SickKids® Pharmacogenomics Report

NAME:
Physician Copy for:
DOB: 01/01/2019
ID #: 1076

SAMPLE REPORT
Test report date: 18/11/2024
Case #: HSC-SAMPLE

Consultation:

Focus Drugs:

Medication List:

Drug Summary:

Therapeutic Category	Use as directed	PGx dosing recommendation available	Consider alternatives
Anticoagulant		Clopidogrel (cardiovascular)	Clopidogrel (neurovascular)
		Warfarin	
Cardiovascular	Atorvastatin	Flecainide	
	Lovastatin	Fluvastatin	
	Metoprolol		
	Pravastatin		
	Propafenone		
	Rosuvastatin		
	Simvastatin		
Dermatology	Abrocitinib		
Gastroenterology	Metoclopramide	Dexlansoprazole	
	Ondansetron	Lansoprazole	
		Omeprazole	
		Pantoprazole	
Genetic disorder	Eliglustat		
Immunology	Azathioprine		
	Tacrolimus		
Infectious Diseases	Efavirenz		
	Voriconazole		

Therapeutic Category	Use as directed	PGx dosing recommendation available	Consider alternatives
Neurology	Brivaracetam	Phenytoin/fosphenytoin	
	Clobazam		
	Pitolisant		
	Siponimod		
	Tetrabenazine		
Oncology	Mercaptopurine	Tamoxifen	
	Thioguanine		
Pain	Oxycodone	Celecoxib	Piroxicam
		Codeine	
		Flurbiprofen	
		Hydrocodone	
		Ibuprofen	
		Meloxicam	
		Tramadol	
Psychiatry	Aripiprazole	Amitriptyline	
	Brexpiprazole	Atomoxetine	
	Clozapine	Citalopram	
	Fluvoxamine	Clomipramine	
	Haloperidol	Desipramine	
	Perphenazine	Doxepin	
	Risperidone	Escitalopram	
	Thioridazine	Imipramine	
	Venlafaxine	Nortriptyline	
	Vortioxetine	Paroxetine	
		Pimozide	
		Sertraline	
		Trimipramine	
		Zuclopenthixol	

Genetic results:

Gene	Genotype	Phenotype	Status
CYP2C19	*1/*2	One functional allele and one non-function allele	Intermediate metabolizer

Gene	Genotype	Phenotype	Status
NUDT15	415C>T CC	Two functional alleles	Normal function
CYP2B6	*1/*1	Two functional alleles	Normal metabolizer
CYP2C9	*2/*2	Two reduced function alleles	Intermediate metabolizer
CYP2D6	*1/*4	One functional allele and one non-function allele	Intermediate metabolizer
CYP3A5	*3/*3	Two non-function alleles	Poor metabolizer
SLCO1B1	*1/*1	Two functional alleles	Normal function
TPMT	*1/*1	Two functional alleles	Normal metabolizer
VKORC1	-1639 G>A AA	Two reduced function alleles	Poor function

Drug/Dosing Recommendations:

Anticoagulant

Warfarin		Moderately reduced CYP2C9 and significantly reduced VKORC1 enzyme activity. An appropriate dose estimation tool based on age group and ancestry should be used to guide warfarin dosing. The Clinical Pharmacogenetics Implementation Consortium (CPIC) recommends that warfarin dosing follows either the Gage and/or IWPC algorithms, both of which drive the web-based algorithm found at warfarindosing.org. The genetic information below can be entered into the warfarindosing.org form to estimate the most appropriate therapeutic dose in patients new to warfarin. After filling in the "Required Patient Information", the following can be entered into the "Genetic Information" section of the form: VKORC1-1639/3673 = AA CYP4F2 V433M = Not available/Pending GGCX rs11676382 = Not available/Pending CYP2C9*2 = TT (Homozygous Mutant) CYP2C9*3 = AA (Wildtype) CYP2C9*5 = CC (Wildtype) CYP2C9*6 = AA (Wildtype)
Clopidogrel (neurovascular)		Reduced CYP2C19 enzyme activity may decrease the conversion of clopidogrel to its active metabolite. This increases the risk for adverse cardiac and cerebrovascular events. Avoid clopidogrel if possible. Consider an alternative P2Y12 inhibitor at standard dose if clinically indicated and no contraindication.
Clopidogrel (cardiovascular)		Reduced CYP2C19 enzyme activity may decrease the conversion of clopidogrel to its active metabolite. This increases the risk for adverse cardiac and cerebrovascular events. If clopidogrel cannot be avoided, consider increasing the dose. Alternatively, consider prasugrel or ticagrelor at standard dose if no contraindication.

