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CNSDOSE TEST REPORT

CNSDose is an advanced tool for the genetic guidance of medications. CNSDose leverages knowledge of liver and blood-brain-barrier genetics, peer-reviewed publications, a randomised controlled trial, as well as non-genetic factors such as drug-drug interactions, lifestyle factors, blackbox warnings, PIM warnings and anticholinergic burden.

REPORT SUMMARY

Patient name:	**Test Patient**	Ordering physician:	**Dr Test Doctor**	Report type:	**Approved**
Patient date of birth:	**1972-02-02**	Ordering facility:		Report approved by:	
CNSDose report date:	**2023-02-07**				

TABLE OF CONTENTS

Current medications	page 2
Medication assessments	page 4
Medication alerts	page 12
Pharmacogenetic results	page 15
How to use this report	page 16
Disclaimers	page 17

TEST RESULTS SUMMARY

CYP1A2	Rapid metaboliser	*1A/*1F
CYP2B6	Normal metaboliser	*1/*1
CYP2C19	Poor metaboliser	*2/*2
CYP2C9	Normal metaboliser	*1/*1
CYP2D6	Poor metaboliser	*4/*5
CYP3A4	Normal metaboliser	*1/*1
CYP3A5	Poor metaboliser	*3/*3
SLCO1B1	Decreased function	*1/*5
UGT1A1	Intermediate metaboliser	*1/*28
*BBB	Medium Efflux	M

*Blood-Brain Barrier
The complete list of test results can be found in the "Pharmacogenetic Results" section of the report.

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CURRENT MEDICATIONS

The assessments below are based on the patients current/intended regimen as provided by the treating physician. To update, or to provide the patients current medication regimen please contact the laboratory at info@incitehealth.com.au.

	ALERTS		PRECAUTIONS				
Medication	**Gene-Drug**	**Drug-Drug**	**Contraindication**	**Lifestyle**	**Blackbox**	**PIM**	**Anticholinergic**
Citalopram	!	!	△	△	△		
Codeine	!	!	△	△	△		
Venlafaxine	!	○	△	△	△		

Expanded Assessment

Medication		Type	Description	Source
Citalopram	!	**Gene-Drug** CYP2C19: PM	Results in higher systemic concentrations and adverse reaction risk (QT prolongation). The maximum recommended dose is 20 mg.	FDA
	!	**Drug-Drug** Codeine	The risk or severity of serotonin syndrome can be increased when Codeine is combined with Citalopram.	DB
	○	**Drug-Drug** Venlafaxine	The risk or severity of serotonin syndrome can be increased when Citalopram is combined with Venlafaxine.	DB
	△	**Contraindication**	Known hypersensitivity to the drug or any of the ingredients With categories: Monoamine Oxidase Inhibitors With drugs: Pimozide	DB
	△	**Lifestyle**	Avoid alcohol. Avoid St. John's Wort. Take with or without food. The absorption is unaffected by food.	DB
Codeine	!	**Gene-Drug** CYP2D6: PM	Where clinically appropriate consider an alternative agent (inefficacy risk).	CPIC
	!	**Drug-Drug** Citalopram	The risk or severity of serotonin syndrome can be increased when Codeine is combined with Citalopram.	DB

! Major prescribing alerts ! Moderate prescribing alerts ○ Standard prescribing alerts △ Additional precautions to consider

Current medications continued on next page

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CURRENT MEDICATIONS (CONTINUED)

Medication		Type	Description	Source
Codeine (continued)	○	**Drug-Drug** Venlafaxine	The risk or severity of serotonin syndrome can be increased when Codeine is combined with Venlafaxine.	DB
	△	**Contraindication**	Known hypersensitivity to the drug or any of the ingredients Patient conditions: Obese or have conditions such as obstructive sleep apnea or severe lung disease, which may increase the risk of serious breathing problems; Age above 12 year; Age below 18 year Patient conditions: Ultrarapid Metabolizer Due to Cytochrome P450 CYP2D6 Variant; To treat cough in patients younger than 18 years old; Post Operative Pain Management in Children With Tonsillectomy/Adenoidectomy; Pain; Paralytic Ileus; Hypercarbia; Acute or severe bronchial asthma; Respiratory depression in the absence of resuscitative equipment	DB
	△	**Lifestyle**	Avoid alcohol. Take with food. Food reduces irritation.	DB
Venlafaxine	!	**Gene-Drug** CYP2D6: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	DPWG
	○	**Drug-Drug** Citalopram	The risk or severity of serotonin syndrome can be increased when Citalopram is combined with Venlafaxine.	DB
	○	**Drug-Drug** Codeine	The risk or severity of serotonin syndrome can be increased when Codeine is combined with Venlafaxine.	DB
	△	**Contraindication**	Known hypersensitivity to the drug or any of the ingredients With categories: Monoamine Oxidase Inhibitors	DB
	△	**Lifestyle**	Avoid alcohol. The safety of using venlafaxine with other CNS-active drugs, including alcohol, has not been evaluated. Avoid St. John's Wort. Co-administration of St. John's Wort may lead to additive serotonergic activity and an increased risk of serotonin syndrome. Take with food. Co-administration with food helps to alleviate or mitigate gastrointestinal upset.	DB

