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myDNA PSYCHOTROPIC

Pharmacogenomic Test

For phcmental2 vy

Date of birth:
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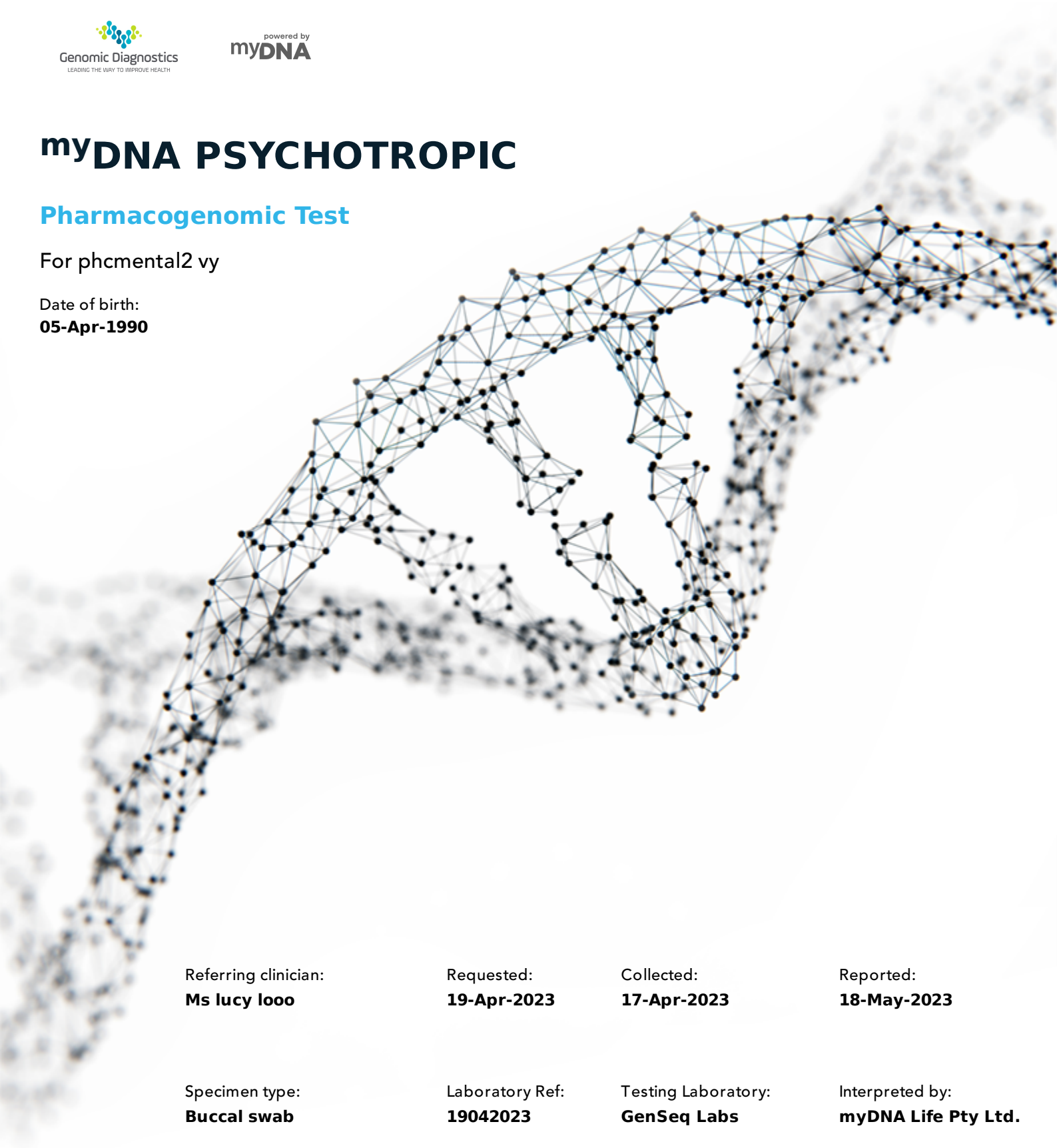


Referring clinician:	Requested:	Collected:	Reported:
Ms lucy looo	**19-Apr-2023**	**17-Apr-2023**	**18-May-2023**
Specimen type:	Laboratory Ref:	Testing Laboratory:	Interpreted by:
Buccal swab	**19042023**	**GenSeq Labs**	**myDNA Life Pty Ltd.**

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 test.

