	**Decreased transporter function**
VKORC1	GG	**Normal VKORC1 enzyme level**

Detailed interpretations of genetic test results are provided at the end of this report.



POTENTIAL DRUG INTERACTIONS

The effect of drug-drug interactions can be additive to the effect of genotype on drug metabolism. Inhibitors can decrease and inducers can increase metabolism, leading to changes in drug concentration and clinical effects.

Comments in the medications of interest and future medications sections only consider the effects of the patient's genotype, not those due to interacting drugs. For the health professional's consideration, the table below identifies which of the patient's current drugs may inhibit or induce those enzymes tested by myDNA. The extent of the inhibition or induction depends on the dose and duration of the therapy. The overall effect on metabolism by a specific enzyme may be estimated by considering both the genetic finding and the potential interacting drug.

MEDICATION	INHIBITOR - MODERATE	INHIBITOR - STRONG	INDUCER
ESOMEPRAZOLE	CYP2C19		

PERSONALIZED MEDICATION GUIDE

Each medication below has been categorized as having major, minor or usual prescribing considerations based on the pharmacogenomic test results. NOTE: These classifications and recommendations do not account for the effect of any inhibitors or inducers. The table is not an all-inclusive list of medications but includes many commonly prescribed medications.

Legend

Consider alternative medication ⚠ | Major prescribing consideration ● | Minor prescribing consideration ● | Usual prescribing consideration ●

CLASS	MAJOR	MINOR	USUAL
ADHD - miscellaneous agents	Atomoxetine	Viloxazine	Methylphenidate
Angiotensin receptor blockers			Irbesartan Losartan
Antianginals		Perhexiline	
Antiarrhythmics	Flecainide Propafenone		
Anticholinergics (genitourinary)		Darifenacin Fesoterodine Tolterodine	
Anticholinesterases		Donepezil Galantamine	
Anticoagulants			Acenocoumarol Prasugrel Ticagrelor Warfarin
Antidepressants - other		Bupropion Mirtazapine Vortioxetine	
Antidepressants - SNRIs	Venlafaxine ⚠	Duloxetine	
Antidepressants - SSRIs	Paroxetine	Fluoxetine Fluvoxamine Sertraline	Citalopram Escitalopram
Antidepressants - TCAs	Amitriptyline Clomipramine Desipramine Doxepin Imipramine Nortriptyline Trimipramine	Amoxapine Protriptyline	

CLASS	MAJOR	MINOR	USUAL
Antidiabetics			Glimepiride Glipizide Glyburide Nateglinide Tolbutamide
Antiemetics		Metoclopramide Ondansetron	
Antiepileptics			Brivaracetam Fosphenytoin Lacosamide Lamotrigine Phenytoin
Antifungals - Azoles			Voriconazole
Antihistamines		Chlorpheniramine Dexchlorpheniramine Promethazine	
Antineoplastics			Cyclophosphamide
Antiplatelet drugs			Clopidogrel
Antipsychotics	Pimozide Thioridazine ⚠	Aripiprazole Aripiprazole Lauroxil Brexpiprazole Chlorpromazine Clozapine Haloperidol Iloperidone Perphenazine Risperidone	Flupenthixol Olanzapine Quetiapine
Antitussives		Dextromethorphan	
Antivirals	Efavirenz	Nevirapine	Atazanavir
Benzodiazepines			Clobazam Diazepam
Beta blockers		Carvedilol Metoprolol Propranolol Timolol	Nebivolol
Calcineurin inhibitors			Tacrolimus
Drugs for alcohol dependence			Naltrexone

CLASS	MAJOR	MINOR	USUAL
Drugs for anxiety and sleep disorders		Pitolisant	
Drugs for gout			Allopurinol
Endocrine drugs		Elagolix	
Haemostatic agents			Avatrombopag Eltrombopag Lusutrombopag
Hypnotics			Melatonin
Immunomodulators and antineoplastics	Tamoxifen ⚠	Gefitinib	Abrocitinib Belzutifan Erdafitinib Methotrexate
Miscellaneous		Cevimeline Eliglustat Lofexidine Meclizine Tamsulosin	Dronabinol Flibanserin Mirabegron Proguanil
Mood stabilisers			Carbamazepine Oxcarbazepine
Neurological drugs		Deutetrabenazine Tetrabenazine Valbenazine	Carisoprodol Siponimod
NSAIDs			Celecoxib Diclofenac Flurbiprofen Ibuprofen Indomethacin Lornoxicam Mefenamic Acid Meloxicam Piroxicam
Oestrogen containing contraceptives			Estetrol Estradiol Ethinylestradiol
Opioid Analgesics	Codeine Tramadol	Hydrocodone Methadone Oliceridine Oxycodone	Alfentanil Buprenorphine Fentanyl Hydromorphone Morphine Sufentanil

CLASS	MAJOR	MINOR	USUAL
Proton pump inhibitors		Dexlansoprazole Lansoprazole Omeprazole Pantoprazole	Esomeprazole Rabeprazole
Psychostimulants		Amphetamine Dextroamphetamine Lisdexamfetamine	
Statins	Atorvastatin Lovastatin ⚠ Pitavastatin Simvastatin ⚠	Fluvastatin Pravastatin Rosuvastatin	

PERSONALIZED PRESCRIBING CONSIDERATIONS

The following tables outline personalized recommendations for future medications.
These tables do not account for the effect of any inhibitors or inducers. The table is not an all-inclusive list of medications but includes many commonly prescribed medications

MAJOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
ATOMOXETINE ADHD - miscellaneous agents	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure is predicted. This may increase the risk of adverse effects.	CPIC[6] provides a moderate recommendation for dosing in children and adults. Refer to CPIC guidelines for details. In summary, Adults: initiate at 40 mg/day. If no clinical response and no adverse events after 2 weeks, increase to 80 mg/day. If inadequate response after 2 weeks, consider use of plasma concentrations 2-4 hours after dosing to guide titration. Children: initiate at 0.5mg/kg/day. If no clinical response and no adverse events after 2 weeks, consider use of plasma concentrations 2-4 hours after dosing to guide titration. Note: FDA-approved drug label[7] recommends maximum doses of 1.4mg/kg/day in children up to 70kg and 100 mg daily in adults or children over 70kg. Note: dosing recommendations should be considered with other clinical factors by the treating clinician(s).
FLECAINIDE Antiarrhythmics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This may increase the risk of concentration-dependent adverse effects.	For indications other than the diagnosis of Brugada syndrome, the DPWG[8] suggests reducing the dose to 75% of the standard dose, recording an ECG and monitoring the plasma concentration. For provocation testing for diagnosis of Brugada syndrome, no specific dose adjustment for flecainide is recommended.
PROPAFENONE Antiarrhythmics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This may increase the risk of concentration-dependent adverse effects.	The DPWG[9] suggests either: 1) adjusting the dose in response to plasma concentration, recording an ECG and being alert to side effects, or 2) selecting an alternative drug (e.g., sotalol, amiodarone).

MAJOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
VENLAFAXINE Antidepressants - SNRIs	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism of venlafaxine into O-desvenlafaxine (also an active drug) is predicted. This will result in increased venlafaxine exposure and reduced O-desvenlafaxine exposure, although there is insufficient evidence supporting the clinical impact.[10] There may be an increased risk of adverse effects, such as gastrointestinal discomfort.	CPIC guidelines[10] suggest no action is recommended based on this genotype. The DPWG[11] recommends: It is not possible to offer adequately substantiated advice for dose reduction based on the literature. 1. Choose an alternative. 2. If an alternative is not an option and side effects occur: a) Reduce the dose b) Check the plasma concentrations of venlafaxine and O-desmethylvenlafaxine (this is not routinely available for venlafaxine). It is not known whether it is possible to reduce the dose to such an extent that effectiveness is maintained without side effects. In general, it is assumed that the effectiveness is determined by the sum of the plasma concentrations of venlafaxine and O-desmethylvenlafaxine. However, the side effects do not appear to be related to this sum.
PAROXETINE Antidepressants - SSRIs	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased paroxetine exposure are predicted. As paroxetine is a strong inhibitor of CYP2D6, the CYP2D6 function is expected to decrease further with ongoing therapy (so-called phenoconversion). As a result of this, the metabolism of paroxetine (and other CYP2D6 substrate drugs) will be slower than is predicted by the genotype. There may be an increased risk of adverse effects.	CPIC[10] guidelines provide an optional recommendation to initiate therapy with a lower starting dose and to use a slower titration schedule as compared to normal metabolizers. It would also be reasonable to monitor for adverse effects. DPWG[12] recommends that no specific action on paroxetine dosing is required based on this genotype.
AMITRIPTYLINE Antidepressants - TCAs	**CYP2D6 - Intermediate metabolizer** **CYP2C19 - Normal metabolizer:** Amitriptyline is metabolized by CYP2C19 into an active metabolite, which is further metabolized by CYP2D6 into an inactive metabolite. Normal metabolism of amitriptyline and reduced metabolism of the active metabolite are predicted.	For use at higher doses such as in the treatment of depression, CPIC[13] provides a moderate recommendation to consider a 25% reduction of the recommended steady-state starting dose and utilisation of therapeutic drug monitoring to guide dose adjustments. Close monitoring for adverse effects is advisable. For use at lower doses such as in treatment of neuropathic pain, standard dosing and prescribing measures apply, with monitoring for adverse effects.
CLOMIPRAMINE Antidepressants - TCAs	**CYP2D6 - Intermediate metabolizer** **CYP2C19 - Normal metabolizer:** Clomipramine is metabolized by CYP2C19 into an active metabolite, which is further metabolized by CYP2D6 into an inactive metabolite. Normal metabolism of clomipramine and reduced metabolism of the active metabolite are predicted.	CPIC[13] provides an optional recommendation to consider a 25% reduction of the recommended steady-state starting dose and utilisation of therapeutic drug monitoring to guide dose adjustments. Close monitoring for adverse effects is advisable. Note that these dosing recommendations only apply to higher initial doses of tricyclic antidepressants for treatment of conditions such as depression.

MAJOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
DESIPRAMINE Antidepressants - TCAs	**CYP2D6 - Intermediate metabolizer:** Reduced desipramine metabolism and increased exposure are predicted. This may increase the risk of adverse effects. Concentration-related adverse effects are less likely to be problematic at the lower doses used for treatment of conditions such as neuropathic pain.	CPIC[13] provides an optional recommendation to consider a 25% reduction of the recommended steady-state starting dose and utilisation of therapeutic drug monitoring to guide dose adjustments. Close monitoring for adverse effects is advisable. Note that these dosing recommendations only apply to higher initial doses of tricyclic antidepressants for treatment of conditions such as depression.
DOXEPIN Antidepressants - TCAs	**CYP2D6 - Intermediate metabolizer** **CYP2C19 - Normal metabolizer:** Doxepin is metabolized by CYP2C19 into an active metabolite, which is further metabolized by CYP2D6 into an inactive metabolite. Normal metabolism of doxepin and reduced metabolism of the active metabolite are predicted.	CPIC[13] provides an optional recommendation to consider a 25% reduction of the recommended steady-state starting dose and utilisation of therapeutic drug monitoring to guide dose adjustments. Close monitoring for adverse effects is advisable. Note that these dosing recommendations only apply to higher initial doses of tricyclic antidepressants for treatment of conditions such as depression.
IMIPRAMINE Antidepressants - TCAs	**CYP2D6 - Intermediate metabolizer** **CYP2C19 - Normal metabolizer:** Imipramine is metabolized by CYP2C19 into an active metabolite, which is further metabolized by CYP2D6 into an inactive metabolite. Normal metabolism of imipramine and reduced metabolism of the active metabolite are predicted.	CPIC[13] provides an optional recommendation to consider a 25% reduction of the recommended steady-state starting dose and utilisation of therapeutic drug monitoring to guide dose adjustments. Close monitoring for adverse effects is advisable. Note that these dosing recommendations only apply to higher initial doses of tricyclic antidepressants for treatment of conditions such as depression.
NORTRIPTYLINE Antidepressants - TCAs	**CYP2D6 - Intermediate metabolizer:** Reduced nortriptyline metabolism and increased exposure are predicted. This may increase the risk of adverse effects. Concentration-related adverse effects are less likely to be problematic at the lower doses used for treatment of conditions such as neuropathic pain.	For use at higher doses such as in the treatment of depression, CPIC[13] provides a recommendation to consider a 25% reduction of the recommended steady-state starting dose and utilisation of therapeutic drug monitoring to guide dose adjustments. Close monitoring for adverse effects is advisable. For use at lower doses such as in treatment of neuropathic pain, standard dosing and prescribing measures apply, with monitoring for adverse effects.
TRIMIPRAMINE Antidepressants - TCAs	**CYP2D6 - Intermediate metabolizer** **CYP2C19 - Normal metabolizer:** Trimipramine is metabolized by CYP2C19 into an active metabolite, which is further metabolized by CYP2D6 into an inactive metabolite. Normal metabolism of trimipramine and reduced metabolism of the active metabolite are predicted.	CPIC[13] provides an optional recommendation to consider a 25% reduction of the recommended steady-state starting dose and utilisation of therapeutic drug monitoring to guide dose adjustments. Close monitoring for adverse effects is advisable. Note that these dosing recommendations only apply to higher initial doses of tricyclic antidepressants for treatment of conditions such as depression.

MAJOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
PIMOZIDE Antipsychotics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This may increase the likelihood of concentration-dependent adverse effects, especially with high doses or if drug-drug interactions occur. There is a theoretically increased risk of QT prolongation (thus torsade de points); the recommendations for a lower dose aim to reduce the risk of excessively high plasma concentration of drug.	DPWG[14] recommends using no more than 80% of the standard maximum dose. Monitor for adverse effects.
THIORIDAZINE Antipsychotics ⚠	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This may potentially increase the risk of concentration-dependent adverse effects. The reduction in clearance of thioridazine may be associated with increased risk of Torsades de pointes and/or sudden death. Other factors contributing to this increased risk include: bradycardia, hypokalaemia, concomitant use of other drugs that prolong QT interval, and presence of congenital prolongation of the QT interval.	Note that the FDA-approved drug label states that thioridazine is contraindicated in patients with reduced activity of CYP2D6.[15] This includes patients with genetic variations leading to reduced activity, or patients with concomitant use of CYP2D6 inhibitors. Drugs that reduce clearance of thioridazine through other mechanisms also increase the risk of adverse events.
EFAVIRENZ Antivirals	**CYP2B6 - Intermediate metabolizer:** Reduced metabolism of efavirenz and higher dose-adjusted trough concentrations compared with normal metabolizers is predicted. This has been associated with an increased risk of concentration-dependent adverse effects, including CNS adverse events.	CPIC and DPWG[16], [17] provide a moderate recommendation to consider initiating efavirenz with decreased dose of 400 mg/day. If therapeutic drug monitoring is available and a decreased dose of efavirenz is prescribed, consider obtaining steady-state plasma efavirenz concentrations to ensure they are in the suggested therapeutic range. The potential benefits and risks of the reduced dose and pill number should be considered.
TAMOXIFEN Immunomodulators and antineoplastics ⚠	**CYP2D6 - Intermediate metabolizer:** Reduced formation of tamoxifen's active metabolite endoxifen by CYP2D6 is predicted. There is conflicting evidence on the effect of this genotype on cancer outcomes. Some studies have shown an increased risk of disease recurrence, whilst others have not shown such effects.	There is controversy whether any treatment changes are required. For the adjuvant treatment of ER+ breast cancer, CPIC guidelines[18] provides a moderate* recommendation to consider hormonal therapy such as an aromatase inhibitor for postmenopausal women or aromatase inhibitor along with ovarian function suppression in premenopausal women. If aromatase inhibitor use is contraindicated, consideration should be given to use a higher but label-approved tamoxifen dose (e.g. 40 mg/day). Avoid CYP2D6 strong to weak inhibitors. *A moderate recommendation means there is close or uncertain balance as to whether the evidence is high quality and desirable effects clearly outweigh undesirable effects.

MAJOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
CODEINE Opioid Analgesics	**CYP2D6 - Intermediate metabolizer** **OPRM1 - Normal mu opioid receptor expression :** Reduced metabolism of codeine by CYP2D6 into its active metabolite morphine is predicted. This could lead to a reduction in analgesic response to codeine. Whilst this OPRM1 genotype has been associated with increased sensitivity to morphine and by extrapolation, to codeine as well, there is insufficient evidence for its clinical significance. Codeine is contraindicated in children under 12 years of age.[2]	Based on the CYP2D6 genotype CPIC[3] provides a moderate recommendation to prescribe codeine according to usual label recommended age or weight specific dosing. Monitor for a reduced clinical response. If response is inadequate and opioid use is warranted, consider a non-tramadol opioid. DPWG [4] provides a recommendation to be alert to possible reduced analgesic effects. In the case of reduced effectiveness, increase the dose or choose a non-tramadol alternative. There is no additional genotype-guided dosing recommendation based on the OPRM1 result.
TRAMADOL Opioid Analgesics	**CYP2D6 - Intermediate metabolizer:** Reduced formation of tramadol's active metabolite is predicted. This could lead to a reduction in analgesic response. Note that tramadol is a serotonergic drug. There is an increased risk of serotonin toxicity when used together with other serotonergic drugs.	CPIC guidelines[3] provide an optional recommendation to use tramadol according to usual label recommended age or weight specific dosing. If no response and opioid use is warranted, consider non-codeine opioid. DPWG guidelines[4] provide a recommendation to be alert to possible reduced analgesic effects. In the case of reduced effectiveness, increase the dose or choose a non-codeine alternative.
ATORVASTATIN Statins	**SLCO1B1 - Decreased transporter function:** This SLCO1B1 genotype is associated with increased atorvastatin exposure compared with a normal function genotype, which may translate to increased risk of atorvastatin related myopathy.[1] Other factors that may further increase this myopathy risk include: higher doses, certain co-administered drugs, female sex, patient frailty, renal failure, hypothyroidism, advanced age, low BMI, intense physical exercise and Asian or African ancestry.	Based on this SLCO1B1 genotype, CPIC guidelines[1] provide a moderate recommendation to prescribe less than or equal to 40 mg as a starting dose and adjust doses based on disease-specific guidelines. Be aware of possible increased risk for myopathy especially for the 40 mg dose. If doses >40mg are needed for desired efficacy, consider combination therapy (i.e. atorvastatin plus non-statin guideline directed medical therapy). Based on this SLCO1B1 genotype, the risk of statin-associated musculoskeletal symptoms (SAMS)[1] is as follows: Atorvastatin 80mg - High SAMS risk If used < 1 year: Consider changing to a statin/dose combination with lower SAMS risk. If used > 1 year without SAMS: it is reasonable to continue. Atorvastatin 40mg - Moderate SAMS risk If used < 4 weeks: Consider changing to a statin/dose combination with lower SAMS risk. If used > 4 weeks without SAMS: it is reasonable to continue. Atorvastatin 10-20mg - Low SAMS risk.

MAJOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
LOVASTATIN Statins ⚠	**SLCO1B1 - Decreased transporter function:** This SLCO1B1 genotype is associated with an increased lovastatin exposure compared with a normal function genotype, which may translate to increased myopathy risk.[1] Other factors that may further increase this myopathy risk: higher doses, certain co-administered drugs, female sex, patient frailty, renal failure, hypothyroidism, advanced age, low BMI, intense physical exercise and Asian or African ancestry.	CPIC guidelines[1] provide a moderate recommendation to prescribe an alternative statin depending on the desired potency. If lovastatin therapy is warranted, limit dose to less than or equal to 20mg daily. Based on this SLCO1B1 genotype, the risk of statin-associated musculoskeletal symptoms (SAMS)[1] is as follows: Lovastatin 40-80mg - High SAMS risk If used < 1 year: Consider changing to a statin/dose combination with lower SAMS risk. If used > 1 year without SAMS: it is reasonable to continue. Lovastatin 20mg - Moderate SAMS risk If used < 4 weeks: Consider changing to a statin/dose combination with lower SAMS risk. If used > 4 weeks without SAMS: it is reasonable to continue.
PITAVASTATIN Statins	**SLCO1B1 - Decreased transporter function:** This SLCO1B1 genotype is associated with an increased pitavastatin exposure compared with a normal function genotype, which may translate to increased myopathy risk.[1] Other factors that may further increase this myopathy risk include: higher doses, certain co-administered drugs, female sex, patient frailty, renal failure, hypothyroidism, advanced age, low BMI, intense physical exercise and Asian or African ancestry.	CPIC guidelines[1] provide a moderate recommendation to prescribe a less than or equal to 2 mg starting dose and adjust doses based on disease-specific guidelines. Be aware of possible increased risk for myopathy, especially for doses >1 mg. If a dose >2 mg is required for desired efficacy, consider an alternative statin or combination therapy (i.e. pitavastatin plus non-statin guideline directed medical therapy). Based on this SLCO1B1 genotype, the risk of statin-associated musculoskeletal symptoms (SAMS)[1] is as follows: Pitavastatin 4mg - High SAMS risk If used < 1 year: Consider changing to a statin/dose combination with lower SAMS risk. If used > 1 year without SAMS: it is reasonable to continue. Pitavastatin 2mg - Moderate SAMS risk If used < 4 weeks: Consider changing to a statin/dose combination with lower SAMS risk. If used > 4 weeks without SAMS: it is reasonable to continue. Pitavastatin 1mg - Low SAMS risk.

MAJOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
SIMVASTATIN Statins ⚠	**SLCO1B1 - Decreased transporter function:** This SLCO1B1 genotype is associated with increased simvastatin exposure and increased myopathy risk compared with the normal function genotype.[1] Other factors that may further increase this myopathy risk include: higher doses, certain co-administered drugs, female sex, patient frailty, renal failure, hypothyroidism, advanced age, low BMI, intense physical exercise and Asian or African ancestry.	Based on this SLCO1B1 genotype, CPIC guidelines[1] provide a strong recommendation to prescribe an alternative statin depending on desired potency. If simvastatin therapy is warranted, limit dose to <20 mg daily. Based on this SLCO1B1 genotype, the risk of statin-associated musculoskeletal symptoms (SAMS)[1] is as follows: Simvastatin 20-40mg - High SAMS risk If used < 1 year: Consider changing to a statin/dose combination with lower SAMS risk. If used > 1 year without SAMS: it is reasonable to continue. Simvastatin 10mg - Moderate SAMS risk If used < 4 weeks: Consider changing to a statin/dose combination with lower SAMS risk. If used > 4 weeks without SAMS: it is reasonable to continue.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
VILOXAZINE ADHD - miscellaneous agents	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and theoretically increased drug exposure is predicted.	No genotype-guided dosing recommendation available. Be alert to adverse effects.
PERHEXILINE Antianginals	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism and increased perhexiline exposure are predicted. There is an increased risk of concentration-dependent adverse effects (hepatotoxicity and peripheral neuropathy), especially if appropriate dose reduction and therapeutic drug monitoring do not occur.	Expect a prolonged time to reach steady-state. Early therapeutic drug monitoring is required when perhexiline is used. A reduced maintenance dose requirement is expected. Monitor closely for concentration-dependent adverse effects.
DARIFENACIN Anticholinergics (genitourinary)	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This may increase the risk of adverse effects. Concomitant use with CYP3A4 inhibiting drugs may be expected to further increase darifenacin exposure and the risk of adverse effects.	No genotype-guided dosing recommendation available. Monitor for adverse effects.
FESOTERODINE Anticholinergics (genitourinary)	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and theoretically increased drug exposure is predicted.	No genotype-guided dosing recommendation available. Be alert to adverse effects.
TOLTERODINE Anticholinergics (genitourinary)	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This may increase the risk of concentration-dependent adverse effects.	No genotype-guided dosing recommendation is available. Monitor for adverse effects.
DONEPEZIL Anticholinesterases	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism via CYP2D6 and increased drug exposure are predicted. This may increase the risk of concentration-dependent adverse effects and a poorer response to therapy.	No genotype-guided dosing recommendation available. Monitor for adverse effects or a poor response to therapy. Note that the CYP2D6 genotype is not expected to affect the metabolism of an alternate cholinesterase inhibitor, rivastigmine.
GALANTAMINE Anticholinesterases	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism via CYP2D6 and increased drug exposure are predicted. This may increase the risk of concentration-dependent adverse effects.	No genotype-guided dosing recommendation available. Monitor for adverse effects or a poor response to therapy. Note that the CYP2D6 genotype is not expected to affect the metabolism of an alternate cholinesterase inhibitor, rivastigmine.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
BUPROPION Antidepressants - other	**CYP2B6 - Intermediate metabolizer:** Individuals with this genotype may have reduced bupropion metabolism and formation of the active metabolite hydroxybupropion (based on studies mainly involving the *6 and *18 alleles), as compared with individuals carrying only normal and/or increased function alleles.[19] Reduced CYP2B6 function may result in reduced effect and/or adverse effects, however, direct evidence is lacking. Other genetic and clinical factors may also affect bupropion metabolism.	Be alert to adverse effects and monitor for adequate clinical response. No genotype-guided dosing recommendation available. Usual prescribing considerations apply.
MIRTAZAPINE Antidepressants - other	**CYP2D6 - Intermediate metabolizer** **CYP1A2 - Normal metabolizer:** Mirtazapine is metabolized by a number of enzymes, including CYP2D6 and CYP1A2. Reduced metabolism by CYP2D6 and normal metabolism by CYP1A2 (less affected by exposure to enzyme inducers such as cigarette smoke) are predicted. There may be increased exposure to mirtazapine and potentially increased clinical effects (therapeutic and/or adverse).	Be alert for adverse effects. Based on the CYP2D6 genotype, DPWG suggests that no specific action on mirtazapine dosing is required.[20]
VORTIOXETINE Antidepressants - other	**CYP2D6 - Intermediate metabolizer:** Reduced vortioxetine metabolism and increased drug exposure is predicted. This may increase the risk of adverse effects.[10]	CPIC guidelines[10] provide a moderate recommendation to initiate therapy with the recommended starting dose.
DULOXETINE Antidepressants - SNRIs	**CYP2D6 - Intermediate metabolizer** **CYP1A2 - Normal metabolizer:** Duloxetine is metabolized by both CYP1A2 and CYP2D6, with CYP1A2 likely to have the major role. Reduced metabolism of duloxetine by CYP2D6 and normal metabolism by CYP1A2 (less affected by exposure to enzyme inducers such as tobacco smoke) is predicted. This may lead to a small increase in exposure to duloxetine. Note that CPIC[10] state that there are currently no recommendations for dosing of duloxetine based on CYP2D6 genotype.	No genotype-guided dosing recommendation available. Be alert to adverse effects.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
FLUOXETINE Antidepressants - SSRIs	**CYP2D6 - Intermediate metabolizer** **CYP2C9 - Normal metabolizer:** The metabolism of fluoxetine is complex due to the involvement of several CYP enzymes (especially CYP2D6 and CYP2C9), the formation of active metabolites and the inhibition of CYP2D6 by fluoxetine and its metabolites. The CYP2D6 genotype predicts increased fluoxetine exposure and reduced formation of the active S-norfluoxetine metabolite. The CYP2C9 genotype predicts normal metabolism via this pathway. However, fluoxetine and its metabolites can strongly inhibit CYP2D6 function, potentially converting the phenotype to a poor metabolizer which can last for up to 9 weeks after cessation of fluoxetine (this is particularly relevant if commencing a drug extensively metabolized by CYP2D6 during this time). This CYP2D6 inhibition is dose and duration of therapy dependent and could potentially lead to late onset adverse effects on a previously tolerated fluoxetine dose.	Based on the CYP2D6 genotype, CPIC[10] and DPWG[21] recommend that no specific action on fluoxetine dosing is required for this genotype. Monitor for altered clinical effect, including adverse effects. If adverse effects are a concern, consider an alternative antidepressant for which normal metabolism is predicted.
FLUVOXAMINE Antidepressants - SSRIs	**CYP2D6 - Intermediate metabolizer** **CYP1A2 - Normal metabolizer:** Fluvoxamine is metabolized by both CYP2D6 (predominant pathway) and CYP1A2. Reduced metabolism by CYP2D6 and normal metabolism by CYP1A2 (not affected by enzyme inducers such as cigarette smoke) are predicted. Fluvoxamine itself will inhibit CYP1A2. There may be increased exposure to fluvoxamine and potentially an increased risk of adverse effects.	Based on the CYP2D6 genotype, CPIC[10] provides a moderate recommendation to initiate therapy with the recommended starting dose. DPWG[12] suggests no specific action on fluvoxamine dosing is required based on this CYP2D6 genotype.
SERTRALINE Antidepressants - SSRIs	**CYP2B6 - Intermediate metabolizer** **CYP2C19 - Normal metabolizer:** Sertraline is metabolized by both CYP2C19 and CYP2B6 into less active compounds. Normal metabolism by CYP2C19 and reduced metabolism by CYP2B6 is predicted.[10]	CPIC[10] guidelines provide a moderate recommendation to initiate therapy with the recommended starting dose. Consider a slower titration schedule and a lower maintenance dose.
AMOXAPINE Antidepressants - TCAs	**CYP2D6 - Intermediate metabolizer:** Slightly reduced metabolism of amoxapine by CYP2D6 is predicted which could theoretically lead to slightly increased amoxapine exposure, although direct evidence is lacking. The FDA notes that systemic concentrations may be altered with this genotype.[22]	No genotype-guided dosing recommendation available. Consider standard dosing. Monitor for adverse effects.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
PROTRIPTYLINE Antidepressants - TCAs	**CYP2D6 - Intermediate metabolizer:** Slightly reduced metabolism of protriptyline by CYP2D6 is predicted which could theoretically lead to slightly increased amoxapine exposure, although direct evidence is lacking.	No genotype-guided dosing recommendation available. Consider standard dosing. Monitor for adverse effects.
METOCLOPRAMIDE Antiemetics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism of metoclopramide by CYP2D6 is predicted. There may be an increased risk of extrapyramidal adverse effects, particularly at higher doses.	No genotype-guided dosing recommendation available. Monitor for adverse effects.
ONDANSETRON Antiemetics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism via CYP2D6 and increased drug exposure are predicted. This may increase the risk of concentration-dependent adverse effects.	CPIC[23] notes that there is insufficient evidence for the clinical impact based on this CYP2D6 genotype. The usual starting dose is suggested. It would be advisable to monitor for adverse effects, especially with the use of higher doses.
CHLORPHENIRAMINE Antihistamines	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism of chlorpheniramine and increased drug exposure are predicted. There may potentially be an increased risk of adverse effects, such as drowsiness, although evidence for this is limited.	No genotype-guided dosing recommendation available. Consider using a lower starting dose. Monitor for adverse effects.
DEXCHLORPHENIRAMINE Antihistamines	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism of dexchlorpheniramine and increased drug exposure are predicted. There may potentially be an increased risk of adverse effects, such as drowsiness, although evidence for this is limited.	No genotype-guided dosing recommendation available. Consider using a lower starting dose. Monitor for adverse effects.
PROMETHAZINE Antihistamines	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism of promethazine and increased drug exposure are predicted. There may potentially be an increased risk of adverse effects, such as drowsiness, although evidence for this is limited.	No genotype-guided dosing recommendation available. Consider using a lower starting dose. Monitor for adverse effects.
ARIPIPRAZOLE Antipsychotics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. Whilst the plasma concentration of the sum of aripiprazole and the active metabolite dehydroaripiprazole may be increased to a limited degree, there is insufficient evidence that this increases the risk of side effects.	Monitor for adverse effects. The DPWG[24] suggests that no specific action on aripiprazole dosing is required with this genotype.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
ARIPIPRAZOLE LAUROXIL Antipsychotics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 is predicted, which could theoretically lead to an increased drug exposure, but there is insufficient evidence that this increases the risk of side effects.	Standard dosing and prescribing measures apply. Monitor for adverse effects. Aristada Initio®: The FDA-approved drug label[25] advises avoiding concomitant use of Aristada Initio with strong CYP3A4 or CYP2D6 inhibitors, or strong CYP3A4 inducers, due to inability for dose modification. Aristada®: If taking concomitant strong CYP3A4 or CYP2D6 inhibitor for more than 2 weeks, the FDA-approved drug label[26] advises reducing the dose of Aristada to the next lower strength; no dosage adjustment is necessary if tolerating 441 mg dose. If taking concomitant strong CYP3A4 and CYP2D6 inhibitors, avoid use of 662mg, 882mg or 1064 mg dose; no dosage adjustment is necessary if tolerating 441 mg dose. If taking concomitant CYP3A4 inducers for more than 2 weeks, increase the 441 mg dose to 662 mg; no dose adjustment for 662 mg, 882 mg or 1062 mg doses.
BREXPIPRAZOLE Antipsychotics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This may increase the risk of concentration-dependent adverse effects.	DPWG guidelines[27] suggest that no specific action on brexpiprazole dosing is required based on this genotype. Monitor for adverse effects.
CHLORPROMAZINE Antipsychotics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism of chlorpromazine by CYP2D6 and slightly increased drug exposure are predicted. The clinical significance is not known, though an increase in adverse effects is possible.	No genotype-guided dosing recommendation available. Monitor for adverse effects.
CLOZAPINE Antipsychotics	**CYP2D6 - Intermediate metabolizer** **CYP1A2 - Normal metabolizer:** Based on the CYP1A2 genotype, normal metabolism is predicted. The highly inducible genotype *1F/*1F is not present and therefore metabolism is less likely to be increased by inducers such as tobacco smoking, daily consumption of cruciferous vegetables or chargrilled meat, and certain medications (e.g. omeprazole). The DPWG guidelines [28] state that there is no gene-drug interaction for CYP1A2 and clozapine. Based on the CYP2D6 genotype, reduced metabolism and increased drug exposure are predicted.	Standard dosing and prescribing measures apply. Monitor for adverse effects. The DPWG guidelines [28] state that no action is required for this CYP2D6 genotype and clozapine.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
HALOPERIDOL Antipsychotics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This may increase the risk of concentration-dependent adverse effects.	Monitor for adverse effects. The DPWG[28] suggests that no specific action on haloperidol dosing is required with this genotype.
ILOPERIDONE Antipsychotics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism of iloperidone by CYP2D6 is predicted which could lead to increased drug exposure.	No genotype-guided dosing recommendation available. Consider standard dosing. Monitor for adverse effects.
PERPHENAZINE Antipsychotics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism of perphenazine by CYP2D6 is predicted which could lead to increased perphenazine exposure.	No genotype-guided dosing recommendation available. Consider standard dosing. Monitor for adverse effects.
RISPERIDONE Antipsychotics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism and increased drug exposure are predicted. This may increase the risk of adverse effects, although there is little evidence to suggest that this is clinically significant. This genetic variation may lead to a decrease in the required maintenance dose.	The DPWG[29] suggests that no specific action on risperidone dosing is required with this genetic result, as the effects on dose may be within the range of normal biological variation. It would be reasonable to be alert to adverse effects and adjust dose according to clinical response.
DEXTROMETHORPHAN Antitussives	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism and increased drug exposure are predicted. This may increase the risk of adverse effects.	No genotype-guided dosing recommendation available. Monitor for adverse effects.
NEVIRAPINE Antivirals	**CYP2B6 - Intermediate metabolizer:** Reduced metabolism by CYP2B6 and increased nevirapine exposure are predicted. This is more likely to be significant with high dosages or if drug-drug interactions occur. There may be an increased risk of Stevens-Johnson Syndrome/TEN with nevirapine treatment in individuals with the 516G>T allele (present in *6) and the 983T>C allele (present in *18), compared with those without these alleles. This is only one of a number of risk factors associated with Stevens-Johnson Syndrome.	No genotype-guided dosing recommendation available. Monitor for adverse effects.
CARVEDILOL Beta blockers	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This could potentially lead to increased clinical effects, although the evidence for this with carvedilol is weak.	DPWG[30] suggests that no specific action on carvedilol dosing is required based on this genotype. Monitor for adverse effects.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
METOPROLOL Beta blockers	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. Clinical consequences are limited mainly to the occurrence of asymptomatic bradycardia.	Be alert to adverse effects such as bradycardia. Where a more gradual reduction in heart rate is desired, or where there are greater concerns for symptomatic bradycardia, DPWG[31] has recommendations to increase the dose in smaller steps and/or prescribe no more than 50% of the standard dose. If currently well tolerated and clinical response has been adequate, a change to therapy may not be required.
PROPRANOLOL Beta blockers	**CYP2D6 - Intermediate metabolizer** **CYP1A2 - Normal metabolizer:** Propranolol is metabolized by both CYP2D6 and CYP1A2 and also has an active metabolite. This genotype predicts reduced metabolism by CYP2D6 and normal metabolism by CYP1A2 (which is less affected by inducers such as cigarette smoke). This could potentially lead to an enhanced beta blocker effect.	No genotype-guided dosing guideline available. Monitor for adverse effects, especially during dose titration.
TIMOLOL Beta blockers	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased systemic drug exposure are predicted. This could theoretically lead to increased clinical effects, however evidence for this is lacking.	Monitor for systemic beta blocker adverse effects such as bradycardia and bronchospasm.
PITOLISANT Drugs for anxiety and sleep disorders	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and theoretically increased drug exposure is predicted.	No genotype-guided dosing recommendation available. Be alert to adverse effects.
ELAGOLIX Endocrine drugs	**SLCO1B1 - Decreased transporter function:** One SLCO1B1*5 variant allele is present. The FDA-approved drug label notes that individuals with two SLCO1B1*5 variant alleles have higher plasma concentrations of elagolix. The clinical significance of the presence of this single *5 variant allele is uncertain.	No genotype-guided dosing recommendation available. Standard dosing and prescribing measures apply. Monitor for adverse effects.
GEFITINIB Immunomodulators and antineoplastics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 is predicted, which could theoretically lead to increased drug exposure. This could increase the risk of adverse effects.	Standard dosing and prescribing measures apply. Monitor for adverse effects and adjust therapy accordingly. The DPWG[32] suggests that no specific action on gefitinib dosing is required with this genetic result.
CEVIMELINE Miscellaneous	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 is predicted, which could theoretically lead to an increased drug exposure. This could increase the risk of adverse effects.	No genotype-guided dosing recommendation available. Standard dosing and prescribing measures apply. Monitor for adverse effects.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
ELIGLUSTAT Miscellaneous	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism of eliglustat and increased drug exposure are predicted. This may increase the risk of adverse effects. However, in the absence of CYP2D6 and CYP3A4 inhibitors, this does not result in a clinically significant increased risk of side effects.[33]	The recommended dose of eliglustat depends on whether CYP3A4 and/or CYP2D6 inhibiting medications are co-prescribed. Refer to DPWG guidelines,[33] FDA-approved drug label[34] or TGA-approved product information[35] for prescribing details.
LOFEXIDINE Miscellaneous	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 is predicted, which could theoretically lead to increased drug exposure. This could increase the risk of adverse effects.	No genotype-guided dosing recommendation available. Standard dosing and prescribing measures apply. Monitor for adverse effects.
MECLIZINE Miscellaneous	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 is predicted, which could theoretically lead to increased drug exposure. This could increase the risk of adverse effects.	No genotype-guided dosing recommendation available. The FDA-approved drug label[36] suggests monitoring for adverse effects and clinical effects, as the genetic polymorphism of CYP2D6 could contribute to large variability in meclizine exposure.
TAMSULOSIN Miscellaneous	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This may could potentially increase the risk of concentration-dependent adverse effects.	No genotype-guided dosing recommendation available. Monitor for adverse effects.
DEUTETRABENAZINE Neurological drugs	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism of deutetrabenazine by CYP2D6 is predicted which could theoretically lead to increased drug exposure, although direct evidence is lacking.	No genotype-guided dosing recommendation available. Monitor for adverse effects.
TETRABENAZINE Neurological drugs	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This may increase the risk of concentration-dependent adverse effects.	The FDA[37] approved drug label advises a maximum daily dose of 100mg, with a maximum recommended single dose of 37.5mg.
VALBENAZINE Neurological drugs	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism of valbenazine by CYP2D6 is predicted which could theoretically lead to increased drug exposure, although direct evidence is lacking.	No genotype-guided dosing recommendation available. Monitor for adverse effects.
HYDROCODONE Opioid Analgesics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 could lead to an increase in hydrocodone exposure and a reduction in exposure to the active metabolite, hydromorphone, thereby potentially reducing the analgesic response. However, there is minimal evidence for this pharmacokinetic or clinical effect.	CPIC[3] provides an optional recommendation to use the hydrocodone label recommended age- or weight-specific dosing. If no response and opioid use is warranted, consider a non-codeine or non-tramadol opioid.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
METHADONE Opioid Analgesics	**CYP2B6 - Intermediate metabolizer:** Slightly reduced metabolism by CYP2B6 and increased methadone exposure are predicted in most instances. However if a *4 allele is present, there is limited evidence suggesting there may be increased methadone metabolism, leading to reduced drug exposure.	No genotype-guided dosing recommendation available. Monitor for an altered clinical effect, including adverse effects, arising from methadone concentrations out of the expected range.
OLICERIDINE Opioid Analgesics	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and theoretically increased drug exposure is predicted.	No genotype-guided dosing recommendation available. Be alert to adverse effects.
OXYCODONE Opioid Analgesics	**CYP2D6 - Intermediate metabolizer:** Reduced exposure to oxycodone's active metabolite, oxymorphone, is predicted. Although this could potentially lead to reduced analgesia, there is limited evidence to suggest that this is clinically significant.	Due to weak evidence for adverse effects and analgesia, CPIC guidelines[3] have no recommendations to support oxycodone dosing. DPWG guidelines[4] also suggest that no specific action on oxycodone dosing is required. Be alert to a reduced analgesic response.
DEXLANSOPRAZOLE Proton pump inhibitors	**CYP2C19 - Normal metabolizer:** This genotype predicts normal metabolism of dexlansoprazole by CYP2C19. However, this rate of metabolism has been associated with a potentially incomplete clinical response in conditions such as oesophagitis and H. pylori.	CPIC guidelines have an optional recommendation to initiate a standard starting daily dose. Consider increasing the dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis, and giving the daily dose in divided doses.[38] If response is inadequate, consider the use of esomeprazole or rabeprazole.
LANSOPRAZOLE Proton pump inhibitors	**CYP2C19 - Normal metabolizer:** This genotype predicts typical metabolism of lansoprazole. However, this rate of metabolism has been associated with a potentially incomplete clinical response in conditions such as oesophagitis and H. pylori, compared to intermediate and poor metabolizers.	CPIC guidelines have a moderate recommendation to initiate a standard starting daily dose. Consider increasing the dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis, and giving the daily dose in divided doses.[38] If response is inadequate, consider the use of esomeprazole or rabeprazole.
OMEPRAZOLE Proton pump inhibitors	**CYP2C19 - Normal metabolizer:** This genotype predicts typical metabolism of omeprazole. However, this rate of metabolism has been associated with a potentially incomplete clinical response in conditions such as oesophagitis and H. pylori, compared to intermediate and poor metabolizers.	CPIC guidelines have a moderate recommendation to initiate a standard starting daily dose. Consider increasing the dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis, and giving the daily dose in divided doses.[38] If response is inadequate, consider use of esomeprazole or rabeprazole.
PANTOPRAZOLE Proton pump inhibitors	**CYP2C19 - Normal metabolizer:** This genotype predicts typical metabolism of pantoprazole. However, this rate of metabolism has been associated with a potentially incomplete clinical response in conditions such as oesophagitis and H. pylori, compared to intermediate and poor metabolizers.	CPIC guidelines have a moderate recommendation to initiate a standard starting daily dose. Consider increasing the dose by 50-100% for the treatment of H. pylori infection and erosive esophagitis, and giving the daily dose in divided doses.[38] If response is inadequate, consider the use of esomeprazole or rabeprazole.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
AMPHETAMINE Psychostimulants	**CYP2D6 - Intermediate metabolizer:** Although the enzymes involved in amphetamine metabolism have not been clearly defined, CYP2D6 is involved in the formation of an active metabolite 4-hydroxy-amphetamine. Reduced metabolism by CYP2D6 is predicted which could lead to variations in amphetamine metabolism.[39]. Whilst this could potentially increase drug exposure, the clinical significance of this has not yet been established.	No genotype-guided dosing recommendation available. Consider standard dosing. It would be reasonable to monitor for adverse effects.
DEXTROAMPHETAMINE Psychostimulants	**CYP2D6 - Intermediate metabolizer:** Dextroamphetamine is eliminated by both the kidney (as unchanged drug) and the liver, with CYP2D6 playing a significant role. Reduced metabolism via CYP2D6 and increased dextroamphetamine exposure is predicted, however the clinical significance of this has not yet been established.	No genotype-guided dosing recommendation available. It would be reasonable to monitor for adverse effects.
LISDEXAMFETAMINE Psychostimulants	**CYP2D6 - Intermediate metabolizer:** Lisdexamfetamine is a prodrug of dextroamphetamine (also known as dexamfetamine). Dextroamphetamine is eliminated by both the kidney (as unchanged drug) and the liver, with CYP2D6 playing a significant role. Reduced metabolism via CYP2D6 and increased dextroamphetamine exposure is predicted, however the clinical significance of this has not yet been established.	No genotype-guided dosing recommendation available. It would be reasonable to monitor for adverse effects.
FLUVASTATIN Statins	**SLCO1B1 - Decreased transporter function** **CYP2C9 - Normal metabolizer:** This SLCO1B1 genotype is associated with an increased exposure to fluvastatin as compared with the normal function genotype; there is typical myopathy risk with doses of less than or equal to 40mg.[1] This CYP2C9 genotype predicts normal metabolism of fluvastatin by this enzyme. Other factors that may further increase this myopathy risk include: higher doses, certain co-administered drugs, female sex, patient frailty, renal failure, hypothyroidism, advanced age, low BMI, intense physical exercise and Asian or African ancestry.	CPIC guidelines[1] provide a moderate recommendation to prescribe the desired starting dose and adjust doses based on disease-specific guidelines. Be aware of possible increased risk for myopathy, especially for doses >40mg daily. Based on this SLCO1B1 genotype, the risk of statin-associated musculoskeletal symptoms (SAMS)[1] is as follows: Fluvastatin 80mg - Moderate SAMS risk If used < 4 weeks: Consider changing to a statin/dose combination with lower SAMS risk. If used > 4 weeks without SAMS: it is reasonable to continue. Fluvastatin 20-40mg - Low SAMS risk.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
PRAVASTATIN Statins	**SLCO1B1 - Decreased transporter function:** This SLCO1B1 genotype is associated with an increased pravastatin exposure compared with a normal function genotype. There is a typical myopathy risk with doses less than or equal to 40mg.[1] Other factors that may further increase this myopathy risk include: higher doses, certain co-administered drugs, female sex, patient frailty, renal failure, hypothyroidism, advanced age, low BMI, intense physical exercise and Asian or African ancestry.	CPIC guidelines[1] provide a moderate recommendation to prescribe the desired starting dose and adjust doses based on disease specific guidelines. Be aware of possible increased risk for myopathy, especially with doses >40mg daily. Based on this SLCO1B1 genotype, the risk of statin-associated musculoskeletal symptoms (SAMS)[1] is as follows: Pravastatin 80mg - Moderate SAMS risk If used < 4 weeks: Consider changing to a statin/dose combination with lower SAMS risk. If used > 4 weeks without SAMS: it is reasonable to continue. Pravastatin 10-40mg - Low SAMS risk.
ROSUVASTATIN Statins	**ABCG2 (rs2231142) - Normal transporter function** **SLCO1B1 - Decreased transporter function:** This SLCO1B1 genotype is associated with an increased rosuvastatin exposure compared with a normal function genotype, however is associated with a typical myopathy risk with doses of rosuvastatin up to 20 mg.[1] This ABCG2 genotype is associated with a typical rosuvastatin exposure and myopathy risk.[1] Other factors that may further increase this myopathy risk include: higher doses, certain co-administered drugs, female sex, patient frailty, renal failure, hypothyroidism, advanced age, low BMI, intense physical exercise and Asian or African ancestry.	CPIC guidelines[1] provide a strong recommendation to prescribe the desired starting dose and adjust doses according to disease-specific and specific population guidelines. Be aware of possible increased risk for myopathy especially for doses over 20 mg. Based on this SLCO1B1 genotype, the risk of statin-associated musculoskeletal symptoms (SAMS)[1] is as follows: Rosuvastatin 40mg - Moderate SAMS risk If used < 4 weeks: Consider changing to a statin/dose combination with lower SAMS risk. If used > 4 weeks without SAMS: it is reasonable to continue. Rosuvastatin 5-20mg - Low SAMS risk.