Cardiovascular

Flecainide		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug. This increases the probability of side effects. Reduction of standard recommended starting dose by 25% may be considered. Monitor according to standard practice. This recommendation does not apply to the flecainide provocation test to diagnose Brugada syndrome.
Metoprolol		Reduced CYP2D6 enzyme activity increases metoprolol exposure. Initiate therapy with standard recommended starting dose. This recommendation is specific to adults, exert caution when extrapolating to pediatric populations.
Propafenone		Reduced CYP2D6 enzyme activity. Initiate therapy with standard recommended starting dose.
Atorvastatin		Normal SLCO1B1 transporter activity, which is related to a standard risk for statin-induced myopathy (muscle toxicity). Initiate therapy with standard recommended starting dose.

Simvastatin		Normal SLCO1B1 transporter activity, which is related to a standard risk for statin-induced myopathy (muscle toxicity). Initiate therapy with standard recommended starting dose. This recommendation is specific to adults, however, preliminary data suggest that this guideline may be extrapolated to children.
Lovastatin		Normal SLCO1B1 transporter activity, which is related to a standard risk for statin-induced myopathy (muscle toxicity). Initiate therapy with standard recommended starting dose.
Pravastatin		Normal SLCO1B1 transporter activity, which is related to a standard risk for statin-induced myopathy (muscle toxicity). Initiate therapy with standard recommended starting dose. This recommendation is specific to adults, however, preliminary data suggest that this guideline may be extrapolated to children.
Rosuvastatin		Normal SLCO1B1 transporter activity, which is related to a standard risk for statin-induced myopathy (muscle toxicity). Initiate therapy with standard recommended starting dose. This recommendation is specific to adults, however, preliminary data suggest that this guideline may be extrapolated to children.
Fluvastatin		Normal SLCO1B1 transporter activity and reduced CYP2C9 enzyme activity, which may be related to an increased risk for statin-induced myopathy (muscle toxicity). In adults, if dose >40 mg needed for desired efficacy, consider an alternative statin or combination therapy. For children, no dosing recommendation is available. For dosing guidance follow disease-specific guidelines and algorithms from the American College of Cardiology, the American Heart Association and CPIC.

Dermatology

Abrocitinib		Reduced CYP2C19 enzyme activity. Initiate therapy with standard recommended starting dose.

Gastroenterology

Lansoprazole		Reduced CYP2C19 enzyme activity may lead to elevated levels of active drug. This increases the probability of clinical effect. Initiate therapy with standard recommended starting dose. For chronic therapy (>12 weeks) and when clinical effect achieved, consider 50% reduction in daily dose and monitor for continued efficacy.
Omeprazole		Reduced CYP2C19 enzyme activity may lead to elevated levels of active drug. This increases the probability of clinical effect. Initiate therapy with standard recommended starting dose. For chronic therapy (>12 weeks) and when clinical effect achieved, consider 50% reduction in daily dose and monitor for continued efficacy.
Pantoprazole		Reduced CYP2C19 enzyme activity may lead to elevated levels of active drug. This increases the probability of clinical effect. Initiate therapy with standard recommended starting dose. For chronic therapy (>12 weeks) and when clinical effect achieved, consider 50% reduction in daily dose and monitor for continued efficacy.

Dexlansoprazole		Reduced CYP2C19 enzyme activity may lead to elevated levels of active drug. This increases the probability of clinical effect. Initiate therapy with standard recommended starting dose. For chronic therapy (>12 weeks) and when clinical effect achieved, consider 50% reduction in daily dose and monitor for continued efficacy.
Ondansetron		Reduced CYP2D6 enzyme activity. Insufficient data is available for this genotype. Initiate therapy with standard recommended starting dose.
Metoclopramide		Reduced CYP2D6 enzyme activity. Initiate therapy with standard recommended starting dose.

Genetic disorder

Eliglustat		Reduced CYP2D6 enzyme activity. Initiate therapy with standard recommended starting dose.