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 four 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.

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.

NO PHARMACOGENOMIC PRESCRIBING CONSIDERATIONS

These medications do not have significant gene-drug interactions identified and standard prescribing considerations apply.

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

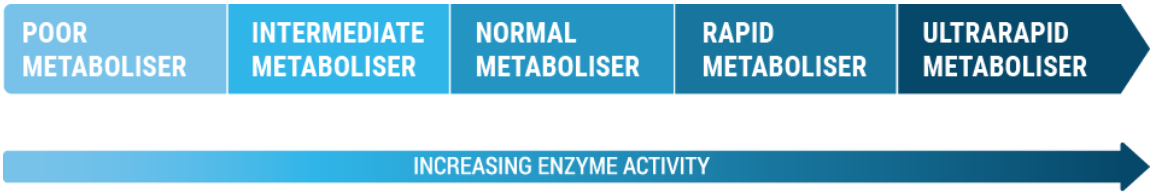
The report consists of the following 4 sections:

1. Genetic test results summary – presents the patient's genotypes for the genes relevant to the medications covered by this report.
2. Medication tables arranged according to the four categories of MAJOR, MINOR, USUAL or NO PHARMACOGENOMIC prescribing considerations.
3. Details of test results – for example, an explanation of how the genotypes have been used to predict CYP enzyme function and the likely general effect on drug metabolism and plasma concentrations (drug exposure).
4. References – list of key peer-reviewed literature that has been used to produce the report.

TEST RESULTS SUMMARY

GENE	GENOTYPE	PREDICTED PHENOTYPE
CYP1A2	*1F/*1F	**Ultrarapid metaboliser (with inducer present)**
CYP2C19	*1/*2	**Intermediate metaboliser**
CYP2C9	*1/*1	**Normal metaboliser**
CYP2D6	*4/*41	**Intermediate metaboliser**
CYP3A4	*1/*1	**Normal metaboliser**

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



ANTIDEPRESSANTS - Important Genes (CYP1A2, CYP2C19, CYP2C9, CYP2D6)

Each antidepressant below has been allocated to a major, minor, usual, or no prescribing considerations quadrant based on the pharmacogenomic test results.
NOTE: These classifications and recommendations do not account for the effect of any inhibitors or inducers and this is not an all-inclusive list of antidepressants.

MAJOR PRESCRIBING CONSIDERATIONS

- AMITRIPTYLINE (TCA)
- CITALOPRAM (SSRI)
- CLOMIPRAMINE (TCA)
- DOSULEPIN (TCA)
- DOXEPIN (TCA)
- ESCITALOPRAM (SSRI)
- IMIPRAMINE (TCA)
- NORTRIPTYLINE (TCA)
- VENLAFAXINE (SNRI)

MINOR PRESCRIBING CONSIDERATIONS

- AGOMELATINE
- DULOXETINE (SNRI)
- FLUOXETINE (SSRI)
- FLUVOXAMINE (SSRI)
- MIANSERIN
- MIRTAZAPINE
- MOCLOBEMIDE
- PAROXETINE (SSRI)
- SERTRALINE (SSRI)
- VORTIOXETINE

USUAL PRESCRIBING CONSIDERATIONS

- NONE

NO PHARMACOGENOMIC PRESCRIBING CONSIDERATIONS

- DESVENLAFAXINE (SNRI)
- SELEGILINE
- TRAZODONE
- VILAZODONE
- LEVOMILNACIPRAN

ANTIPSYCHOTICS - Important Genes (CYP1A2, CYP2D6, CYP3A4)

Each antipsychotic below has been allocated to a major, minor, usual, or no prescribing considerations quadrant based on the pharmacogenomic test results.
NOTE: These classifications and recommendations do not account for the effect of any inhibitors or inducers and this is not an all-inclusive list of antipsychotics.