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
METHYLPHENIDATE ADHD - miscellaneous agents	**CYP2D6 - Intermediate metabolizer** **COMT - Normal to high COMT enzyme activity:** DPWG guidelines[40],[41] state that there is no gene-drug interaction for methylphenidate with CYP2D6 and COMT.	No dosage recommendation is currently available based on the genetic findings.
IRBESARTAN Angiotensin receptor blockers	**CYP2C9 - Normal metabolizer:** Normal metabolism of irbesartan by CYP2C9 is predicted.	Standard dosing and prescribing measures apply.
LOSARTAN Angiotensin receptor blockers	**CYP2C9 - Normal metabolizer:** Normal formation of losartan's active metabolite by CYP2C9 and a typical clinical response is predicted.	Standard dosing and prescribing measures apply.
ACENOCOUMAROL Anticoagulants	**VKORC1 - Normal VKORC1 enzyme level** **CYP2C9 - Normal metabolizer:** Normal metabolism of acenocoumarol by CYP2C9 is predicted. Normal amount of VKORC1 present (the enzyme inhibited by acenocoumarol). Overall acenocoumarol sensitivity is predicted to be normal.	No widely used or label approved genotype-guided dosing algorithm. Usual prescribing considerations apply.
PRASUGREL Anticoagulants	**CYP2C19 - Normal metabolizer:** DPWG[5] states that there is no gene-drug interaction for CYP2C19 and prasugrel.	No genotype-guided dosing recommendation available for this genotype. Standard dosing and prescribing measures apply.
TICAGRELOR Anticoagulants	**CYP2C19 - Normal metabolizer:** DPWG[42] states that there is no gene-drug interaction for ticagrelor and CYP2C19.	No genotype-guided dosing recommendation available for this genotype. Standard dosing and prescribing measures apply.
WARFARIN Anticoagulants	**VKORC1 - Normal VKORC1 enzyme level** **CYP2C9 - Normal metabolizer:** Normal metabolism of warfarin by CYP2C9 is predicted. Normal amount of VKORC1 (the enzyme warfarin inhibits). The combined CYP2C9 and VKORC1 results predict warfarin sensitivity to be normal.	CYP2C9 and VKORC1 - For patients already taking warfarin (e.g. more than 5 doses), dose adjustment is guided by INR. For patients initiating warfarin, there are CPIC[43] recommendations to reach the therapeutic dose. The summary of CPIC recommendations include consideration of the use of validated published pharmacogenetic algorithms[44],[45] available at warfarindosing.org that take into account clinical details as well as genetic findings. See CPIC guidelines for further details. If the patient identifies to be of African ancestry, CPIC provides recommendations for special dosing requirements for warfarin.
CITALOPRAM Antidepressants - SSRIs	**CYP2C19 - Normal metabolizer:** Normal metabolism of citalopram by CYP2C19 is predicted.	CPIC guidelines[10] provide a strong recommendation to initiate therapy with the recommended starting dose.
ESCITALOPRAM Antidepressants - SSRIs	**CYP2C19 - Normal metabolizer:** Normal metabolism of escitalopram by CYP2C19 is predicted.	CPIC guidelines[10] provide a strong recommendation to initiate therapy with the recommended starting dose.