! Major prescribing alerts ! Moderate prescribing alerts ○ Standard prescribing alerts △ Additional precautions to consider

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MEDICATION ASSESSMENTS

The psychotropic medication guidance detailed below is based on a combined analysis of the patient's hepatic and blood brain barrier genetics.

	DOSAGE			ALERTS		PRECAUTIONS		
Medication	**Lower**	**Average**	**Higher**	**Gene-Drug**	**Drug-Drug**	**Blackbox**	**PIM**	**Anticholinergic**
Alzheimers								
Donepezil	●							
Galantamine	●							
Anti-ADHD agents								
Atomoxetine	●					△		
Clonidine	●					△		
Dexamfetamine	●					△		
Guanfacine		●						
Lisdexamfetamine		●				△		
Methylphenidate		●				△		
Modafinil		●						
Antidepressants								
Agomelatine			●					
Amitriptyline				!		△		△

The medications listed below are associated with major gene-drug prescribing alerts. Avoidance may be clinically appropriate, as directed by FDA, CPIC or DPWG guidelines.

Amitriptyline, Citalopram, Clomipramine, Clopidogrel, Codeine, Desipramine, Doxepin, Escitalopram, Imipramine, Nortriptyline, Paroxetine, Simvastatin, Tamoxifen, Venlafaxine, Voriconazole

! Major prescribing alerts ! Moderate prescribing alerts ○ Standard prescribing alerts △ Additional precautions to consider

Medication assessments continued on next page

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MEDICATION ASSESSMENTS (CONTINUED)

	DOSAGE			ALERTS		PRECAUTIONS		
Medication	**Lower**	**Average**	**Higher**	**Gene-Drug**	**Drug-Drug**	**Blackbox**	**PIM**	**Anticholinergic**
Antidepressants (continued)								
Bupropion		●				△		
Citalopram				❗	⚠	△		
Clomipramine				❗		△		
Desipramine				❗		△		△
Desvenlafaxine		●				△		
Dothiepin	●							△
Doxepin				❗		△		△
Duloxetine		●				△		
Escitalopram				❗		△		△
Fluoxetine	●					△		△
Fluvoxamine	●					△		
Imipramine				❗				△
Mianserin	●							
Milnacipran		●				△		
Mirtazapine	●					△		

❗ **The medications listed below are associated with major gene-drug prescribing alerts. Avoidance may be clinically appropriate, as directed by FDA, CPIC or DPWG guidelines.**

Amitriptyline, Citalopram, Clomipramine, Clopidogrel, Codeine, Desipramine, Doxepin, Escitalopram, Imipramine, Nortriptyline, Paroxetine, Simvastatin, Tamoxifen, Venlafaxine, Voriconazole

❗ Major prescribing alerts ⚠ Moderate prescribing alerts ○ Standard prescribing alerts △ Additional precautions to consider

Medication assessments continued on next page

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MEDICATION ASSESSMENTS (CONTINUED)

	DOSAGE			ALERTS		PRECAUTIONS		
Medication	**Lower**	**Average**	**Higher**	**Gene-Drug**	**Drug-Drug**	**Blackbox**	**PIM**	**Anticholinergic**
Antidepressants (continued)								
Moclobemide	●							
Nortriptyline				❗		△		△
Paroxetine				❗		△		△
Reboxetine		●						
Sertraline	●					△		
Venlafaxine				❗	○	△		
Vortioxetine	●					△		
Antipsychotics								
Amisulpride		●						
Aripiprazole	●					△		△
Asenapine		●				△		
Brexpiprazole	●					△		
Cariprazine	●					△		
Chlorpromazine	●							△
Clozapine	●			△		△		△