MAJOR PRESCRIBING CONSIDERATIONS

- ZUCLOPENTHIXOL

MINOR PRESCRIBING CONSIDERATIONS

- ARIPIPRAZOLE
- BREXPIPRAZOLE
- CHLORPROMAZINE
- CLOZAPINE
- HALOPERIDOL
- OLANZAPINE
- RISPERIDONE

USUAL PRESCRIBING CONSIDERATIONS

- FLUPENTHIXOL
- QUETIAPINE

NO PHARMACOGENOMIC PRESCRIBING CONSIDERATIONS

- ASENAPINE
- LURASIDONE
- PALIPERIDONE
- ZIPRASIDONE

OTHER PSYCHOTROPICS - Important Genes (CYP2C19, CYP2D6)

This section includes medications that belong to the following groups: ADHD stimulants and non-stimulants, mood stabilizers, hypnotics and anxiolytics. Each medication below has been allocated to a major, minor, usual, or no prescribing considerations quadrant based on the pharmacogenomic test results. NOTE: These classifications and recommendations do not account for the effect of any inhibitors or inducers and this is not an all-inclusive list of psychotropic medications.

MAJOR PRESCRIBING CONSIDERATIONS

- ATOMOXETINE

MINOR PRESCRIBING CONSIDERATIONS

- CLOBAZAM (BENZODIAZEPINE)
- DEXAMPHETAMINE (PSYCHOSTIMULANT)
- DIAZEPAM (BENZODIAZEPINE)
- LISDEXAMFETAMINE (PSYCHOSTIMULANT)

USUAL PRESCRIBING CONSIDERATIONS

- NONE

NO PHARMACOGENOMIC PRESCRIBING CONSIDERATIONS

- ALPRAZOLAM (BENZODIAZEPINE)
- CLONAZEPAM (BENZODIAZEPINE)
- CLONIDINE
- DEXMETHYLPHENIDATE (PSYCHOSTIMULANT)
- GUANFACINE
- LORAZEPAM (BENZODIAZEPINE)
- METHYLPHENIDATE (PSYCHOSTIMULANT)
- OXAZEPAM (BENZODIAZEPINE)
- TEMAZEPAM (BENZODIAZEPINE)
- ZOLPIDEM

ANTIDEPRESSANTS

The following tables provide reference information to consider for antidepressants categorized as having major, minor or usual prescribing considerations, based on the genetic test results. This information is intended as a guide and to be considered in addition to other clinical information as part of a comprehensive clinical review by the clinician. NOTE: These classifications and recommendations do not account for the effect of any inhibitors or inducers.