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
GLIMEPIRIDE Antidiabetics	**CYP2C9 - Normal metabolizer:** Normal metabolism of glimepiride by CYP2C9 is predicted.	Standard dosing and prescribing measures apply.
GLIPIZIDE Antidiabetics	**CYP2C9 - Normal metabolizer:** Normal metabolism of glipizide by CYP2C9 is predicted.	Standard dosing and prescribing measures apply.
GLYBURIDE Antidiabetics	**CYP2C9 - Normal metabolizer:** Normal metabolism of glyburide by CYP2C9 is predicted.	Standard dosing and prescribing measures apply.
NATEGLINIDE Antidiabetics	**CYP2C9 - Normal metabolizer:** Normal metabolism of nateglinide by CYP2C9 is predicted.	Standard dosing and prescribing measures apply.
TOLBUTAMIDE Antidiabetics	**CYP2C9 - Normal metabolizer:** Normal metabolism of tolbutamide by CYP2C9 is predicted.	DPWG[46] states that there is no action needed for this gene-drug interaction.
BRIVARACETAM Antiepileptics	**CYP2C19 - Normal metabolizer:** Normal metabolism of brivaracetam by CYP2C19 is predicted.	Standard dosing and prescribing measures apply. The FDA-approved drug label for brivaracetam states that those using inhibitors of CYP2C19 may require dose reduction.[47]
FOSPHENYTOIN Antiepileptics	**HLA-B*15:02 (rs144012689) - Normal risk of certain hypersensitivity reactions** **CYP2C9 - Normal metabolizer:** Fosphenytoin is a prodrug of phenytoin. The rs144012689 TT result provides a high prediction of the absence of HLA-B*15:02 allele. Normal metabolism of phenytoin by CYP2C9 is predicted.	Where HLA-B*15:02 is absent, in the presence of a CYP2C9 normal metabolizer genotype, CPIC guidelines[48] provide a strong recommendation that no adjustments are needed from typical dosing strategies; subsequent doses should be adjusted according to therapeutic drug monitoring and clinical response. Be aware that this rs144012689 is a screening test only, and furthermore an HLA-B*15:02 negative test does not eliminate the risk of phenytoin-induced SJS/TEN; if the patient develops any rash or hypersensitivity reactions on fosphenytoin, then discontinuation should be considered in accordance with standard prescribing guidelines.[49]
LACOSAMIDE Antiepileptics	**CYP2C19 - Normal metabolizer:** Normal metabolism of lacosamide by CYP2C19 is predicted.	Standard dosing and prescribing measures apply.
LAMOTRIGINE Antiepileptics	**HLA-B*15:02 (rs144012689) - Normal risk of certain hypersensitivity reactions:** The rs144012689 TT result provides a high prediction of the absence of HLA-B*15:02 allele.	No genotype-guided dosing recommendations are available where the HLA-B*15:02 is absent. Be aware that this rs144012689 is a screening test only, and furthermore a HLA-B*15:02 negative test does not eliminate the risk of lamotrigine-induced SJS/TEN; if the patient develops any rash or hypersensitivity reactions on lamotrigine, then discontinuation should be considered in accordance with standard prescribing guidelines.[50]

