Bumrungrad Personalized Medication Review

Test Data

HN 987654321

Bumrungrad International HOSPITAL

Personalized Medication Review

Name Test Data HN 987654321 Date of birth: 1st Jan 1989

Collected Date: 1st Aug 2024

Reported Date: 7th Aug 2024

Personalized Medicine report

Genetic Testing for Drug Allergy
Pharmacogenomics for *HLA-A* and *HLA-B* **

In reference to the current database of drug-gene association, your results of *HLA-A* and *HLA-B* testing, which are related to drug allergy suggest that,

- You have **a normal/ low risk of drugs induced severe cutaneous reaction if the following medications are used**,
  (1.) Carbamazepine (antiepileptic)
  (2.) Oxcarbazepine (antiepileptic)
  (3.) Co-trimoxazole (antibiotic)
  (4.) Dapsone (antibiotic)
  (5.) Abacavir (antiviral)
  (6.) Nevirapine (antiviral)
  (7.) Allopurinol (anti-hyperuricemia)

  Therefore, the medications can be used per standard dosing guideline. However, if you are a naive person, other common reactions, such as hives or rashes should also be monitored.

Personalized Medication Review

Name Test Data HN 987654321 Date of birth: 1st Jan 1989

Collected Date: 1st Aug 2024

Reported Date: 30th Aug 2024

Personalized Medicine report

Genetic Testing for Drug Metabolism
Pharmacogenomics panel (11 genes)

Current medications

Azathioprine (Imuran®) is a medicine used for treatment of irritable bowel syndrome (IBS). It is metabolized via TPMT (Thiopurine-*S*-methyltransferase) and NUDT15 (Nucleoside diphosphate-linked moiety X motif 15) enzyme. Since you have a normal function of *TPMT* and *NUDT15* gene, the medication can be used as per standard dosing guideline. However, its side effects, such as nausea, vomiting, low white blood cell count and increase risk of infection should be observed. Moreover, blood testing will be routinely monitored by the doctor while using this medication.

Regarding your **Mesalazine (Pentasa®)** and supplements which are **MTV** and **Omega-3** , the response including the efficacy and side effects of them could not be predicted from the genetic testing for drug metabolism (PGx panel-BH MedGene).

Bring the lists of your current medications and supplements to the hospital every visit, so that the doctor and/or a pharmacist can recheck the possible side effects and interaction among them.

Note: The prediction is based on simply the genetic profile. Other factors such as patient's current condition, kidney and liver function, and drug interaction among drugs, etc. may also be considered by the doctor if your medication treatment would be adjusted.

Reviewed by R. Ph 1

Pharmacy License No. 87654

Approved by: R. Ph 2

Pharmacy License No. 45678

ห้องปฏิบัติการเภสัชพันธุศาสตร์

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PHARMACOGENOMICS AND PERSONALIZED MEDICINE REPORT

Name-Surname :		**Age :**		**Gender :**	
Hospital Number :		**Hospital/Source :**			
Specimen :		**Phone/Fax :**			
Ethnicity :		**Requested date :**			
Physician :		**Reported date :**			

***HLA* genotyping test for Carbamazepine profile (TEST CODE 410074)**

***HLA* allele :**		
Possibility genotype† :	***HLA-A*02:07/02:03***	***HLA-B*46:01/55:02***
Drug-Gene	Genotype	Therapeutic recommendation
Abacavir *(HLA-B*57:01)*	Negative *HLA-B*57:01*	Abacavir can be used per standard dosing guideline with a normal/low risk of Abacavir hypersensitivity.
Allopurinol *(HLA-B*58:01)*	Negative *HLA-B*58:01*	Allopurinol can be used per standard dosing guideline with a normal/low risk of Allopurinol-induced MPE, SJS, TEN, DRESS.
Carbamazepine *(HLA-B*15:02/ HLA-B75* family/*HLA-A*31:01)*	Negative *HLA-B*15:02*	Carbamazepine can be used per standard dosing guideline with a normal/low risk of Carbamazepine-induced MPE, DRESS and SJS/TEN.
	Negative *HLA-A*31:01*	
Co-trimoxazole *(HLA-B*13:01, HLA-B*...*	Negative *HLA-B*13:02*	Co-trimoxazole can be used per standard dosing guideline with a normal/low risk of Co-trimoxazole-induced SJS, TEN, DRESS.
	Negative *HLA-B*13:01*	
Dapsone *(HLA-B*13:01)*	Negative *HLA-B*13:01*	Dapsone can be used follow standard guideline with a lower risk of Dapsone-induced drug hypersensitivity.
Nevirapine *(HLA-B*35:05)*	Negative *HLA-B*35:05*	Nevirapine can be used per standard dosing guideline with a normal/low risk of Nevirapine-induced skin rash.
Oxcarbazepine *(HLA-B*15:02)*	Negative *HLA-B*15:02*	Oxcarbazepine can be used per standard dosing guideline with a normal/low risk of Oxcarbazepine -induced SJS, TEN.