MAJOR PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
AMITRIPTYLINE TCA	**CYP2D6 - Intermediate metaboliser** **CYP2C19 - Intermediate metaboliser:** Amitriptyline is metabolised by CYP2C19 into an active metabolite, which is further metabolised by CYP2D6 into an inactive metabolite. Reduced metabolism of both amitriptyline and its active metabolite are predicted.	For use at higher doses such as in the treatment of depression, CPIC[1] 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. For use at lower doses such as in treatment of neuropathic pain, standard dosing and prescribing measures apply, with monitoring of adverse effects.
CITALOPRAM SSRI	**CYP2C19 - Intermediate metaboliser:** Reduced metabolism of citalopram by CYP2C19 and increased drug exposure are predicted. This may increase the likelihood of adverse effects, especially with higher doses or if drug-drug interactions occur.	CPIC guidelines[2] provide a strong recommendation to initiate therapy with the recommended starting dose. Monitor for adverse effects. DPWG guidelines recommend not exceeding the following doses: 30mg as tablets or 22mg as drops for adults up to 65 years; 15mg as tablets or 10mg as drops for adults 65 years and over.[3]
CLOMIPRAMINE TCA	**CYP2D6 - Intermediate metaboliser** **CYP2C19 - Intermediate metaboliser:** Clomipramine is metabolised by CYP2C19 into an active metabolite, which is further metabolised by CYP2D6 into an inactive metabolite. Reduced metabolism of both clomipramine and its active metabolite are predicted.	CPIC[1] 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.
DOSULEPIN TCA	**CYP2D6 - Intermediate metaboliser** **CYP2C19 - Intermediate metaboliser:** Dosulepin is metabolised by CYP2C19 into an active metabolite, which is further metabolised by CYP2D6 into an inactive metabolite. Reduced metabolism of both Dosulepin and its active metabolite are predicted.	CPIC[1] 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 TCA	**CYP2D6 - Intermediate metaboliser** **CYP2C19 - Intermediate metaboliser:** Doxepin is metabolised by CYP2C19 into an active metabolite, which is further metabolised by CYP2D6 into an inactive metabolite. Reduced metabolism of both doxepin and its active metabolite are predicted.	CPIC[1] 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.
ESCITALOPRAM SSRI	**CYP2C19 - Intermediate metaboliser:** Reduced metabolism of escitalopram by CYP2C19 and increased drug exposure are predicted. This may increase the likelihood of adverse effects, especially with higher doses or if drug-drug interactions occur.	CPIC guidelines[2] provide a strong recommendation to initiate therapy with the recommended starting dose. Monitor for adverse effects. DPWG guidelines recommend not exceeding 75% of the standard maximum dose, i.e. a maximum of 15 mg/day for adults up to 65 years and 7.5 mg/day for adults 65 years and over.[3]