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
PHENYTOIN Antiepileptics	**HLA-B*15:02 (rs144012689) - Normal risk of certain hypersensitivity reactions** **CYP2C9 - Normal metabolizer:** The rs144012689 TT result provides a high prediction of the absence of HLA-B*15:02 allele. Normal metabolism of phenytoin by CYP2C9 is predicted.	Where HLA-B*15:02 is absent, in the presence of a CYP2C9 normal metabolizer genotype, CPIC guidelines[48] provide a strong recommendation that no adjustments are needed from typical dosing strategies; subsequent doses should be adjusted according to therapeutic drug monitoring and clinical response. Be aware that this rs144012689 is a screening test only, and furthermore an HLA-B*15:02 negative test does not eliminate the risk of phenytoin-induced SJS/TEN; if the patient develops any rash or hypersensitivity reactions on phenytoin, then discontinuation should be considered in accordance with standard prescribing guidelines.[51],[48]
VORICONAZOLE Antifungals - Azoles	**CYP2C19 - Normal metabolizer:** Normal voriconazole metabolism by CYP2C19 is predicted.	CPIC guidelines[52] provide a strong recommendation to initiate therapy with the recommended standard of care dosing.
CYCLOPHOSPHAMIDE Antineoplastics	**CYP2C19 - Normal metabolizer:** Normal metabolism of cyclophosphamide by CYP2C19 into its active metabolite is predicted.	No genotype-guided dosing recommendation available.
CLOPIDOGREL Antiplatelet drugs	**CYP2C19 - Normal metabolizer:** Normal formation of clopidogrel's active metabolite by CYP2C19 is predicted.	CPIC guidelines[53] provide a strong recommendation to use the label-recommended dosage if clopidogrel is being prescribed for cardiovascular or neurovascular indications.
FLUPENTHIXOL Antipsychotics	**CYP2D6 - Intermediate metabolizer:** DPWG guidelines[54] state that there is no gene-drug interaction for flupenthixol and CYP2D6.	No dosage recommendation is currently available based on the genetic findings.
OLANZAPINE Antipsychotics	**CYP1A2 - Normal metabolizer:** Normal metabolism by CYP1A2 is predicted. The highly inducible CYP1A2 genotype *1F/*1F is not present and therefore metabolism is less likely to be increased by inducers such as tobacco smoking, daily consumption of cruciferous vegetables or chargrilled meat and certain medications (e.g. omeprazole). Although olanzapine is metabolized to a lesser extent by CYP2D6, the DPWG guidelines[28] state that there is no gene-drug interaction for either CYP1A2 or CYP2D6 and olanzapine.	No genotype-guided dosing recommendation is available. Standard dosing and prescribing measures apply.
QUETIAPINE Antipsychotics	**CYP3A4 - Normal metabolizer:** Normal metabolism of quetiapine by CYP3A4 is predicted. Although quetiapine is also metabolized to a lesser extent by CYP2D6, the DPWG guidelines[28] state that there is no gene-drug interaction for CYP2D6 and quetiapine.	Standard dosing and prescribing measures apply.

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
ATAZANAVIR Antivirals	**CYP3A5 - Poor metabolizer:** Poor metabolism of atazanavir via CYP3A5 is predicted. However, target drug exposure is expected to be in the normal range because this is a common CYP3A5 phenotype amongst Caucasians, for whom dosing was developed, and there are other enzymes involved in the metabolism of atazanavir. Note that a test for a variation in the UGT1A1 gene is available. This test is useful for predicting the risk of atazanavir-induced hyperbilirubinemia, and if results are available, they may be considered in addition to the CYP3A5 results.	CYP3A5 - Usual prescribing considerations apply.
CLOBAZAM Benzodiazepines	**CYP2C19 - Normal metabolizer:** Clobazam is metabolized by CYP3A4 into an active metabolite, N-desmethylclobazam, which is responsible for most of the therapeutic effect. N-desmethylclobazam is further metabolized by CYP2C19 into an inactive metabolite. Normal metabolism of clobazam's active metabolite is predicted. (Note that the effect of variations in CYP3A4 has not been described).	Standard dosing and prescribing measures apply.
DIAZEPAM Benzodiazepines	**CYP2C19 - Normal metabolizer:** Diazepam is metabolized by CYP3A4 and CYP2C19 into active metabolites, including desmethyldiazepam, which has a long half-life. The CYP2C19 genotype predicts normal CYP2C19-mediated metabolism of both diazepam and desmethyldiazepam. (Note that the effect of variations in the CYP3A4 gene on diazepam metabolism have not been described).	Standard dosing and prescribing measures apply.
NEBIVOLOL Beta blockers	**CYP2D6 - Intermediate metabolizer:** Reduced nebivolol metabolism by CYP2D6 and increased drug exposure are predicted. However, this has not been convincingly linked to increased beta blocking effects.	No genotype-guided dosing recommendation is available. Be alert for excessive beta blockade.
TACROLIMUS Calcineurin inhibitors	**CYP3A5 - Poor metabolizer:** Poor metabolism of tacrolimus is predicted. Higher dose-adjusted trough concentrations and increased chance of achieving concentration targets are also predicted. This phenotype is the most common in Caucasian populations and tacrolimus dosing procedures were developed for these patients.	For use in transplant recipients, other than in liver transplant where donor and recipient livers are of different genotypes, CPIC guidelines[55] recommend using the standard recommended starting dose. Therapeutic drug monitoring should guide ongoing dose adjustments . In liver transplants where the transplanted liver has a different genotype from the recipient's genotype, there is insufficient evidence to support a dose recommendation.[55]

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
NALTREXONE Drugs for alcohol dependence	**OPRM1 - Normal mu opioid receptor expression :** There is currently insufficient evidence to support an association between the OPRM1 genotype and the response to naltrexone. It has been suggested that the AA genotype may be associated with a reduced response to naltrexone (compared to patients with the AG or GG genotype) in the management of alcohol use disorder in a few studies, however in other studies and a recent meta-analysis, this was not observed.[56]	CPIC guidelines[3] state that there is insufficient evidence to provide a recommendation for naltrexone dosing based on OPRM1 genotype. It would be reasonable to monitor for a reduced clinical response and appropriate modifications to therapy if required.
ALLOPURINOL Drugs for gout	**ABCG2 (rs2231142) - Normal transporter function:** This genotype is associated with typical excretion of uric acid by the kidneys and intestine.	Standard dosing and prescribing measures apply.
AVATROMBOPAG Haemostatic agents	**CYP2C9 - Normal metabolizer** **F5 (rs6025) - No Factor V Leiden variant detected** **F2 (rs1799963) - No prothrombin G20210A variant detected:** Normal metabolism of avatrombopag by CYP2C9 is predicted. This individual is a non-carrier of Factor V Leiden and non-carrier of the prothrombin G20210A variant, and based on these genotypes, is not at increased risk of thrombosis. This risk may also be influenced by other genetic and clinical factors.	CYP2C9 - For treatment of chronic immune thrombocytopenia, the FDA-approved drug label[57] and TGA-approved product information[58] advises a reduced dose with concomitant use of a moderate or strong dual inhibitor of CYP2C9 and CYP3A4 due to the increased risk of toxicity. It advises an increased starting dose with concomitant use of a moderate or strong dual inducer of CYP2C9 and CYP3A4 due to a possible reduction in efficacy. F5 and F2 - The FDA-approved drug label and TGA-approved product information states that the risk for thrombosis should be considered in patients with risk factors for thromboembolism, including genetic prothrombotic conditions (e.g. Factor V Leiden, prothrombin 20210A, Antithrombin deficiency or Protein C or S deficiency).[57],[58]
ELTROMBOPAG Haemostatic agents	**F5 (rs6025) - No Factor V Leiden variant detected:** This individual is a non-carrier of Factor V Leiden and based on this genotype, is not at increased risk of thrombosis. This risk may also be influenced by other genetic and clinical factors.	The FDA-approved drug label states that the risk for thromboembolism should be considered in patients with known risk factors for thromboembolism (e.g., Factor V Leiden, ATIII deficiency, antiphospholipid syndrome, chronic liver disease).[59]
LUSUTROMBOPAG Haemostatic agents	**F5 (rs6025) - No Factor V Leiden variant detected** **F2 (rs1799963) - No prothrombin G20210A variant detected:** This individual is a non-carrier of Factor V Leiden and non-carrier of the prothrombin G20210A variant, and based on these genotypes, is not at increased risk of thrombosis. This risk may also be influenced by other genetic and clinical factors.	The FDA-approved drug label states that the risk for thrombosis should be considered in patients with risk factors for thromboembolism, including genetic prothrombotic conditions (e.g. Factor V Leiden, prothrombin 20210A, Antithrombin deficiency or Protein C or S deficiency).[60]

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
MELATONIN Hypnotics	**CYP1A2 - Normal metabolizer:** Normal metabolism of melatonin by CYP1A2 is predicted. Metabolism is much less likely to be increased by inducers such as tobacco smoking, daily consumption of cruciferous vegetables or chargrilled meat, and certain medications (e.g. omeprazole).	Standard dosing and prescribing measures apply.
ABROCITINIB Immunomodulators and antineoplastics	**CYP2C19 - Normal metabolizer:** Normal metabolism of abrocitinib by CYP2C19 is predicted.	Standard dosing and prescribing measures apply.
BELZUTIFAN Immunomodulators and antineoplastics	**CYP2C19 - Normal metabolizer:** Normal metabolism of belzutifan by CYP2C19 is predicted.	Standard dosing and prescribing measures apply.
ERDAFITINIB Immunomodulators and antineoplastics	**CYP2C9 - Normal metabolizer:** Normal metabolism of erdafitinib by CYP2C9 is predicted.	Standard dosing and prescribing measures apply.
METHOTREXATE Immunomodulators and antineoplastics	**MTHFR (rs1801133) - Normal MTHFR enzyme activity:** Although there has been some association with this MTHFR genotype and a decreased risk of methotrexate adverse effects compared to the TT or TC genotypes, there is also conflicting evidence. The DPWG guidelines[61] has stated that there is no gene-drug interaction therefore it is determined not to be clinically actionable.	No dosage recommendation is currently available based on the genetic findings.
DRONABINOL Miscellaneous	**CYP2C9 - Normal metabolizer:** Normal metabolism of dronabinol by CYP2C9 is predicted.	Standard dosing and prescribing measures apply.
FLIBANSERIN Miscellaneous	**CYP2C19 - Normal metabolizer:** Normal metabolism of flibanserin by CYP2C19 is predicted.	Standard dosing and prescribing measures apply.
MIRABEGRON Miscellaneous	**CYP2D6 - Intermediate metabolizer:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This may could potentially increase the risk of concentration-dependent adverse effects.	No genotype-guided dosing recommendation available. Monitor for adverse effects.
PROGUANIL Miscellaneous	**CYP2C19 - Normal metabolizer:** Normal metabolism of proguanil by CYP2C19 into its active metabolite cycloguanil is predicted.	No genotype-guided dosing recommendation available.