Notes: Abbreviation; CBZ = carbamazepine, OxCBZ = oxcarbazepine, SJS = Steven-Johnson's syndrome, TEN = toxic epidermal necrolysis, MPE = maculopapular exanthema DRESS = drug reaction with eosinophilia and systemic symptoms

†The *HLA-A* XX:XX* and *HLA-B*XX:XX* allele were determined by PCR-SSOP method which is intermediate resolution *HLA* typing. This report is based on The Common and Well-Documented (CWD) database.

Interpreted by

PERSONALISED MEDICATION REPORT

For

Date of birth:	myDNA ID:	Pathology No:	Sample type:
Collected:	Received:	Reported:	Doctor:

Personalised Medication Report

for

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

Name:		DOB:		Collected:	
Address:		myDNA ID:		Received:	
		Pathology No:		Reported:	
Doctor:					

Sample type and quality: **Buccal. The sample quality was assessed and deemed to be satisfactory according to the laboratory's acceptance criteria.**

Clinical Notes:

REPORT SUMMARY

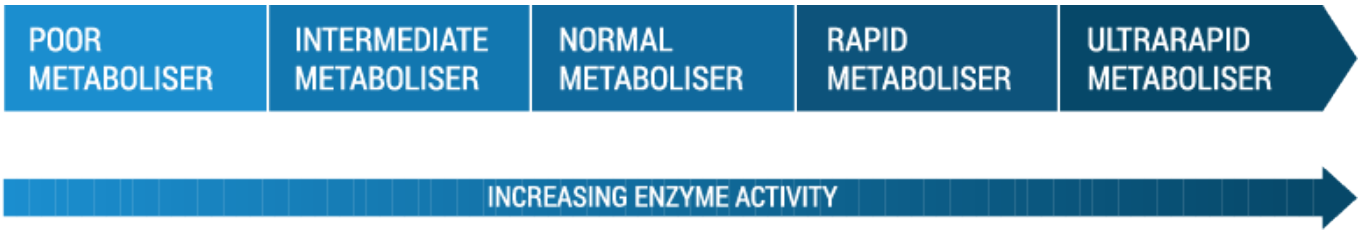
MEDICATIONS OF INTEREST OVERVIEW
MEDICATIONS THAT DO NOT HAVE PRESCRIBING CONSIDERATIONS BASED ON myDNA TEST
mesalazine, multivitamin, omega 3, tobacco smoke

GENETIC TEST RESULTS OVERVIEW

GENE	GENOTYPE	PREDICTED PHENOTYPE	GENE	GENOTYPE	PREDICTED PHENOTYPE
CYP2D6	*1/*1	Normal metaboliser	*CYP3A5*	*3/*3	Poor metaboliser
CYP2C19	*1/*1	Normal metaboliser	*SLCO1B1*	*1/*1	Normal transporter function
CYP2C9	*1/*2	Intermediate metaboliser	*CYP2B6*	*1/*6	Intermediate metaboliser
VKORC1	AG	Moderately reduced VKORC1 enzyme level	*OPRM1*	AA	Normal mu opioid receptor expression
CYP1A2	*1F/*1F	Ultrarapid metaboliser (with inducer present)	*ABCG2* (rs2231142)	CC	Normal transporter function
CYP3A4	*1/*1	Normal metaboliser			

Detailed interpretations of genetic test results are provided in the *pharmacogenomic interpretation* section below.

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



OTHER INFORMATION
Please note that the myDNA medication test does not cover TPMT genotyping, used to predict the dose and risk of myelosuppression of thiopurine drugs (azathioprine and 6-MP). TPMT genotype testing can be ordered through myDNA for Australian patients and may be Medicare subsidised. For non-Australian patients, consult your local pathology provider for TPMT genotype testing.