MAJOR PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
IMIPRAMINE TCA	**CYP2D6 - Intermediate metaboliser** **CYP2C19 - Intermediate metaboliser:** Imipramine is metabolised by CYP2C19 into an active metabolite, which is further metabolised by CYP2D6 into an inactive metabolite. Reduced metabolism of both imipramine and its active metabolite are predicted. This may increase the risk of adverse effects.	CPIC[1] 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 TCA	**CYP2D6 - Intermediate metaboliser:** 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[1] 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.
VENLAFAXINE SNRI	**CYP2D6 - Intermediate metaboliser:** 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. There may be an increased risk of adverse effects, such as gastrointestinal discomfort.	The DPWG[4] 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.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
AGOMELATINE	**CYP1A2 - Ultrarapid metaboliser (with inducer present):** Increased agomelatine metabolism and reduced plasma concentrations are predicted[5, 6]. This effect is expected to be enhanced with exposure to enzyme inducers such as tobacco smoking, daily consumption of cruciferous vegetables or chargrilled meat, and certain medications (e.g. omeprazole). The clinical significance of this has not yet been established.	No genotype-guided dosing recommendation available. It would be reasonable to monitor for an adequate clinical response.
DULOXETINE SNRI	**CYP2D6 - Intermediate metaboliser** **CYP1A2 - Ultrarapid metaboliser (with inducer present):** Duloxetine is metabolised by both CYP1A2 and CYP2D6, with CYP1A2 likely to have the major role. Reduced duloxetine metabolism by CYP2D6 and increased metabolism by CYP1A2 in patients exposed to enzyme inducers (e.g. cigarette smoke) are predicted. The overall effect on duloxetine plasma concentrations and clinical response is difficult to predict.	No genotype-guided dosing recommendation available. Monitor for an altered clinical response.
FLUOXETINE SSRI	**CYP2D6 - Intermediate metaboliser** **CYP2C9 - Normal metaboliser:** 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 metaboliser which can last for up to 9 weeks after cessation of fluoxetine (this is particularly relevant if commencing a drug extensively metabolised 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, DPWG[7] recommends 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 SSRI	**CYP2D6 - Intermediate metaboliser** **CYP1A2 - Ultrarapid metaboliser (with inducer present):** Fluvoxamine is metabolised by both CYP2D6 (predominant pathway) and CYP1A2. Reduced metabolism by CYP2D6 and increased metabolism by CYP1A2 in the presence of enzyme inducers such as cigarette smoke are predicted. Note that fluvoxamine itself will inhibit CYP1A2, which could negate the effect of enzyme induction, especially with increasing dose. Whilst difficult to predict, the exposure to fluvoxamine may be increased. There is some evidence that increased drug exposure is associated with adverse effects, such as gastrointestinal upset.	Based on the CYP2D6 genotype, CPIC[2] provides a moderate recommendation to initiate therapy with the recommended starting dose. DPWG [8] suggests no specific action on fluvoxamine dosing is required based on this CYP2D6 genotype.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
MIANSERIN	**CYP2D6 - Intermediate metaboliser:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This could potentially increase the risk of adverse effects.	No genotype guided dosing recommendation is available. Be alert for adverse effects.
MIRTAZAPINE	**CYP2D6 - Intermediate metaboliser** **CYP1A2 - Ultrarapid metaboliser (with inducer present):** Mirtazapine is metabolised by a number of enzymes, including CYP2D6 and CYP1A2. Reduced metabolism by CYP2D6 and increased metabolism by CYP1A2 in the presence of enzyme inducers (e.g. cigarette smoking) are predicted. The overall effect on plasma concentrations and clinical effects is difficult to predict.	Monitor for altered clinical effect. Based on the CYP2D6 genotype, DPWG suggests that no specific action on mirtazapine dosing is required.[9]
MOCLOBEMIDE	**CYP2C19 - Intermediate metaboliser:** Reduced metabolism by CYP2C19 and increased moclobemide exposure are predicted. There may be an increased risk of adverse effects.	DPWG[10] suggests that no specific action on moclobemide dosing is required with this genotype. Monitor for adverse effects.
PAROXETINE SSRI	**CYP2D6 - Intermediate metaboliser:** 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 phenocopying). 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 increased adverse effects.	CPIC[2] guidelines provide a moderate recommendation to initiate therapy with the recommended starting dose. It would also be reasonable to monitor closely for adverse effects. DPWG[3] recommends that no specific action on paroxetine dosing is required based on this genotype.
SERTRALINE SSRI	**CYP2C19 - Intermediate metaboliser:** Reduced metabolism when compared to extensive metabolisers is predicted.[2] However, the DPWG classifies this genetic result as having a minor influence on sertraline plasma concentration and no effect on side effects.[3]	CPIC guidelines[2] provide a strong recommendation to initiate therapy with the recommended starting dose. The DPWG guideline states that there is not enough evidence to recommend adjustment of therapy.[3]
VORTIOXETINE	**CYP2D6 - Intermediate metaboliser:** Reduced vortioxetine metabolism and increased drug exposure is predicted. This may increase the risk of adverse effects, although direct evidence is lacking.	No genotype-guided dosing recommendation available. Be alert for adverse effects.

ANTIPSYCHOTICS

The following tables provide reference information to consider for antipsychotics categorized as having major, minor or usual prescribing considerations, based on the genetic test results. This information is intended as a guide and to be considered in addition to other clinical information as part of a comprehensive clinical review by the clinician. NOTE: These classifications and recommendations do not account for the effect of any inhibitors or inducers.

MAJOR PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
ZUCLOPENTHIXOL	**CYP2D6 - Intermediate metaboliser:** Reduced metabolism and increased drug exposure are predicted. This may increase the risk of adverse effects.	The DPWG[11] advises starting with 75% of the standard dose or selecting an alternative drug according to current guidelines.