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
CARBAMAZEPINE Mood stabilisers	**HLA-A*31:01 (rs1061235) - Normal risk of certain hypersensitivity reactions** **HLA-B*15:02 (rs144012689) - Normal risk of certain hypersensitivity reactions:** The rs1061235 AA result provides a high prediction of the absence of the HLA-A*31:01 allele. The rs144012689 TT result provides a high prediction of the absence of the HLA-B*15:02 allele. This result is associated with a normal or reduced risk of cutaneous hypersensitivity reactions to carbamazepine (such as Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)), drug reaction with eosinophilia and systemic symptoms (DRESS) and maculopapular exanthema (MPE).	It would be reasonable to cautiously consider the use of carbamazepine as per standard prescribing guidelines.[62] Be aware that this is a screening test only, if the patient develops any rash or hypersensitivity reactions during treatment with carbamazepine, then discontinuation should be considered in accordance with standard prescribing guidelines.[63]
OXCARBAZEPINE Mood stabilisers	**HLA-B*15:02 (rs144012689) - Normal risk of certain hypersensitivity reactions:** The rs144012689 TT result provides a high prediction of the absence of the HLA-B*15:02 allele. This result is associated with a normal or reduced risk of cutaneous hypersensitivity reactions to oxcarbazepine (such as Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)).	It would be reasonable to cautiously consider the use of oxcarbazepine as per standard prescribing guidelines.[62] Be aware that this is a screening test only, if the patient develops any rash or hypersensitivity reactions on oxcarbazepine, then discontinuation should be considered in accordance with standard prescribing guidelines.[64]
CARISOPRODOL Neurological drugs	**CYP2C19 - Normal metabolizer:** Normal metabolism of carisoprodol by CYP2C19 is predicted.	Standard dosing and prescribing measures apply.
SIPONIMOD Neurological drugs	**CYP2C9 - Normal metabolizer:** Normal metabolism of siponimod by CYP2C9 is predicted.	The FDA-approved drug label[65] states that in patients with the CYP2C9 *1/*1 genotype, treatment initiation should be with a 5-day titration using the starter pack, starting at 0.25 mg daily and gradually increasing until the maintenance dose of 2 mg on Day 6 of treatment.
CELECOXIB NSAIDs	**CYP2C9 - Normal metabolizer:** Normal metabolism of celecoxib by CYP2C9 is predicted.	CPIC guidelines[66] have a strong recommendation to initiate therapy with the recommended starting dose. In accordance with prescribing information, use the lowest effective dose for the shortest duration required.
DICLOFENAC NSAIDs	**CYP2C9 - Normal metabolizer:** Diclofenac is partially metabolized by CYP2C9 and metabolism via this pathway is expected to be normal[67].	CPIC guidelines[66] state that there is insufficient evidence to provide a recommendation to guide clinical practice at this time. Standard dosing and prescribing measures apply.
FLURBIPROFEN NSAIDs	**CYP2C9 - Normal metabolizer:** Normal metabolism of flurbiprofen by CYP2C9 is predicted.	CPIC guidelines[66] have a strong recommendation to initiate therapy with the recommended starting dose. In accordance with prescribing information, use the lowest effective dose for the shortest duration required.

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
IBUPROFEN NSAIDs	**CYP2C9 - Normal metabolizer:** Normal metabolism of ibuprofen by CYP2C9 is predicted[68].	CPIC guidelines[66] have a strong recommendation to initiate therapy with the recommended starting dose. In accordance with prescribing information, use the lowest effective dose for the shortest duration required.
INDOMETHACIN NSAIDs	**CYP2C9 - Normal metabolizer:** Indomethacin is only partially metabolized by CYP2C9 and metabolism via this pathway is expected to be normal.[69]	CPIC guidelines[66] state that there is insufficient evidence to provide a recommendation to guide clinical practice at this time. Standard dosing and prescribing measures apply.
LORNOXICAM NSAIDs	**CYP2C9 - Normal metabolizer:** Normal metabolism of lornoxicam by CYP2C9 is predicted.	CPIC guidelines[66] have a strong recommendation to initiate therapy with the recommended starting dose. In accordance with prescribing information, use the lowest effective dose for the shortest duration required.
MEFENAMIC ACID NSAIDs	**CYP2C9 - Normal metabolizer:** Normal metabolism of mefenamic acid by CYP2C9 is predicted.[70]	Standard dosing and prescribing measures apply.
MELOXICAM NSAIDs	**CYP2C9 - Normal metabolizer:** Normal metabolism of meloxicam by CYP2C9 is predicted.	CPIC guidelines[66] have a strong recommendation to initiate therapy with the recommended starting dose. In accordance with prescribing information, use the lowest effective dose for the shortest duration required.
PIROXICAM NSAIDs	**CYP2C9 - Normal metabolizer:** Normal metabolism of piroxicam by CYP2C9 is predicted.	CPIC guidelines[66] have a strong recommendation to initiate therapy with the recommended starting dose. In accordance with prescribing information, use the lowest effective dose for the shortest duration required.
ESTETROL Oestrogen containing contraceptives	**F5 (rs6025) - No Factor V Leiden variant detected** **F2 (rs1799963) - No prothrombin G20210A variant detected:** The GG genotype (non-carrier of Factor V Leiden) is not associated with increased risk of thrombosis. This risk may also be influenced by other genetic and clinical factors. The GG genotype (non-carrier of the prothrombin G20210A variant) is not associated with increased risk of thrombosis. Other genetic and clinical factors may also influence the risk of thrombosis in patients taking oral contraceptives. The use of oestrogen containing contraceptives has been associated with increased risk of thrombosis, regardless of genotype.	No genotype-guided dosing recommendations available. Consider standard dosing and monitoring.

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
ESTRADIOL Oestrogen containing contraceptives	**F5 (rs6025) - No Factor V Leiden variant detected** **F2 (rs1799963) - No prothrombin G20210A variant detected:** The GG genotype (non-carrier of Factor V Leiden) is not associated with increased risk of thrombosis. This risk may also be influenced by other genetic and clinical factors. The GG genotype (non-carrier of the prothrombin G20210A variant) is not associated with increased risk of thrombosis. Other genetic and clinical factors may also influence the risk of thrombosis in patients taking oral contraceptives. The use of oestrogen containing contraceptives has been associated with increased risk of thrombosis, regardless of genotype.	No genotype-guided dosing recommendations available. Consider standard dosing and monitoring.
ETHINYLESTRADIOL Oestrogen containing contraceptives	**F5 (rs6025) - No Factor V Leiden variant detected** **F2 (rs1799963) - No prothrombin G20210A variant detected:** The GG genotype (non-carrier of Factor V Leiden) is not associated with increased risk of thrombosis. This risk may also be influenced by other genetic and clinical factors. The GG genotype (non-carrier of the prothrombin G20210A variant) is not associated with increased risk of thrombosis. Other genetic and clinical factors may also influence the risk of thrombosis in patients taking oral contraceptives. The use of oestrogen containing contraceptives has been associated with increased risk of thrombosis, regardless of genotype.	No genotype-guided dosing recommendations available. Consider standard dosing and monitoring.

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
ALFENTANIL Opioid Analgesics	**OPRM1 - Normal mu opioid receptor expression** **COMT - Normal to high COMT enzyme activity:** OPRM1 - Whilst the AA genotype has been associated with increased sensitivity to some opioid analgesics, there is no effect or insufficient evidence for adverse events, opioid dose requirements, analgesia, or change in opioid dependence/withdrawal therapy for alfentanil. COMT - No effect for opioid adverse events. Insufficient evidence for an association between COMT rs4680 genotype, analgesia and opioid dose requirements.	CPIC[3] states that there is insufficient evidence to provide a recommendation to guide clinical practice at this time. Standard dosing and prescribing measures apply.
BUPRENORPHINE Opioid Analgesics	**OPRM1 - Normal mu opioid receptor expression** **COMT - Normal to high COMT enzyme activity:** OPRM1 - Whilst the AA genotype has been associated with increased sensitivity to some opioid analgesics, there is no effect or insufficient evidence for adverse events, opioid dose requirements, analgesia, or change in opioid dependence/withdrawal therapy for buprenorphine. COMT - No effect for opioid adverse events. Insufficient evidence for an association between COMT rs4680 genotype, analgesia and opioid dose requirements.	CPIC[3] states that there is insufficient evidence to provide a recommendation to guide clinical practice at this time. Standard dosing and prescribing measures apply.
FENTANYL Opioid Analgesics	**OPRM1 - Normal mu opioid receptor expression** **COMT - Normal to high COMT enzyme activity:** OPRM1 - Whilst the AA genotype has been associated with increased sensitivity to some opioid analgesics, there is no effect for fentanyl adverse events and analgesia. There has also been mixed evidence for an association between OPRM1 rs1799971 and fentanyl dose requirements. COMT - No effect for opioid adverse events. Insufficient evidence for an association between COMT rs4680 genotype, analgesia and opioid dose requirements.	CPIC[3] states that there is insufficient evidence to provide a recommendation to guide clinical practice at this time. Standard dosing and prescribing measures apply.

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
HYDROMORPHONE Opioid Analgesics	**OPRM1 - Normal mu opioid receptor expression** **COMT - Normal to high COMT enzyme activity:** OPRM1 - Whilst the AA genotype has been associated with increased sensitivity to some opioid analgesics, there is no effect or insufficient evidence for adverse events, opioid dose requirements, analgesia, or change in opioid dependence/withdrawal therapy for hydromorphone. COMT - No effect for opioid adverse events. Insufficient evidence for an association between COMT rs4680 genotype, analgesia and opioid dose requirements.	CPIC[3] states that there is insufficient evidence to provide a recommendation to guide clinical practice at this time. Standard dosing and prescribing measures apply.
MORPHINE Opioid Analgesics	**OPRM1 - Normal mu opioid receptor expression** **COMT - Normal to high COMT enzyme activity:** OPRM1 - Whilst the AA genotype has been associated with increased sensitivity to morphine (including reduced morphine consumption, lower pain scores, and a higher rate of nausea) there is insufficient evidence for its clinical significance. COMT - Although the GG genotype has been associated with higher consumption of morphine in some studies, there are conflicting results in other studies.	CPIC[3] states that there is insufficient evidence to provide a recommendation to guide clinical practice at this time. Standard dosing and prescribing measures apply.
SUFENTANIL Opioid Analgesics	**OPRM1 - Normal mu opioid receptor expression** **COMT - Normal to high COMT enzyme activity:** OPRM1 - Whilst the AA genotype has been associated with increased sensitivity to some opioid analgesics, there is no effect or insufficient evidence for adverse events, opioid dose requirements, analgesia, or change in opioid dependence/withdrawal therapy for sufentanil. COMT - No effect for opioid adverse events. Insufficient evidence for an association between COMT rs4680 genotype, analgesia and opioid dose requirements.	CPIC[3] states that there is insufficient evidence to provide a recommendation to guide clinical practice at this time. Standard dosing and prescribing measures apply.
ESOMEPRAZOLE Proton pump inhibitors	**CYP2C19 - Normal metabolizer:** Typical metabolism of esomeprazole by CYP2C19 is predicted. Note that this genotype has a lesser effect with esomeprazole and rabeprazole compared to other PPIs.	Standard dosing and prescribing measures apply. If response is inadequate, consider a trial of rabeprazole as an alternative.