❗ **The medications listed below are associated with major gene-drug prescribing alerts. Avoidance may be clinically appropriate, as directed by FDA, CPIC or DPWG guidelines.**

Amitriptyline, Citalopram, Clomipramine, Clopidogrel, Codeine, Desipramine, Doxepin, Escitalopram, Imipramine, Nortriptyline, Paroxetine, Simvastatin, Tamoxifen, Venlafaxine, Voriconazole

❗ Major prescribing alerts ⚠ Moderate prescribing alerts ○ Standard prescribing alerts △ Additional precautions to consider

Medication assessments continued on next page

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MEDICATION ASSESSMENTS (CONTINUED)

	DOSAGE			ALERTS		PRECAUTIONS		
Medication	**Lower**	**Average**	**Higher**	**Gene-Drug**	**Drug-Drug**	**Blackbox**	**PIM**	**Anticholinergic**
Antipsychotics (continued)								
Haloperidol	●					△		
Lurasidone		●				△		
Olanzapine		●				△		△
Paliperidone	●					△		
Quetiapine		●				△		△
Risperidone	●					△		
Ziprasidone		●				△		△
Anxiolytics & Hypnotics								
Alprazolam		●				△		
Bromazepam		●						
Buspirone		●						
Clobazam	●					△		
Clonazepam		●				△		
Diazepam	●					△		
Diphenhydramine	●							△

The medications listed below are associated with major gene-drug prescribing alerts. Avoidance may be clinically appropriate, as directed by FDA, CPIC or DPWG guidelines.

Amitriptyline, Citalopram, Clomipramine, Clopidogrel, Codeine, Desipramine, Doxepin, Escitalopram, Imipramine, Nortriptyline, Paroxetine, Simvastatin, Tamoxifen, Venlafaxine, Voriconazole

Major prescribing alerts Moderate prescribing alerts Standard prescribing alerts △ Additional precautions to consider

Medication assessments continued on next page

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MEDICATION ASSESSMENTS (CONTINUED)

	DOSAGE			ALERTS		PRECAUTIONS		
Medication	**Lower**	**Average**	**Higher**	**Gene-Drug**	**Drug-Drug**	**Blackbox**	**PIM**	**Anticholinergic**
Anxiolytics & Hypnotics (continued)								
Flunitrazepam		●						
Melatonin			●					
Midazolam		●				△		
Nitrazepam		●						
Propranolol	●							
Suvorexant		●						
Temazepam		●				△		
Zolpidem		●				△		
Zopiclone		●						
Mood stabilizers / Anticonvulsants								
Brivaracetam	●							
Carbamazepine		●		△		△		
Lamotrigine		●				△		△
Perampanel		●				△		
Rufinamide		●						

The medications listed below are associated with major gene-drug prescribing alerts. Avoidance may be clinically appropriate, as directed by FDA, CPIC or DPWG guidelines.

Amitriptyline, Citalopram, Clomipramine, Clopidogrel, Codeine, Desipramine, Doxepin, Escitalopram, Imipramine, Nortriptyline, Paroxetine, Simvastatin, Tamoxifen, Venlafaxine, Voriconazole

● Major prescribing alerts ● Moderate prescribing alerts ○ Standard prescribing alerts △ Additional precautions to consider

Medication assessments continued on next page

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MEDICATION ASSESSMENTS (CONTINUED)

	DOSAGE			ALERTS		PRECAUTIONS		
Medication	**Lower**	**Average**	**Higher**	**Gene-Drug**	**Drug-Drug**	**Blackbox**	**PIM**	**Anticholinergic**
Mood stabilizers / Anticonvulsants (continued)								
Topiramate		●						
Valproate (Valproic acid)		●				△		
Other Psychotropic								
Bromocriptine		●						
Cabergoline		●						
Dapoxetine		●						
Disulfiram		●				△		
Naloxone		●						
Naltrexone		●				△		
Nicotine		●						
Rasagiline		●						
Ropinirole		●						
Rotigotine		●						
Selegiline		●						

The medications listed below are associated with major gene-drug prescribing alerts. Avoidance may be clinically appropriate, as directed by FDA, CPIC or DPWG guidelines.

