OTHER MEDICATIONS

The following tables outline personalised recommendations for other medications.

NOTE: These tables do not account for the effect of any inhibitors or inducers. The table is not an all-inclusive list of other medications.

MEDICATIONS WITH *MINOR* 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[17] 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[18] 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).
Clobazam (Benzodiazepine)	***CYP2C19* - Rapid 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. The CYP2C19 genotype predicts increased metabolism of clobazam's active metabolite and a possible reduction in clinical effects. (Note that the effect of variations in CYP3A4 has not been described).	No genotype-guided dosing recommendation available. Be alert to a reduced clinical response.

MEDICATION	INTERPRETATION	RECOMMENDATION
	exposure are predicted. The clinical significance of this is uncertain.	
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[14] 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.[13]
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[15] suggest 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. Be alert to adverse effects and adjust dose according to clinical response.
Zuclopenthixol	***CYP2D6* - Intermediate metaboliser:** Reduced metabolism and increased drug exposure are predicted. This may increase the risk of adverse effects.	The DPWG[16] advises starting with 75% of the standard dose or selecting an alternative drug according to current guidelines.

MEDICATIONS WITH *USUAL* PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
Quetiapine	***CYP3A4* - Normal metaboliser:** Normal metabolism of quetiapine is predicted.	Standard dosing and prescribing measures apply.

ANTIPSYCHOTICS

The following tables outline personalised recommendations for antipsychotics.

NOTE: These tables do not account for the effect of any inhibitors or inducers. The table is not an all-inclusive list of antipsychotics.

MEDICATIONS WITH *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[10] 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[11] suggests 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.[12] Based on the CYP2D6 genotype, reduced metabolism and increased drug	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.[13]

MEDICATION	INTERPRETATION	RECOMMENDATION
	dependent and could potentially lead to late onset adverse effects on a previously tolerated fluoxetine dose.	
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[1] provides a strong recommendation to initiate therapy with the recommended starting dose. DPWG [9] suggests no specific action on fluvoxamine dosing is required based on this CYP2D6 genotype.
Paroxetine (SSRI)	***CYP2D6* - Intermediate metaboliser:** Reduced metabolism 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[1] guidelines provide a strong recommendation to initiate therapy with the recommended starting dose. It would also be reasonable to monitor closely for adverse effects.
Sertraline (SSRI)	***CYP2C19* - Rapid metaboliser:** Increased metabolism by CYP2C19 could increase the probability of reduced plasma concentrations, and potentially reduce the clinical effects. However, there is limited evidence linking this genotype with increased sertraline metabolism and reduced drug exposure.	CPIC[1] provides an optional recommendation to initiate therapy with the recommended starting dose. If the clinical response is not adequate despite standard maintenance dosing, CPIC suggests considering an alternative antidepressant not predominantly metabolised by CYP2C19.

MEDICATION	INTERPRETATION	RECOMMENDATION
	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.	
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[7] 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.
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	Based on the CYP2D6 genotype, DPWG[8] 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.

MEDICATIONS WITH *MINOR* PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
Agomelatine	**CYP1A2 - Ultrarapid metaboliser (with inducer present):** Increased agomelatine metabolism and reduced plasma concentrations are predicted, especially with exposure to enzyme inducers such as tobacco smoking, daily consumption of cruciferous vegetables or chargrilled meat, and certain medications (e.g. omeprazole). One study demonstrated a significant reduction in plasma concentrations of agomelatine with this genotype.[5] The relationship of changes in plasma concentration to patient response to agomelatine is not clear.	No genotype-guided dosing recommendation available. Monitor for a reduced clinical effect.
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.[6]
Moclobemide	**CYP2C19 - Rapid metaboliser:** Increased metabolism by CYP2C19 and reduced plasma concentrations are predicted. The clinical significance of this is not known, though reduced effects could be anticipated.	No genotype-guided dosing recommendation available. Be alert to a reduced clinical response.
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.
Duloxetine (SNRI)	**CYP2D6 - Intermediate metaboliser** **CYP1A2 - Ultrarapid metaboliser (with inducer present):** Duloxetine is metabolised by both CYP1A2 and CYP2D6, with CYP1A2	No genotype-guided dosing recommendation available. Monitor for an altered clinical response.