Immunology

Azathioprine		Normal TPMT and NUDT15 enzyme activity. Initiate therapy with standard recommended starting dose.
Tacrolimus		CYP3A5 non-expressors have low enzyme activity, which is found in the majority of the population. Initiate therapy with standard recommended starting dose and utilize therapeutic drug monitoring to guide dose adjustments.

Infectious Diseases

Voriconazole		Reduced CYP2C19 enzyme activity. Initiate therapy with standard recommended starting dose.
Efavirenz		Normal CYP2B6 enzyme activity. Initiate therapy with standard recommended starting dose.

Neurology

Phenytoin/fosphenytoin		Moderately reduced CYP2C9 enzyme activity may lead to elevated levels of active drug. This increases the probability of side effects. Initiate therapy with standard recommended starting dose. Consider reducing maintenance dose by 25% and monitor according to clinical standard practice.
Clobazam		Reduced CYP2C19 enzyme activity. Initiate therapy with standard recommended starting dose.
Tetrabenazine		Reduced CYP2D6 enzyme activity. Initiate therapy with standard recommended starting dose.
Siponimod		Reduced CYP2C9 enzyme activity may lead to elevated levels of active drug. Initiate therapy with the standard recommended starting dose.
Brivaracetam		Reduced CYP2C19 enzyme activity may lead to elevated levels of active drug. Initiate therapy with standard recommended starting dose.
Pitolisant		Reduced CYP2D6 enzyme activity. Initiate therapy with standard recommended starting dose.

Oncology

Tamoxifen		Reduced CYP2D6 enzyme activity decreases the conversion of tamoxifen to its active metabolite (e.g., endoxifen). This can result in reduced clinical effect. Consider an alternative treatment (e.g., aromatase inhibitors in post-menopausal women), or increase the standard recommended starting dose 1.5 to 2-fold and utilize therapeutic drug monitoring of endoxifen.
Mercaptopurine		Normal TPMT and NUDT15 enzyme activity. Initiate therapy with standard recommended starting dose.
Thioguanine		Normal TPMT and NUDT15 enzyme activity. Initiate therapy with standard recommended starting dose.

Pain

Codeine		Reduced CYP2D6 enzyme activity decreases the conversion of codeine to its more potent metabolite. This may have an effect on analgesia. Initiate therapy with standard recommended starting dose. If codeine is not effective, consider a dose increase or an alternative treatment that is not affected by CYP2D6 metabolism (e.g., acetaminophen, NSAID, morphine and non-opioid analgesics).
Oxycodone		Reduced CYP2D6 enzyme activity. Limited data is available to associate this variation with a weaker analgesic effect. Be alert to symptoms of insufficient pain relief. NOTE: Codeine and tramadol are NOT good alternatives because their metabolism is also affected by CYP2D6 activity.
Tramadol		Reduced CYP2D6 enzyme activity may decrease the conversion of tramadol to its more potent metabolite. This may have an effect on analgesia. Initiate therapy with standard recommended starting dose. If tramadol is not effective select an alternative treatment that is not affected by CYP2D6 metabolism (e.g., acetaminophen, NSAID, morphine and non-opioid analgesics). NOTE: Codeine, hydrocodone and oxycodone are NOT good alternatives because their metabolism is also affected by CYP2D6 activity.
Celecoxib		Moderately reduced CYP2C9 enzyme activity may lead to elevated levels of active drug. This may increase the probability of toxicities. Initiate therapy with lowest recommended starting dose. Titrate dose upward to clinical effect or maximum recommended dose with caution.
Flurbiprofen		Moderately reduced CYP2C9 enzyme activity may lead to elevated levels of active drug. This may increase the probability of toxicities. Initiate therapy with the lowest recommended starting dose. Titrate dose upward to clinical effect or the maximum recommended dose with caution.
Piroxicam		Moderately reduced CYP2C9 enzyme activity may lead to elevated levels of active drug. This may increase the probability of toxicities. Select an alternative drug that is not affected by CYP2C9 metabolism or choose an NSAID metabolized by CYP2C9 but with a shorter half-life.
Ibuprofen		Moderately reduced CYP2C9 enzyme activity may lead to elevated levels of active drug. This may increase the probability of toxicities. Initiate therapy with the lowest recommended starting dose. Titrate dose upward to clinical effect or the maximum recommended dose with caution.