Amitriptyline, Citalopram, Clomipramine, Clopidogrel, Codeine, Desipramine, Doxepin, Escitalopram, Imipramine, Nortriptyline, Paroxetine, Simvastatin, Tamoxifen, Venlafaxine, Voriconazole

● Major prescribing alerts ⓘ Moderate prescribing alerts ○ Standard prescribing alerts △ Additional precautions to consider

Medication assessments continued on next page

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MEDICATION ASSESSMENTS (CONTINUED)

	DOSAGE			ALERTS		PRECAUTIONS		
Medication	**Lower**	**Average**	**Higher**	**Gene-Drug**	**Drug-Drug**	**Blackbox**	**PIM**	**Anticholinergic**
Non-psychotropic								
Atazanavir								
Carvedilol				⚠				
Celecoxib						△		
Clopidogrel				❗		△		
Codeine				❗	⚠	△		
Efavirenz						△		
Esomeprazole				⚠		△		
Flecainide				⚠		△		
Flurbiprofen						△		
Gefitinib				⚠				
Irinotecan						△		
Lansoprazole								
Metoclopramide				⚠		△		
Metoprolol				⚠		△		
Omeprazole				⚠				

❗ **The medications listed below are associated with major gene-drug prescribing alerts. Avoidance may be clinically appropriate, as directed by FDA, CPIC or DPWG guidelines.**

Amitriptyline, Citalopram, Clomipramine, Clopidogrel, Codeine, Desipramine, Doxepin, Escitalopram, Imipramine, Nortriptyline, Paroxetine, Simvastatin, Tamoxifen, Venlafaxine, Voriconazole

❗ Major prescribing alerts ⚠ Moderate prescribing alerts ○ Standard prescribing alerts △ Additional precautions to consider

Medication assessments continued on next page

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MEDICATION ASSESSMENTS (CONTINUED)

	DOSAGE			ALERTS		PRECAUTIONS		
Medication	**Lower**	**Average**	**Higher**	**Gene-Drug**	**Drug-Drug**	**Blackbox**	**PIM**	**Anticholinergic**
Non-psychotropic (continued)								
Ondansetron								
Oxycodone						△		
Pantoprazole				ⓘ				
Phenytoin						△		
Piroxicam						△		
Raltegravir								
Rosuvastatin								
Simvastatin				❗				
Tacrolimus				○		△		
Tamoxifen				❗		△		
Tramadol				ⓘ		△		△
Voriconazole				❗		△		
Warfarin						△		

❗ **The medications listed below are associated with major gene-drug prescribing alerts. Avoidance may be clinically appropriate, as directed by FDA, CPIC or DPWG guidelines.**

Amitriptyline, Citalopram, Clomipramine, Clopidogrel, Codeine, Desipramine, Doxepin, Escitalopram, Imipramine, Nortriptyline, Paroxetine, Simvastatin, Tamoxifen, Venlafaxine, Voriconazole

❗ Major prescribing alerts ⓘ Moderate prescribing alerts ○ Standard prescribing alerts △ Additional precautions to consider

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MEDICATION ALERTS

Medications listed below may be associated with significant gene-drug or drug-drug prescribing alerts, as directed by FDA, CPIC or DPWG guidelines. Avoidance may be indicated, please review carefully.

Medication		Type	Description	Source
Amitriptyline	!	**Gene-Drug** CYP2C19: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	CPIC
	!	**Gene-Drug** CYP2D6: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	CPIC
Carbamazepine	△	**Gene-Drug**	HLA testing recommended in patients of Asian ethnicity.	FDA
Carvedilol	!	**Gene-Drug** CYP2D6: PM	Results in higher systemic concentrations and higher adverse reaction risk (dizziness).	FDA
Citalopram	!	**Gene-Drug** CYP2C19: PM	Results in higher systemic concentrations and adverse reaction risk (QT prolongation). The maximum recommended dose is 20 mg.	FDA
	!	**Drug-Drug** Codeine	The risk or severity of serotonin syndrome can be increased when Codeine is combined with Citalopram.	DB
	○	**Drug-Drug** Venlafaxine	The risk or severity of serotonin syndrome can be increased when Citalopram is combined with Venlafaxine.	DB
Clomipramine	!	**Gene-Drug** CYP2C19: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	CPIC
	!	**Gene-Drug** CYP2D6: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	CPIC
Clopidogrel	!	**Gene-Drug** CYP2C19: PM	Results in lower systemic active metabolite concentrations, lower antiplatelet response, and may result in higher cardiovascular risk. Consider use of another platelet P2Y12 inhibitor.	FDA
Clozapine	△	**Gene-Drug**	Serum level monitoring recommended.	FDA
Codeine	!	**Gene-Drug** CYP2D6: PM	Where clinically appropriate consider an alternative agent (inefficacy risk).	CPIC