MEDICATION	INTERPRETATION	RECOMMENDATION
	plasma concentrations of clomipramine are predicted. Reduced metabolism of the active metabolite is predicted.	therapeutic drug monitoring to guide dose adjustments.
Dothiepin (TCA)	***CYP2D6* - Intermediate metaboliser** ***CYP2C19* - Rapid metaboliser:** Dothiepin is metabolised by CYP2C19 into an active metabolite, which is further metabolised by CYP2D6 into an inactive metabolite. Slightly increased metabolism and reduced plasma concentrations of dothiepin are predicted. Reduced metabolism of the active metabolite is predicted.	CPIC[2] provides an optional recommendation to consider an alternative drug not metabolized by CYP2C19, such as nortriptyline. If dothiepin is required, consider therapeutic drug monitoring to guide dose adjustments.
Doxepin (TCA)	***CYP2D6* - Intermediate metaboliser** ***CYP2C19* - Rapid metaboliser:** Doxepin is metabolised by CYP2C19 into an active metabolite, which is further metabolised by CYP2D6 into an inactive metabolite. Slightly increased metabolism and reduced plasma concentrations of doxepin are predicted. Reduced metabolism of the active metabolite is predicted.	CPIC[2] provides an optional recommendation to consider an alternative drug not metabolized by CYP2C19, such as nortriptyline. If doxepin is required, consider therapeutic drug monitoring to guide dose adjustments.
Imipramine (TCA)	***CYP2D6* - Intermediate metaboliser** ***CYP2C19* - Rapid metaboliser:** Imipramine is metabolised by CYP2C19 into an active metabolite, which is further metabolised by CYP2D6 into an inactive metabolite. Slightly increased metabolism and reduced plasma concentrations of imipramine are predicted. Reduced metabolism of the active metabolite is predicted.	CPIC[2] provides an optional recommendation to consider an alternative drug not metabolized by CYP2C19, such as nortriptyline. If imipramine is required, consider therapeutic drug monitoring to guide dose adjustments.
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[3,4] provides a recommendation to consider a 25% reduction of the recommended starting dose. 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.

ANTIDEPRESSANTS

The following tables outline personalised recommendations for antidepressants.

NOTE: These tables do not account for the effect of any inhibitors or inducers. The table is not an all-inclusive list of antidepressants.

MEDICATIONS WITH ***MAJOR*** PRESCRIBING CONSIDERATIONS

MEDICATION	INTERPRETATION	RECOMMENDATION
Citalopram (SSRI)	***CYP2C19*** **- Rapid metaboliser:** Increased metabolism of citalopram by CYP2C19 and reduced drug exposure are predicted. This may increase the likelihood of therapeutic failure.	CPIC guidelines[1] provide a moderate recommendation to consider an alternative antidepressant not predominantly metabolised by CYP2C19. If the clinical response has been adequate, a change to therapy may not be required.
Escitalopram (SSRI)	***CYP2C19*** **- Rapid metaboliser:** Increased metabolism of escitalopram by CYP2C19 and reduced drug exposure are predicted. This may increase the likelihood of therapeutic failure.	CPIC guidelines[1] provide a moderate recommendation to consider an alternative antidepressant not predominantly metabolised by CYP2C19. If the clinical response has been adequate, a change to therapy may not be required.
Amitriptyline (TCA)	***CYP2D6*** **- Intermediate metaboliser** ***CYP2C19*** **- Rapid metaboliser:** Amitriptyline is metabolised by CYP2C19 into an active metabolite, which is further metabolised by CYP2D6 into an inactive metabolite. Slightly increased metabolism and reduced plasma concentrations of amitriptyline are predicted. There may be an increased risk of therapeutic failure with amitriptyline. Reduced metabolism of the active metabolite is predicted.	For use at higher doses such as in the treatment of depression, CPIC[2] provides an optional recommendation to consider an alternative drug not metabolized by CYP2C19, such as nortriptyline. If amitriptyline is required, consider therapeutic drug monitoring to guide dose adjustments. For use at lower doses such as in treatment of neuropathic pain, if currently well tolerated and clinical response has been adequate, a change to therapy may not be required. Nortriptyline may be more suitable from a metabolism perspective. If using nortriptyline, monitor for adverse effects.
Clomipramine (TCA)	***CYP2D6*** **- Intermediate metaboliser** ***CYP2C19*** **- Rapid metaboliser:** Clomipramine is metabolised by CYP2C19 into an active metabolite, which is further metabolised by CYP2D6 into an inactive metabolite. Slightly increased metabolism and reduced	CPIC[2] provides an optional recommendation to consider an alternative drug not metabolized by CYP2C19, such as nortriptyline. If clomipramine is required, consider