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
ARIPIPRAZOLE	**CYP2D6 - Intermediate metaboliser:** 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[12] suggests that no specific action on aripiprazole dosing is required with this genotype.
BREXPIPRAZOLE	**CYP2D6 - Intermediate metaboliser:** Reduced metabolism by CYP2D6 and increased drug exposure are predicted. This may increase the risk of concentration-dependent adverse effects.	DPWG guidelines[13] suggest that no specific action on brexpiprazole dosing is required based on this genotype. Monitor for adverse effects.
CHLORPROMAZINE	**CYP2D6 - Intermediate metaboliser:** 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	**CYP2D6 - Intermediate metaboliser** **CYP1A2 - Ultrarapid metaboliser (with inducer present):** Based on the CYP1A2 genotype, increased metabolism of clozapine and reduced drug exposure are predicted, especially in the presence of inducers such as tobacco smoking, daily consumption of cruciferous vegetables or chargrilled meat, and certain medications (e.g. omeprazole). This CYP1A2 genotype has also been associated with a reduced clinical response to clozapine, which is more marked in smokers.[14] Based on the CYP2D6 genotype, reduced metabolism and increased drug exposure are predicted. The clinical significance of this is uncertain.	No genotype-guided dosing recommendation available. Monitor for reduced clinical effect, especially in a patient exposed to enzyme inducers. If exposure to enzyme inducers stops abruptly (e.g. tobacco smoking cessation) monitor for emergent concentration-dependent adverse effects. Some authorities have recommended a dose reduction at the time of smoking cessation.[15]
HALOPERIDOL	**CYP2D6 - Intermediate metaboliser:** 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[16] suggests that no specific action on haloperidol dosing is required with this genotype.
OLANZAPINE	**CYP1A2 - Ultrarapid metaboliser (with inducer present):** Increased metabolism of olanzapine and reduced drug exposure are predicted, especially in the presence of inducers such as tobacco smoking, daily consumption of cruciferous vegetables or chargrilled meat, and certain medications (e.g. omeprazole).This genotype has been associated with a reduced clinical response to olanzapine independent of smoking, but this has not been confirmed in all studies.	No genotype-guided dosing recommendation available. Monitor for reduced clinical effect, especially in a patient exposed to enzyme inducers. If exposure to enzyme inducers stops abruptly (e.g. tobacco smoking cessation) monitor for emergent concentration-dependent adverse effects. Some authorities have recommended a dose reduction at the time of smoking cessation.[15]

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
RISPERIDONE	**CYP2D6 - Intermediate metaboliser:** 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[17] 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.

USUAL PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
FLUPENTHIXOL	**CYP2D6 - Intermediate metaboliser:** DPWG guidelines[18] state that there is no gene-drug interaction for flupenthixol and CYP2D6.	No dosage recommendation is currently available based on the genetic findings.
QUETIAPINE	**CYP3A4 - Normal metaboliser:** Normal metabolism of quetiapine by CYP3A4 is predicted.	Standard dosing and prescribing measures apply.

OTHER PSYCHOTROPICS

The following tables provide reference information to consider for other psychotropics categorized as having major, minor or usual prescribing considerations, based on the genetic test results. This information is intended as a guide and to be considered in addition to other clinical information as part of a comprehensive clinical review by the clinician. NOTE: These classifications and recommendations do not account for the effect of any inhibitors or inducers.

MAJOR PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
ATOMOXETINE	**CYP2D6 - Intermediate metaboliser:** Reduced metabolism by CYP2D6 and increased drug exposure is predicted. This may increase the risk of adverse effects.	CPIC[19] 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[20] 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).

MINOR PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
CLOBAZAM Benzodiazepine	**CYP2C19 - Intermediate metaboliser:** Clobazam is metabolised by CYP3A4 into an active metabolite, N-desmethylclobazam, which is responsible for most of the therapeutic effect. N-desmethylclobazam is further metabolised by CYP2C19 into an inactive metabolite. Reduced metabolism of clobazam's active metabolite and a possible increase in clinical effects is predicted. (Note that the effect of variations in CYP3A4 has not been described).	No genotype-guided dosing recommendation available. Be alert to increased clinical effects.
DEXAMPHETAMINE Psychostimulant	**CYP2D6 - Intermediate metaboliser:** Dexamphetamine is eliminated by both the kidney (as unchanged drug) and the liver, with CYP2D6 playing a significant role. Reduced metabolism via CYP2D6 and increased dexamphetamine 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.
DIAZEPAM Benzodiazepine	**CYP2C19 - Intermediate metaboliser:** Diazepam is metabolised by CYP3A4 and CYP2C19 into active metabolites, including desmethyldiazepam, which has a long half-life. The CYP2C19 genotype predicts reduced metabolism of both diazepam and desmethyldiazepam, increased plasma concentrations and possibly increased clinical effects (including prolonged sedation). (Note that the effect of variations in the CYP3A4 gene on diazepam metabolism have not been described).	If excessive clinical effects (e.g. sedation) are problematic, consider reducing the dose or prescribing an alternative benzodiazepine not extensively metabolised by CYP2C19, such as oxazepam or lorazepam.
LISDEXAMFETAMINE Psychostimulant	**CYP2D6 - Intermediate metaboliser:** 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.