Meloxicam		Moderately reduced CYP2C9 enzyme activity may lead to elevated levels of active drug. This may increase the probability of toxicities. Initiate therapy with 50% of the lowest recommended starting dose. Titrate upward to clinical effect to a maximum of 50% of the recommended dose. Upward dose titration should not occur until after steady state is reached (at least 7 days). Alternatively, consider a different drug that is not affected by CYP2C9 metabolism or an NSAID metabolized by CYP2C9 but with a shorter half-life.
Hydrocodone		Reduced CYP2D6 enzyme activity. Limited data is available to associate this variation with a weaker analgesic effect. Initiate therapy with standard recommended starting dose. If hydrocodone is not effective, consider an alternative treatment that is not affected by CYP2D6 metabolism (e.g., acetaminophen, NSAID, morphine and non-opioid analgesics).

Psychiatry

Amitriptyline		Reduced CYP2C19 and CYP2D6 enzyme activity may lead to altered levels of active drug and its metabolites. This may increase the probability of side effects. Consider reducing the starting dose by 25% and utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.
Citalopram		Reduced CYP2C19 enzyme activity may lead to elevated levels of active drug. This may increase the probability of side effects. Initiate therapy with recommended starting dose. Consider a slower titration schedule and lower maintenance dose.
Clomipramine		Reduced CYP2C19 and CYP2D6 enzyme activity may lead to altered levels of active drug and its metabolites. This may increase the probability of side effects. Consider reducing the starting dose by 25% and utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.
Desipramine		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug. This increases the probability of side effects. Consider reducing the starting dose by 25%. Utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.
Doxepin		Reduced CYP2C19 and CYP2D6 enzyme activity may lead to altered levels of active drug and its metabolites. This may increase the probability of side effects. Consider reducing the starting dose by 25% and utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.
Escitalopram		Reduced CYP2C19 enzyme activity may lead to elevated levels of active drug. This may increase the probability of side effects. Initiate therapy with recommended starting dose. Consider a slower titration schedule and lower maintenance dose.
Fluvoxamine		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug. This may increase the probability of side effects. Initiate therapy with standard recommended starting dose.
Imipramine		Reduced CYP2C19 and CYP2D6 enzyme activity may lead to altered levels of active drug and its metabolites. This may increase the probability of side effects. Consider reducing the starting dose by 25% and utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.

Nortriptyline		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug. This increases the probability of side effects. Consider reducing the starting dose by 25%. Utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.
Paroxetine		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug. This may increase the probability of side effects. Consider a lower starting dose and slower titration schedule.
Trimipramine		Reduced CYP2C19 and CYP2D6 enzyme activity may lead to altered levels of active drug and its metabolites. This may increase the probability of side effects. Consider reducing the starting dose by 25% and utilize therapeutic drug monitoring to guide dose adjustments. This recommendation only applies to higher initial doses, for example used in conditions such as depression.
Venlafaxine		Reduced CYP2D6 enzyme activity. Clinical guidelines do not contain dosing recommendations for CYP2D6 intermediate metabolizers due to the lack of scientific evidence. Initiate therapy with standard recommended starting dose.
Aripiprazole		Reduced CYP2D6 enzyme activity. Initiate therapy with standard recommended starting dose.
Atomoxetine		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug. This increases the probability of side effects. Initiate therapy with standard recommended starting dose and monitor according to clinical standard practice. Consider to reduce the dose in case side effects occur and monitor for persistence of clinical effect.
Haloperidol		Reduced CYP2D6 enzyme activity. Initiate therapy with standard recommended starting dose.
Risperidone		Reduced CYP2D6 enzyme activity. Initiate therapy with standard recommended starting dose.
Thioridazine		Reduced CYP2D6 enzyme activity. Initiate therapy with standard recommended starting dose.
Brexpiprazole		Reduced CYP2D6 enzyme activity may lead to increased levels of active drug. Current evidence suggests that the probability of side effects or clinical effect is not influenced by this genotype. Initiate therapy with standard recommended starting dose.
Clozapine		Reduced CYP2D6 enzyme activity. Initiate therapy with standard recommended starting dose.
Pimozide		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug. This may increase the probability of side effects. Inconsistent recommendations are available. As per DPWG, do not exceed 80% of the standard recommended starting dose. As per product monograph, initiate therapy with standard recommended starting dose.
Vortioxetine		Reduced CYP2D6 enzyme activity. Initiate therapy with standard recommended starting dose.
Zuclopenthixol		Reduced CYP2D6 enzyme activity may lead to elevated levels of active drug. As per DPWG, a reduction of the standard recommended starting dose by 25% may be considered. Titrate the dose based on clinical effect.
Perphenazine		Reduced CYP2D6 enzyme activity. Initiate therapy with standard recommended starting dose.