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
Tobacco Smoke			CYP1A2

FUTURE MEDICATIONS

The following tables outline personalised recommendations for future medications.

NOTE: 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.

MEDICATIONS WITH *MAJOR* PRESCRIBING CONSIDERATIONS

MEDICATION (DRUG CATEGORY)	INTERPRETATION	RECOMMENDATION
Acenocoumarol (Anticoagulants)	***VKORC1* - Moderately reduced VKORC1 enzyme level** ***CYP2C9* - Intermediate metaboliser:** Slightly reduced metabolism of acenocoumarol by CYP2C9 is predicted. Reduced amount of VKORC1 present (the enzyme acenocoumarol inhibits). Overall increased sensitivity to acenocoumarol, an increased risk of both supratherapeutic INR and bleeding, and a lower dose requirement are predicted.	Based on the CYP2C9 and VKORC1 genotypes, DPWG[1,2] states that no specific action is required for dosing of acenocoumarol. Genetic variation may lead to a decrease in the required maintenance dose, however there is insufficient evidence that this causes problems when therapy is initiated as usual, i.e. with frequent INR monitoring.
Warfarin (Anticoagulants)	***VKORC1* - Moderately reduced VKORC1 enzyme level** ***CYP2C9* - Intermediate metaboliser:** Slightly reduced metabolism of warfarin by CYP2C9 is predicted. Reduced amount of VKORC1 (the enzyme warfarin inhibits). The combined CYP2C9 and VKORC1 results predict increased warfarin sensitivity and increased risk of supratherapeutic INR.	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[3] recommendations to reach the therapeutic dose. The summary of CPIC recommendations include consideration of the use of validated published pharmacogenetic algorithms[4,5] 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.
Efavirenz (Antivirals)	***CYP2B6* - Intermediate metaboliser:** Reduced metabolism of efavirenz and higher dose-adjusted trough	CPIC and DPWG[6, 7] provide a moderate recommendation to consider initiating efavirenz with decreased dose of 400 mg/day.

MEDICATIONS WITH *MAJOR* PRESCRIBING CONSIDERATIONS		
MEDICATION (DRUG CATEGORY)	INTERPRETATION	RECOMMENDATION
	concentrations compared with normal metabolisers is predicted. This has been associated with an increased risk of concentration-dependent adverse effects, including CNS adverse events.	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.
Fluvastatin (Statins)	*SLCO1B1* - Normal transporter function *CYP2C9* - Intermediate metaboliser: This SLCO1B1 genotype is associated with typical statin exposure and myopathy risk.[8] This CYP2C9 genotype predicts increased fluvastatin exposure as compared with normal metabolisers, which may translate to increased myopathy risk.[8] 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[8] provide a moderate recommendation to prescribe less than or equal to 40mg daily as a starting dose and adjust doses based on disease-specific guidelines. If doses >40mg are required for desired efficacy, consider an alternative statin or combination therapy (i.e. fluvastatin plus non-statin guideline directed medical therapy).

MEDICATIONS WITH *MINOR* PRESCRIBING CONSIDERATIONS				
DRUG CATEGORY	MEDICATION	GENE(S) INVOLVED	POTENTIAL CLINICAL ISSUES	PUBLISHED GUIDELINES
ADHD - miscellaneous agents	Atomoxetine	*CYP2D6*	Reduced / inadequate response	*CPIC*[9], *FDA*[10]
Angiotensin receptor blockers	Irbesartan	*CYP2C9*	Increased therapeutic and/or adverse effects	-
Antidepressants - other	Agomelatine	*CYP1A2*	Reduced / inadequate response	-
	Bupropion	*CYP2B6*	Altered response	-
	Mirtazapine	*CYP2D6* *CYP1A2*	Reduced / inadequate response	-
Antidepressants - SNRIs	Duloxetine	*CYP2D6* *CYP1A2*	Reduced / inadequate response	*CPIC*[11]
Antidepressants - SSRIs	Sertraline	*CYP2B6* *CYP2C19*	Increased therapeutic and/or adverse effects	*CPIC*[11]
Antidiabetics	Gliclazide	*CYP2C9* *CYP2C19*	Increased therapeutic and/or adverse effects	*DPWG*[12]
	Glimepiride	*CYP2C9*	Increased therapeutic and/or adverse effects	*DPWG*[13]
	Glyburide	*CYP2C9*	Increased therapeutic and/or adverse effects	*DPWG*[14]
Antiepileptics	Fosphenytoin	*CYP2C9*	Adverse effects	*CPIC*[15]
	Phenytoin	*CYP2C9*	Adverse effects	*CPIC*[15]