GENETIC TEST RESULTS

GENE	GENOTYPE	PREDICTED PHENOTYPE
CYP1A2	*1F/*1F	**Ultrarapid metaboliser (with inducer present):** Due to the presence of two *1F alleles, this individual is predicted to have an ultrarapid metaboliser phenotype. Enzyme activity is highest in the presence of inducers, such as tobacco smoke, regular consumption of cruciferous vegetables or chargrilled meats, and certain drugs. For a drug extensively metabolised by CYP1A2, drug exposure and clinical effects may either be reduced (for an active drug) or increased (for a prodrug).
CYP2C19	*1/*2	**Intermediate metaboliser:** This individual is predicted to have an intermediate metaboliser phenotype due to the presence of one normal function allele and one no function allele. For a drug extensively metabolised by CYP2C19, 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).
CYP2C9	*1/*1	**Normal metaboliser:** Due to the presence of two normal function alleles, this individual is predicted to have a normal metaboliser phenotype. For a drug extensively metabolised by CYP2C9, drug exposure and clinical effects may be expected to lie within the normal range.
CYP2D6	*4/*41	**Intermediate metaboliser:** Due to the presence of one reduced function allele and one no function allele, this individual is predicted to have an intermediate metaboliser phenotype. For a drug extensively metabolised 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 metaboliser:** The *22 allele is not present and this individual is expected to have a normal metaboliser phenotype. Whilst many drugs are known to be metabolised by CYP3A4, relatively few genetic variations have been found that affect metabolism of a limited number of these drugs.

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This report has been prepared by the myDNA Clinical Team

Laboratory Results provided by:

GenSeq Labs (NATA 20082)

myDNA DISCLAIMER

Response to medications is complex and may also be influenced by other genetic and non-genetic factors which are not tested for (e.g. patient adherence to prescription regimen, concurrent illness, drug-drug interactions). This report is just one clinical factor which is intended to be considered in addition to other clinical information as part of a comprehensive medical evaluation by the treating clinician. It is advised that medications should not be changed solely based on this report and it is the responsibility of the treating clinician to consider all information relating to the patient to determine the most appropriate course of treatment. Unless instructed by their doctor, patients are advised not to alter the dose or stop any medications based on this report.

Clinical monitoring should occur for all psychotropic medications. It is not intended to imply that drugs listed in this report are approved for certain indications or that they have comparable efficacy or safety. Note that prescribing of some of the listed medications for psychiatric conditions may be considered off-label and approved drug labels should be consulted for guidance regarding their use.

This report outlines gene-drug interactions for the medications listed. Allergic reactions cannot be detected by this test. The test does not detect all known variants in the genes tested.

This report is written assuming the clinician will explain the results of the report to the tested individual and any resulting implications for both the individual or family members. The report follows FDA guidelines to inform the ordering clinician about results and meaning of the test and that the clinician has the responsibility for arranging all further explanatory counseling.

The pharmacogenomic guidance in this report primarily applies to adult patients over the age of 18 years. Therefore, clinician discretion should be exercised if the guidance in this report is applied to patients under the age of 18 years other than otherwise stated.