Sertraline		Reduced CYP2C19 and normal CYP2B6 enzyme activity may lead to altered levels of active drug and its metabolites. Initiate therapy with recommended starting dose. Consider a slower titration schedule and lower maintenance dose.

Legend:

	Use as directed	Use label recommended dosage and administration
	Use with caution	Use with caution - read detailed recommendation for potential dose adjustment
	Consider alternatives	Select alternative treatment if possible -read detailed recommendation for details.

DISCLAIMER

Genotyping of CYP2B6, CYP2C19, CYP2C9, CYP2D6, CYP3A5, NUDT15, SLCO1B1, TPMT and VKORC1 will be carried out using the Agena MassARRAY® platform. DNA samples are normalized to a concentration of 10 ng/uL, and 2uL per well is used for PCR amplification and primer extension with iPLEX, iPLEX Veridose Core, and Veridose CYP2D6 CNV reagents. A thermal cycler, Biorad C1000, is used for amplification. The extension products are dispensed onto a CPM 384 spectrochip Array using the Agena 384 chip prep module and detected using a MassARRAY MALDI-TOF mass spectrometer which provides genotyping and quantification. Haplotype reports are automatically generated using the Typer software and the ADME PGx Pro software, according to the manufacturer's standard protocols. Results are processed to generate SNP calls automatically, using the MassARRAY® TyperAnalyzer software (Agena Biosciences, San Diego, CA, USA), and then manually reviewed by the operator to validate the allele calls. Automatic SNP calls that are of concern will be removed.

Variants tested predict the following genotypes/haplotypes: CYP2D6 *1,*2,*3,*4*,*5,*6,*7,*8,*9,*10,*11,*12,*14A,*14B,*15,*17,*18,*19,*20,*29,*41,*69; CYP2D6 Copy Number Variant (CNV) analysis is performed using the Agena Veridose CYP2D6 CNV panel, which detects both CNV's and hybrid alleles and includes 22 assays to interrogate 7 regions (5', exon 1, intron 2, intron 4, intron 6, intron 7 and exon 9) of the CYP2D6 gene; CYP2B6 *1, *4, *6, *9, *18, *22; CYP2C19 *1,*2,*3,*4A,*4B,*5,*6,*7,*8,*17,*22,*35; CYP2C9 *1,*2,*3*4,*5,*6,*8,*11,*12,*13,*15,*25,*27; CYP3A5 *1,*2,*3*6,*7; NUDT15 rs116855232 (415C>T); SLCO1B1 *1, *5 (rs4149056); TPMT *1, *2, *3A, *3B, *4; and VKORC1 *1,*2 (-1639G>A).

Genetic variants not tested by this assay can contribute to an individual's efficiency of drug metabolism. This report is based on the technology and testing of certain variants listed above and may not fully take into account other factors that may affect drug sensitivity or efficacy such as co-medication, physical conditions, diet, smoking or the clinical context of the patient. The interpretation of this test may be affected by DNA rearrangements, blood transfusion, bone marrow transplantation or other rare events; these events can affect the testing and could cause false positive or false negative results. The interpretive report provided focuses on medications and genes with published pharmacogenomic practice guidance by professional organizations such as CPIC: Clinical Pharmacogenetics Implementation Consortium, DPWG: Dutch Pharmacogenetics Working Group, CPNDS: Canadian Pharmacogenomics Network for Drug Safety and FDA: U.S. Food and Drug Administration. The test used to prepare this report is a clinical investigational test; the test results are to be used for clinical research purposes only. Pharmacogenetic testing does not replace the need for therapeutic drug and clinical monitoring. It should be noted that the data interpretation outlined in this report is based on current understanding of genes and variants at the time of reporting. Patients are responsible for obtaining updates of this report, as necessary, in the future. The treating physician has ultimate responsibility for a patient's treatment plan, including treatment decisions made on the basis of this report. Neither the Hospital for Sick Children nor its employees or agents, shall have any liability to any person or entity with regard to claims, loss, damage arising, or alleged to arise, directly or indirectly, from the use of information contained in this report.