! Major prescribing alerts ! Moderate prescribing alerts ○ Standard prescribing alerts △ Additional precautions to consider

Medication alerts continued on next page

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MEDICATION ALERTS (CONTINUED)

Medication		Type	Description	Source
Codeine (CONTINUED)	!	**Drug-Drug** Citalopram	The risk or severity of serotonin syndrome can be increased when Codeine is combined with Citalopram.	DB
	○	**Drug-Drug** Venlafaxine	The risk or severity of serotonin syndrome can be increased when Codeine is combined with Venlafaxine.	DB
Desipramine	!	**Gene-Drug** CYP2D6: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	CPIC
Doxepin	!	**Gene-Drug** CYP2D6: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	CPIC
	!	**Gene-Drug** CYP2C19: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	CPIC
Escitalopram	!	**Gene-Drug** CYP2C19: PM	Consider dose reduction (tolerability risk). In adults up to 65 years, do not exceed 20mg/day as tablets or 16mg/day as drops. In adults 65 years or older, do not exceed 10mg/day as tablets or 8mg/day as drops. (QTc prolongation risk).	DPWG
Esomeprazole	!	**Gene-Drug** CYP2C19: PM	Results in higher systemic concentrations.	FDA
Flecainide	!	**Gene-Drug** CYP2D6: PM	Consider 50% reduction of standard dose (tolerability risk). Therapeutic drug monitoring recommended.	DPWG
Gefitinib	!	**Gene-Drug** CYP2D6: PM	Results in higher systemic concentrations and higher adverse reaction risk. Monitor for adverse reactions.	FDA
Imipramine	!	**Gene-Drug** CYP2D6: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	CPIC
	!	**Gene-Drug** CYP2C19: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	CPIC
Metoclopramide	!	**Gene-Drug** CYP2D6: PM	Results in higher systemic concentrations and higher adverse reaction risk. The recommended dosage is lower. Refer to FDA labeling for specific dosing recommendations.	FDA

! Major prescribing alerts ! Moderate prescribing alerts ○ Standard prescribing alerts △ Additional precautions to consider

Medication alerts continued on next page

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MEDICATION ALERTS (CONTINUED)

Medication		Type	Description	Source
Metoprolol	⚠	**Gene-Drug** CYP2D6: PM	Results in higher systemic concentrations.	FDA
Nortriptyline	!	**Gene-Drug** CYP2D6: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	CPIC
Omeprazole	⚠	**Gene-Drug** CYP2C19: PM	Results in higher systemic concentrations.	FDA
Pantoprazole	⚠	**Gene-Drug** CYP2C19: PM	Results in higher systemic concentrations. Consider dosage reduction in children who are poor metabolizers. No dosage adjustment is needed for adult patients who are poor metabolizers.	FDA
Paroxetine	!	**Gene-Drug** CYP2D6: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	CPIC
Simvastatin	!	**Gene-Drug** SLCO1B1 / rs4149056: T/C	Where clinically appropriate consider an alternative agent (toxicity risk).	DPWG
Tacrolimus	○	**Gene-Drug** CYP3A5: PM	Standard dosing appropriate. Therapeutic drug monitoring recommended.	CPIC
Tamoxifen	!	**Gene-Drug** CYP2D6: PM	Where clinically appropriate consider an alternative agent (inefficacy risk).	CPIC
Tramadol	⚠	**Gene-Drug** CYP2D6: PM	Consider dose elevation (inefficacy risk).	DPWG
Venlafaxine	!	**Gene-Drug** CYP2D6: PM	Where clinically appropriate consider an alternative agent (toxicity risk).	DPWG
	○	**Drug-Drug** Citalopram	The risk or severity of serotonin syndrome can be increased when Citalopram is combined with Venlafaxine.	DB
	○	**Drug-Drug** Codeine	The risk or severity of serotonin syndrome can be increased when Codeine is combined with Venlafaxine.	DB
Voriconazole	!	**Gene-Drug** CYP2C19: PM	Where clinically appropriate consider an alternative agent.	CPIC

! Major prescribing alerts ⚠ Moderate prescribing alerts ○ Standard prescribing alerts △ Additional precautions to consider