Disclaimer of Liability

This myDNA report does not serve as medical advice and does not substitute clinical monitoring. myDNA is not liable for any clinical decisions made based on the results provided in this report as this remains the responsibility of the treating clinician. myDNA strongly believes that this report should be considered as part of a comprehensive medical evaluation by the treating clinician.

The information provided in the report is believed to be accurate and complete at the date reported and is based on the current evidence in the scientific literature. However, the scientific literature is routinely updated as new information becomes available and therefore, the reported drug classifications and clinical considerations may change from the original published version of the report. While myDNA believes the information of this report is accurate and complete, myDNA does not provide any warranties of any kind relating to how the information provided in this report is used or applied by the treating clinician.

TEST METHODOLOGY AND LIMITATIONS

Pharmacogenomics testing and clinical interpretation was performed by GenSeq Labs (a subsidiary of myDNA) in a NATA accredited laboratory (NATA accredited lab No 20082). DNA is extracted from a blood or cheek swab sample and SNP genotyping is performed using open array technology (Life Technologies QuantStudio 12K). CYP2D6 copy number is established by real time PCR (QuantStudio 6), allowing for quantification of up to 4 copies. 3D PCR (QuantStudio 3D) is used to determine which allele is duplicated. The genomic regions listed in this report were tested using the Life Technologies® QuantStudio System; there is a possibility that the tested individual is a carrier for additional, undetected variants that may affect results. Although molecular tests are highly accurate, rare diagnostic errors may occur that interfere with analysis. Sources of these errors include sample mix-up, trace contamination, and other technical errors. The presence of additional variants nearby may interfere with variant detection. Genetic counselling is recommended to properly review and explain these results to the tested individual. Allergic reactions cannot be detected by this genetic test. The test does not detect all known variants in the genes tested. If an individual carries a rare variant not covered by the test, the phenotype may be inaccurately reported. The interpretation and clinical recommendations are based on the above results as reported by GenSeq Labs and also uses information provided to myDNA by the referring healthcare professionals. This report also assumes correct labelling of sample tubes and that the sample is from the indicated patient.

TEST PANEL OF GENES AND VARIANTS

The following clinically actionable alleles are tested: CYP1A2 *1F(LRG_1274:g.5732C>A); CYP2C19 *2(NG_008384.3:g.24179G>A), *3(NG_008384.3:g.22973G>A), *9 (NG_008384.3:g.17809G>A) *17(NG_008384.3:g.4220C>T); CYP2C9 *2(LRG_1195:g.9133C>T), *3(LRG_1195:g.48139A>C), *5 (LRG_1195:g.48144C>G), *6 (LRG_1195:g.16126del), *8 (LRG_1195:g. 9152G>A), *11 (LRG_1195:g. 48067C>T), *27 (LRG_1195:g. 9152G>T); CYP2D6 *2 (LRG_303:g.7870C>T), *3 (LRG_303:g.7569del), *4 (LRG_303:g.[5119C>T; 6047G>A]), *5 (del(CYP2D6)), *6 (LRG_303:g.6727del), *7 (LRG_303:g.7955A>C), *8 (LRG_303:g.[6778G>T; 7870C>T), *9 (LRG_303:g. 7635_7637del), *10 (LRG_303:g.5119C>T), *12 (LRG_303:g.[5143G>A; 7870C>T]), *114 (LRG_303:g.[5119C>T;6778G>A ;7870C>T]), *14 (LRG_303:g.[6778G>A ;7870C>T]), *17 (LRG_303:g.[6041C>T;7870C>T], *29 (LRG_303:g.[7870C>T;8203G>A], *36 (NC_000022.10:g.[42526694G>A ;42522624_42522669con42536337_42536382]), *41(LRG_303:g.[7870C>T; 8008G>A]) and CYP3A4 *22(NG_008421.1:g.20493C>T). The *1 allele denotes the absence of any variant and is designated as the wild type. The *1A allele denotes the absence of the *1F variant for CYP1A2. Only a single variant SNP is tested for the CYP1A2 and CYP3A4 genes. All variants are named using the HGVS nomenclature.