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REPORT SUMMARY

Unless instructed by their doctor, patients are advised not to alter the dose or stop any medications.

Name:	**Janelle Marie Courcha**	DOB:	**11-Sep-2002**	Collected:	**24-Mar-2021**
Address:	**9 Parkhurst Avenue, Hilbert, WA, 6112**	myDNA ID:	**104449**	Received:	**30-Mar-2021**
		Pathology No:	**160715P0H7G1**	Reported:	**13-Apr-2021**
Doctor:	**Dr Morenikeji Komaiya**	Copy to:			
Sample type and quality:	**Buccal. The sample quality was assessed and deemed to be satisfactory according to the laboratory's acceptance criteria.**				

SUBMITTED MEDICATIONS

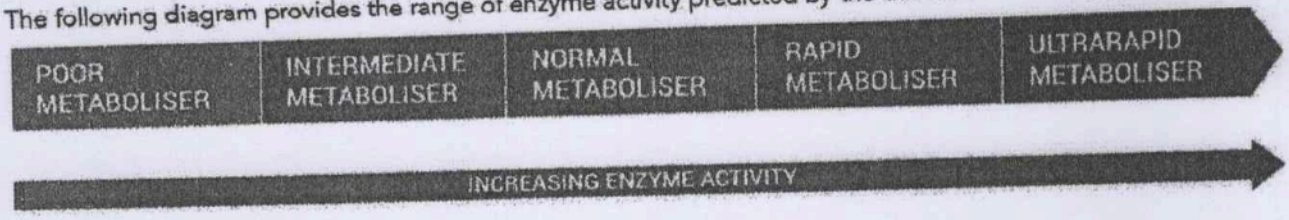
agomelatine (Valdoxan), dexamphetamine

GENETIC TEST RESULTS SUMMARY

GENE	GENOTYPE	PREDICTED PHENOTYPE
CYP2D6	*4/*41	Intermediate metaboliser
CYP2C19	*1/*17	Rapid metaboliser
CYP2C9	*1/*1	Normal metaboliser
CYP1A2	*1F/*1F	Ultrarapid metaboliser (with inducer present)
CYP3A4	*1/*1	Normal metaboliser

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

The following diagram provides the range of enzyme activity predicted by the this test.



ABOUT THIS REPORT

Overview

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 significant effect to drug response is predicted. There may be guidelines recommending consideration be given to a change in the dose or the medication type, in order to minimise the risk of the potential clinical issue noted.
- Minor prescribing considerations – Altered drug response is possible, but the clinical significance is either thought to be minor or there is insufficient data available. Consider monitoring for the clinical issue noted in this report and any guideline prescribing recommendations.
- Usual prescribing considerations – Genetic results are not predicted to affect drug response, 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.

For many medications covered in this report, international, peer reviewed prescribing guidelines are available and these are included in our report.

The two major guidelines are those of the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Royal Dutch Pharmacists Association – Pharmacogenetics Working Group (DPWG).

Report breakdown

The report consists of the following sections:

- Genetic test results summary – presents the patients genotypes for the genes relevant to the medications covered by this report
- Medication tables arranged according to the three categories
- Details of test results – 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 (exposure)
- References – the major references used for the report. More detailed references are available by contacting myDNA.

As part of our clinical service, we have a team of clinical experts available to answer any questions you may have about this report or about pharmacogenomics in general.