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PHARMACOGENETIC RESULTS

Requisition number:	IH-0000-0000-0305	**Clinical testing performed by:**		**Lab director:**	
Patient name:	Test Patient	Incite Health		**Lab accreditation number:**	020374
Patient date of birth:	1972-02-02	PO Box 8004, Burwood Heights			
Sample identifier:	EX-01	VIC 3151, Australia			
Sample collection date:	2023-02-01				
Received at lab date:	2023-02-06				

TEST RESULTS

ABCB1	
rs1045642	A/A
rs2032582	A/A
rs2229109	C/C
ABCC1	
rs212090	T/T
ABCG2	
rs2231137	C/C
rs2231142	T/T
COMT	
rs4680	G/A
OPRM1	
rs1799971	A/A
VKORC1	
rs9923231	C/C

CYP1A2	**Rapid metaboliser**	***1A/*1F**
CYP2B6	**Normal metaboliser**	***1/*1**
CYP2C19	**Poor metaboliser**	***2/*2**
CYP2C9	**Normal metaboliser**	***1/*1**
CYP2D6	**Poor metaboliser**	***4/*5**
CYP3A4	**Normal metaboliser**	***1/*1**
CYP3A5	**Poor metaboliser**	***3/*3**
SLCO1B1	**Decreased function**	***1/*5**
UGT1A1	**Intermediate metaboliser**	***1/*28**

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HOW TO USE THIS REPORT

DOSING GUIDELINES

In the "Medication Assessments" section of the report, the dosage columns "Lower", "Average" and "Higher" describe the dose range at which the medications are likely to be tolerable and effective for the patient, where:

Less preferred

LOWER DOSE

Genetically for this patient, the medications listed are likely tolerable and effective at the very low end of the recommended dose range.

Preferred

AVERAGE DOSE

Genetically for this patient, the medications listed are likely tolerable and effective at average recommended doses, so may be preferred.

Less preferred

HIGHER DOSE

Genetically for this patient, the medications listed are likely tolerable and effective at the very high end of the recommended dose range. Upward dose titration may be clinically appropriate.

Prescribers can use the dosing guidelines in one of three recommended ways:

Option 1: Where the patient has already started on a medication, if the selected medication comes back in the lower-dose column, no need to increase the dose - await efficacy to emerge over the subsequent month. If the selected medication comes back in the average-dose column, escalate the dose to the average manufacturer recommended dose and await efficacy to emerge over the subsequent month. If the selected medication comes back in the higher-dose column, escalate the dose to the high end of the manufacturer recommended dose range (as tolerated) and await efficacy to emerge over the subsequent month. As non-genetic factors will significantly effect dosing in some patients, always continue to use clinical acumen in dosing.

Option 2: If medications are listed in the average-dose column, select one of these medications and initiate at average manufacturer recommended dose - await efficacy to emerge over the subsequent month. There remains scope for the dose to be adjusted up or down if non-genetic factors impact optimal clinical dosing.

Option 3: If no medications are listed in the average-dose column, select a medication in the lower-dose column, initiate at a low dose and await a month for efficacy to emerge. If all medications are listed in the higher-dose column (high hepatic and BBB block) start a medication at average dose and after a few days escalate the dose (as tolerated) toward the upper end of the manufacturer recommended dose range, then await efficacy to emerge over the subsequent month.

REPORT KEYS

Phenotype abbreviations

UM Ultrarapid metaboliser

RM Rapid metaboliser

NM Normal metaboliser

IM Intermediate metaboliser

PM Poor metaboliser

Icons

Major prescribing alerts

Moderate prescribing alerts

Standard prescribing alerts

Additional precautions to consider

Guideline source

DB DrugBank / www.drugbank.ca

FDA U.S. Food & Drug Administration / www.fda.gov

CPIC Clinical Pharmacogenetics Implementation Consortium / www.cpicpgx.org

DPWG Dutch Pharmacogenetics Working Group / www.upgx.eu

PIM: "Potentially Inappropriate Medications" warnings apply to patients 65 years of age, or older.

Not evaluated: Any medication listed in the patients current/intended regimen that is not included in the current CNSDose panel; such medications are not evaluated for gene-drug interactions.

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DISCLAIMERS

METHODOLOGY

Analysis was performed using methods developed and validated by Incite Health. Patient genomic DNA was analyzed by the MassARRAY® System using primers and probes designed by Agena Bioscience and Incite Health. This assay detects the variants and alleles listed below.