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION DRUG CATEGORY	INTERPRETATION	RECOMMENDATION
RABEPRAZOLE Proton pump inhibitors	**CYP2C19 - Normal metabolizer:** Normal metabolism of rabeprazole by CYP2C19 is predicted. Note that this genotype has a lesser effect with rabeprazole and esomeprazole compared to other PPIs.	Standard dosing and prescribing measures apply. If the response to rabeprazole is inadequate, consider a trial of esomeprazole as an alternative agent.

DETAILED PHARMACOGENOMIC TEST RESULTS

GENE	GENOTYPE	PREDICTED PHENOTYPE
ABCG2 (rs2231142)	CC	**Normal transporter function:** This individual has two copies of the normal allele which predicts normal function of the ABCG2 encoded transporter. This transporter is relevant for the clearance of certain medications such as rosuvastatin.
COMT	GG	**Normal to high COMT enzyme activity:** The COMT enzyme is involved in the metabolism of catecholamine. The GG contains two normal alleles (G) for the COMT gene predicting higher activity of the COMT enzyme compared to the AG/AA genotypes.
CYP1A2	*1A/*1F	**Normal metabolizer:** Due to the presence of only one copy of the *1F allele, this individual is predicted to have a normal metabolizer phenotype. Normal metabolism of CYP1A2 substrate drugs is predicted. Furthermore, metabolism is not expected to be increased by exposure to inducers such as tobacco smoking and certain dietary components and drugs.
CYP2B6	*1/*6	**Intermediate metabolizer:** This individual is predicted to have an intermediate metabolizer phenotype due to the presence of one normal function allele and one decreased function allele. Due to technical difficulties in unambiguously determining this genotype, the individual's other possible genotype is *4/*9 which also predicts an intermediate metabolizer phenotype. For a drug extensively metabolized by CYP2B6, drug exposure and clinical effects may either be increased (for an active drug) or decreased (for a prodrug). This individual is at risk of experiencing adverse effects (active drug) or therapeutic failure (prodrug).
CYP2C19	*1/*1	**Normal metabolizer:** Due to the presence of two copies of normal function alleles, this individual is predicted to have a normal metabolizer phenotype. For a drug extensively metabolized by CYP2C19, drug exposure and clinical effects may be expected to lie within the normal range.
CYP2C9	*1/*1	**Normal metabolizer:** Due to the presence of two normal function alleles, this individual is predicted to have a normal metabolizer phenotype. For a drug extensively metabolized by CYP2C9, drug exposure and clinical effects may be expected to lie within the normal range.
CYP2D6	*4/*41	**Intermediate metabolizer:** Due to the presence of one reduced function allele and one no function allele, this individual is predicted to have an intermediate metabolizer phenotype. For a drug extensively metabolized by CYP2D6, drug exposure and clinical effects may either be increased (for an active drug) or decreased (for a prodrug). The individual is at risk of experiencing adverse effects (active drug) or therapeutic failure (prodrug).
CYP3A4	*1/*1	**Normal metabolizer:** The *22 allele is not present and this individual is expected to have a normal metabolizer phenotype. Whilst many drugs are known to be metabolized by CYP3A4, relatively few genetic variations have been found that affect metabolism of a limited number of these drugs.
CYP3A5	*3/*3	**Poor metabolizer:** Due to the presence of two no function alleles, this individual is predicted to have a poor metabolizer phenotype (CYP3A5 non-expresser). CYP3A5 is known to metabolize certain drugs, including tacrolimus. Note that this individual's phenotype is the most common one amongst Caucasians.

GENE	GENOTYPE	PREDICTED PHENOTYPE
F2 (rs1799963)	GG	**No prothrombin G20210A variant detected:** This individual has the GG genotype for F2 rs1799963, i.e. the prothrombin G20210A variant was not detected. Based on this genotype, the patient does not have an increased risk of venous thrombosis and embolism. The presence of other genetic variants may contribute to an increased risk of thrombosis, such as Factor V Leiden (F5 in this test), antithrombin deficiency or Protein C or S deficiency.[71], [72] Note that other genetic and clinical factors influence the risk of thrombosis in any individual.
F5 (rs6025)	GG	**No Factor V Leiden variant detected:** This individual has the GG genotype for F5 rs6025, i.e., Factor V Leiden was not detected. Based on this genotype, the patient does not have an increased risk of venous thrombosis and embolism. The presence of other genetic variants may contribute to an increased risk of thrombosis, such as the prothrombin G20210A variant (F2 in this test), antithrombin deficiency or Protein C or S deficiency.[71], [72] Note that other genetic and clinical factors influence the risk of thrombosis in any individual.
HLA A*31:01 (rs1061235)	AA	**Normal risk of certain hypersensitivity reactions:** Testing for a specific rs1061235 variant may be utilized as a screening test for the presence of HLA-A*31:01. HLA-A*31:01 is an allele which, if present, has been associated with hypersensitivity reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, maculopapular eruptions, and drug reaction with eosinophilia and systemic symptoms (DRESS) with carbamazepine. This AA result provides a high prediction of the absence of the HLA-A*31:01 allele. The negative predictive value for this test has been shown to be 100%.[73] The clinical utility for testing for this variant appears to be particularly relevant for carbamazepine, with the FDA-approved drug label noting that the risks and benefits of carbamazepine therapy should be weighed before considering carbamazepine in patients known to be positive for HLA-A*31:01.[63]
HLA B*15:02 (rs144012689)	TT	**Normal risk of certain hypersensitivity reactions:** Testing for a specific rs144012689 variant may be utilized as a screening test for the presence of HLA-B*15:02. HLA-B*15:02 is an allele which, if present, is associated with serious cutaneous hypersensitivity reactions (such as Stevens-Johnson syndrome and toxic epidermal necrolysis) for certain medications. This TT result provides a high prediction of the absence of the HLA-B*15:02 allele. The negative predictive value for this test has been shown to be 100%.[74] The clinical utility of testing for this variant appears to be particularly relevant for carbamazepine and oxcarbazepine, as there is more limited evidence for other medications. The FDA-approved drug label notes that HLA-B*15:02 is found almost exclusively in patients with Asian ancestry across broad areas of Asia and that patients with ancestry in genetically at risk populations should be screened for the presence of HLA-B*15:02 prior to initiating treatment with carbamazepine.[63] It is noted that this should also be considered prior to initiating treatment with oxcarbazepine.
MTHFR (rs1801133)	CC	**Normal MTHFR enzyme activity:** Due to the presence of two normal C alleles of the C677T polymorphism, normal MTHFR enzyme activity is predicted. The risk of low folate and high homocysteine are unlikely to be influenced by the genetic result.

GENE	GENOTYPE	PREDICTED PHENOTYPE
OPRM1	AA	**Normal mu opioid receptor expression :** The AA genotype contains two normal alleles for the OPRM1 gene which encodes the mu opioid receptor. Whilst the evidence around OPRM1 genetic variation continues to develop, it appears that this result is associated with increased sensitivity to certain opioids (in particular, morphine) compared to those with the variant allele (G). These findings are supported by a number of cohort studies and at least two meta-analyses[75],[76] however, this is not shown in all studies. For naltrexone in the management of alcohol use disorder, some studies have shown an association of this result with a reduced response compared to those with the variant allele. Note the frequency of the variant allele (G) is higher in people of Asian ancestry (around 40%) than European ancestry (around 15%).
SLCO1B1	*1/*5	**Decreased transporter function:** This individual carries one copy of the decreased function *5 allele and is predicted to have decreased function of the *SLCO1B1* encoded transporter. Decreased clearance of certain medications such as simvastatin is expected.
VKORC1	GG	**Normal VKORC1 enzyme level:** The VKORC1 enzyme is predicted to be present in normal amounts and the response to warfarin will be normal. The *CYP2C9* genotype should also be considered together with the *VKORC1* genotype for calculating the initial warfarin dose.

ADDITIONAL GENES WITH EMERGING EVIDENCE

This section contains genes that have limited evidence for clinical implementation and are not utilized in how medications are classified under major, minor, usual or no pharmacogenomic prescribing considerations. The data has been included for informational purposes only and there are currently no recommendations to alter prescribing based on genotype.

GENE	GENOTYPE	COMMENTS
ABCB1	TT	ABCB1 encodes p-glycoprotein, an efflux transporter that transports many agents out of cells. The TT genotype is associated with lower expression and activity of ABCB1. This finding has been associated with better treatment efficacy of some antiemetic medications (such as granisetron and ondansetron). Individuals with this genetic result tend to have a better control rate of nausea and vomiting compared to individuals with CC and CT genotypes. There are currently no recommendations to alter prescribing.
ADRA2A	GC	This genetic result may be associated with some improvement in response to methylphenidate compared to CC carriers,[77] however, study results are conflicting. There are currently no recommendations to alter prescribing.
APOE (rs7412)	CC	The ApoE gene encodes a protein which is used to form lipoproteins. The ApoE lipoprotein is involved in cholesterol metabolism. This ApoE genotype is associated with lower plasma concentration of APOE. This finding has been shown to result in reduced LDL-C lowering response to atorvastatin treatment compared to CT and TT individuals. There are currently no recommendations to alter prescribing.
CES1A1	GG	Individuals with this genetic result may have increased metabolism of methylphenidate[78] compared to AA or AG carriers. There are currently no recommendations to alter prescribing.
DRD2	GG	This genotype may be associated with a potential reduced risk of adverse effects to some antipsychotics, such as tardive dyskinesia or hyperprolactinaemia compared to the AA or AG genotypes. There are currently no recommendations to alter prescribing.
HTR2A	GG	This genetic result may be associated with an increased risk of side effects for certain SSRIs compared to AG or AA carriers,[79] however, this has not been shown in all studies and there are currently no recommendations to alter prescribing.
SLC6A4	S/S	This genetic result (two short alleles of the 5HTTLPR) has been associated with some reduction in SSRI response in individuals of Caucasian ancestry compared with LS or LL carriers.[80] However, there are conflicting studies, particularly in other populations. There are currently no recommendations to alter prescribing.
UGT1A4	*1/*1	Individuals with this genetic result may have increased drug exposure of lamotrigine[81] and olanzapine[82] compared to *3/*3 carriers. However, there is conflicting evidence in relation to this effect and there are currently no recommendations to alter prescribing.
UGT2B15	*1/*1	Individuals with this genetic result may have increased clearance of certain benzodiazepines, such as lorazepam[83] and oxazepam[84] compared to *2/*2 carriers. However there is limited evidence for this effect and there are currently no recommendations to alter prescribing.