MEDICATIONS WITH *MINOR* PRESCRIBING CONSIDERATIONS				
DRUG CATEGORY	MEDICATION	GENE(S) INVOLVED	POTENTIAL CLINICAL ISSUES	PUBLISHED GUIDELINES
Antipsychotics	Clozapine	*CYP2D6* *CYP1A2*	Reduced / inadequate response	*DPWG*[16]
	Olanzapine	*CYP1A2*	Reduced / inadequate response	*DPWG*[16]
Antivirals	Nevirapine	*CYP2B6*	Adverse effects	-
Beta blockers	Propranolol	*CYP2D6* *CYP1A2*	Altered response	-
Haemostatic agents	Avatrombopag	*CYP2C9*	Altered response	*FDA*[17], *TGA*[18]
Miscellaneous	Dronabinol	*CYP2C9*	Adverse effects	-
	Lesinurad	*CYP2C9*	Adverse effects	-
NSAIDs	Celecoxib	*CYP2C9*	Increased therapeutic and/or adverse effects	*CPIC*[19]
	Flurbiprofen	*CYP2C9*	Adverse effects	*CPIC*[19]
	Ibuprofen	*CYP2C9*	Adverse effects	*CPIC*[19]
	Lornoxicam	*CYP2C9*	Adverse effects	*CPIC*[19]
	Meloxicam	*CYP2C9*	Adverse effects	*CPIC*[19]
	Piroxicam	*CYP2C9*	Adverse effects	*CPIC*[19]
	Tenoxicam	*CYP2C9*	Adverse effects	*CPIC*[19]
Opioid Analgesics	Methadone	*CYP2B6*	Altered response	-
Proton pump inhibitors	Dexlansoprazole	*CYP2C19*	Reduced / inadequate response	*CPIC*[20]
	Lansoprazole	*CYP2C19*	Reduced / inadequate response	*CPIC*[20]
	Omeprazole	*CYP2C19*	Reduced / inadequate response	*CPIC*[20]
	Pantoprazole	*CYP2C19*	Reduced / inadequate response	*CPIC*[20]

MEDICATIONS WITH *USUAL* PRESCRIBING CONSIDERATIONS				
DRUG CATEGORY	MEDICATION	GENE(S) INVOLVED	POTENTIAL CLINICAL ISSUES	PUBLISHED GUIDELINES
ADHD - miscellaneous agents	Viloxazine	*CYP2D6*	No altered effect predicted by genotype	-
Angiotensin receptor blockers	Losartan	*CYP2C9*	No altered effect predicted by genotype	-
Antianginals	Perhexiline	*CYP2D6*	No altered effect predicted by genotype	-
Antiarrhythmics	Flecainide	*CYP2D6*	No altered effect predicted by genotype	-
	Propafenone	*CYP2D6*	No altered effect predicted by genotype	-
Anticholinergics (genitourinary)	Darifenacin	*CYP2D6*	No altered effect predicted by genotype	-
	Fesoterodine	*CYP2D6*	No altered effect predicted by genotype	-
	Tolterodine	*CYP2D6*	No altered effect predicted by genotype	-
Anticholinesterases	Donepezil	*CYP2D6*	No altered effect predicted by genotype	-
	Galantamine	*CYP2D6*	No altered effect predicted by genotype	-
Anticoagulants	Prasugrel	*CYP2C19*	No altered effect predicted by genotype	*DPWG*[21]
	Ticagrelor	*CYP2C19*	No altered effect predicted by genotype	*DPWG*[22]
Antidepressants - other	Mianserin	*CYP2D6*	No altered effect predicted by genotype	-