CYP2D6	*2, *3, *4, *5, *6, *7, *8, *9, *10, *11, *12, *14A, *14B, *15, *17, *18, *19, *20, *29, *36, *41 and duplications & hybrids.
CYP2C9	*2, *3, *4, *5, *6, *8, *11, *12, *13, *15
CYP2C19	*2, *3, *4, *5, *6, *7, *8, *17
CYP1A2	*1A, *1C, *1F, *1K, *7, *11
CYP3A4	*2, *17, *22
CYP3A5	*2, *3, *6, *7
CYP2B6	*6, *18
UGT1A1	*28, *36, *37
ABCB1	rs1045642, rs2032582, rs2229109
ABCC1	rs212090
ABCG2	rs2231137, rs2231142
COMT	rs4680
OPRM1	rs1799971
SLCO1B1	rs4149056
VKORC1	rs9923231

ASSAY LIMITATIONS

Rare variants not detected by this assay may be present but not reported. Such undetected genetic and/or non-genetic factors such as drug-drug interactions, may impact the phenotype.

Test performance may be limited by the presence of PCR inhibitors in the patient's sample or by a low quantity or quality of extracted DNA. These interferents and limitations typically produce failure to amplify (no result) rather than an inaccurate result. The presence of rare or otherwise unidentified nearby variants may also affect test performance at the targeted locations. Test results and clinical interpretation may be inaccurate in patients who have undergone tissue transplant therapy.

Disclaimers continued on next page

cnsdose.

DISCLAIMERS (CONTINUED)

LIABILITY DISCLAIMERS

Warning: All medication decisions & adjustments must be in consultation with the treating clinician.

*Genetic guidance is from combined hepatic metaboliser and blood-brain-barrier permeability status. Non-genetic factors influence central nervous system (CNS) bioavailability & dosing. Renal & hepatic impairment, brain trauma, & advanced age may necessitate dose reduction. Medication interactions, smoking and certain foods may influence dosing. The clinical utility of CNSDose is based on level 1b evidence – a double blind randomized controlled trial with narrow confidence intervals [1, 2]. The report is over 85% accurate in determining Desvenlafaxine dosage for remission in Caucasians with co-morbidity free depression [3]. Utility in other ethnicities is undetermined. Efficacy of CNSDose in depression with comorbidities has not been established, but is currently being studied. The report is to be used as just one optional part of the clinical decision making process [3-6]. Regular review by an experienced clinician is needed to gauge efficacy, tolerability, and safety of medication [3-6]. The report is clinical grade (not investigational) and complies with relevant jurisdictional partner laboratory regulations. Bupropion, Citalopram, Levomilnacipran, Trazodone, Vilazodone, & Vortioxetine were not included in the original clinical trials which only examined the report listed antidepressants. [1,2]. However, guidance is based on the same methods used in the clinical trials, but such guidance should be used with greater caution. Some listed medications may not be available in certain countries. United States prescribers to consider 'pharmacogenomic biomarkers in drug labelling': https://www.fda.gov/drugs/science-and-research-drugs/table-pharmacogenomic-biomarkers-drug-labeling. CNSDose is a registered trademark, with patent pending.

[1] Singh AB (2015). Improved antidepressant remission in major depression via a pharmacokinetic pathway polygene pharmacogenetic report. Clinical Psychopharmacology Neuroscience, 13.2:150. [2] Bousman CA & Hopwood M (2016). Commercial pharmacogenetic-based decision-support tools in psychiatry. The Lancet Psychiatry, 3.6:585-590. [3] van Westrhenen, Roos, et al. (2021) "Policy and Practice Review: A First Guideline on the Use of Pharmacogenetics in Clinical Psychiatric Practice." Frontiers in pharmacology 12: 187. [4] Malhi, Gin S., et al. (2021) "The 2020 Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders." Australian & New Zealand Journal of Psychiatry 55.1 : 7-117. [5] Eap, C. B., et al. (2021) "Tools for optimising pharmacotherapy in psychiatry (therapeutic drug monitoring, molecular brain imaging and pharmacogenetic tests): focus on antidepressants." The World Journal of Biological Psychiatry : 1-68. [6] Arranz, M. J., Salazar, J., & Hernández, M. H. (2021). Pharmacogenetics of antipsychotics: Clinical utility and implementation. Behavioural Brain Research, 401, 113058.