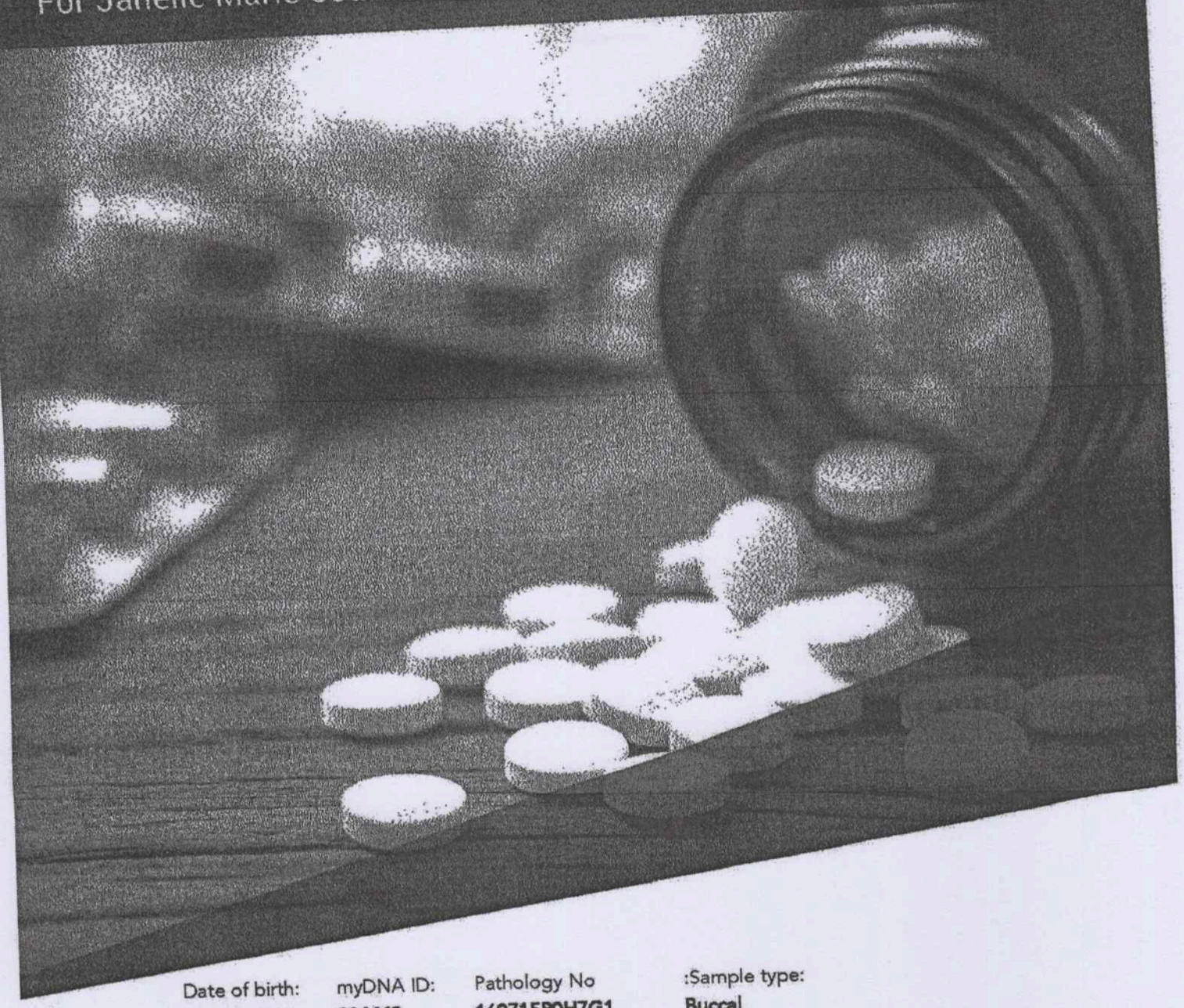
If you have any such queries, please call our clinical team on +61 3 8582 0301.

myDNA

RECOMMENDATIONS FOR HEALTHCARE PROFESSIONALS

PERSONALISED MENTAL HEALTH MEDICATION REPORT

For Janelle Marie Courcha



Date of birth:	myDNA ID:	Pathology No	:Sample type:
11-Sep-2002	**104449**	**160715P0H7G1**	**Buccal**
Collected:	Received:	Reported:	Doctor:
24-Mar-2021	**30-Mar-2021**	**13-Apr-2021**	**Dr Morenikeji Komaiya**