MEDICATIONS WITH *USUAL* PRESCRIBING CONSIDERATIONS				
DRUG CATEGORY	MEDICATION	GENE(S) INVOLVED	POTENTIAL CLINICAL ISSUES	PUBLISHED GUIDELINES
	Hydrocodone	*CYP2D6*	No altered effect predicted by genotype	*CPIC*[34]
	Morphine	*OPRM1*	Associated with increased sensitivity to morphine	*CPIC*[34]
	Oliceridine	*CYP2D6*	No altered effect predicted by genotype	-
	Oxycodone	*CYP2D6*	No altered effect predicted by genotype	*CPIC*[34]
	Tramadol	*CYP2D6*	No altered effect predicted by genotype	*CPIC*[34]
Proton pump inhibitors	Esomeprazole	*CYP2C19*	No altered effect predicted by genotype	-
	Rabeprazole	*CYP2C19*	No altered effect predicted by genotype	-
Psychostimulants	Amphetamine	*CYP2D6*	No altered effect predicted by genotype	-
	Dextroamphetamine	*CYP2D6*	No altered effect predicted by genotype	-
	Lisdexamfetamine	*CYP2D6*	No altered effect predicted by genotype	-
Statins	Atorvastatin	*SLCO1B1*	No altered effect predicted by genotype	*CPIC*[8]
	Lovastatin	*SLCO1B1*	No altered effect predicted by genotype	*CPIC*[8]
	Pitavastatin	*SLCO1B1*	No altered effect predicted by genotype	*CPIC*[8]
	Pravastatin	*SLCO1B1*	No altered effect predicted by genotype	*CPIC*[8]
	Rosuvastatin	*ABCG2 (rs2231142) SLCO1B1*	No altered effect predicted by genotype	*CPIC*[8]
	Simvastatin	*SLCO1B1*	No altered effect predicted by genotype	*CPIC*[8]

LEGEND:
CPIC = Clinical Pharmacogenetics Implementation Consortium
DPWG = The Royal Dutch Pharmacists Association – Pharmacogenetics Working Group
TGA = Therapeutic Goods Administration (Australia)
FDA = Food and Drug Administration (US)

CPIC and DPWG guidelines are available on the PharmGKB website www.pharmgkb.org/view/dosing-guidelines.do

PHARMACOGENOMIC INTERPRETATION

EXPLANATION OF GENETIC RESULTS		
GENE	GENOTYPE	PREDICTED FUNCTION
CYP2D6	*1/*1	*CYP2D6* - Normal metaboliser Due to the presence of two copies of normal function alleles, this individual is predicted to have a normal metaboliser phenotype. For a drug extensively metabolised by CYP2D6, drug exposure and clinical effects may be expected to lie within the normal range.

EXPLANATION OF GENETIC RESULTS		
GENE	GENOTYPE	PREDICTED FUNCTION
CYP2C19	*1/*1	*CYP2C19* - Normal metaboliser Due to the presence of two copies of normal function alleles, this individual is predicted to have a normal metaboliser phenotype. For a drug extensively metabolised by CYP2C19, drug exposure and clinical effects may be expected to lie within the normal range.
CYP2C9	*1/*2	*CYP2C9* - Intermediate metaboliser Due to the presence of one normal function allele and one decreased function allele, this individual is predicted to have an intermediate metaboliser phenotype. For a drug extensively metabolised by CYP2C9, drug exposure and clinical effects may either be increased (for an active drug) or decreased (for a prodrug). As the decreased function allele is associated with only a small reduction in enzyme function, this variation may only be significant for certain medications, with high dosages or if drug-drug interactions occur.
VKORC1	AG	*VKORC1* - Moderately reduced VKORC1 enzyme level The VKORC1 enzyme is predicted to be present in moderately reduced amounts and the response to warfarin will be enhanced. The *CYP2C9* genotype should also be considered together with the *VKORC1* genotype for calculating the initial warfarin dose.
CYP1A2	*1F/*1F	*CYP1A2* - 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).
CYP3A4	*1/*1	*CYP3A4* - 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 for a limited number of these drugs.
CYP3A5	*3/*3	*CYP3A5* - Poor metaboliser Due to the presence of two no function alleles, this individual is predicted to have poor metaboliser phenotype (CYP3A5 non-expresser). CYP3A5 is known to metabolise certain drugs, including tacrolimus. Note that this individual's phenotype is the most common one amongst Caucasians.
SLCO1B1	*1/*1	*SLCO1B1* - Normal transporter function The decreased function *5 allele is not present and this individual is predicted to have normal function of the *SLCO1B1* encoded transporter. The transporter is important for the clearance of certain drugs, including simvastatin.
CYP2B6	*1/*6	*CYP2B6* - Intermediate metaboliser This individual is predicted to have an intermediate metaboliser 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 metaboliser phenotype. For a drug extensively metabolised 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).