



ARUP Test Code: 3001535  
Collection Date: 01/28/2025  
Received in lab: 01/29/2025  
Completion Date: 02/03/2025

**TPMT2 Specimen Whole Blood**

**Patient Results**

Gene	Genotype	Flag	Phenotype	Flag
TPMT	*1/*3A		Intermediate	A
NUDT15	*1/*1		Normal	

**TPMT2 Interpretation**

See Note

One no function allele was identified in the TPMT gene, suggesting an intermediate metabolizer phenotype and susceptibility to dose-related toxicity from standard doses of thiopurine drugs. Dose reduction of thiopurine drugs may be required. See drug labeling and clinical consensus guidelines for more details about dosing.

No variant alleles were identified in the NUDT15 gene, suggesting a normal metabolizer phenotype and that standard doses of thiopurines are appropriate. See drug labeling and clinical consensus guidelines for more details about dosing.

Recommendation: Guidelines for genotype - based dosing are published by the Clinical Pharmacogenetics Implementation Consortium(CPIC) and can be found at: <https://cpicpgx.org/> and <https://www.pharmgkb.org/>.

This result has been reviewed and approved by [REDACTED]

**Interpretive Comments**

BACKGROUND INFORMATION: TPMT and NUDT15

CHARACTERISTICS: Thiopurine drug therapy is used for autoimmune diseases, inflammatory bowel disease, acute lymphoblastic leukemia, and to prevent rejection after solid organ transplant. The inactivation of thiopurine drugs is catalyzed in part by thiopurine methyltransferase (TPMT) and nudix hydrolase 15 (NUDT15). Variants in the TPMT and/or NUDT15 genes are associated with an accumulation of cytotoxic metabolites leading to increased risk of drug-related toxicity with standard doses of thiopurine drugs. These effects on thiopurine catabolism can be additive.

INHERITANCE: Autosomal codominant.



CAUSE: TPMT and NUDT15 variants affect enzyme expression or activity.

VARIANTS TESTED:

(Variants are numbered according to NM\_000367 transcript for TPMT and the NM\_018283 transcript for NUDT15)

\*1: Indicative of no detected targeted variants and an assumption of functional allele.

TPMT\*2: rs1800462, c.238G>C

TPMT\*3A: rs1800460, c.460G>A; rs1142345, c.719A>G

TPMT\*3B: rs1800460, c.460G>A

TPMT\*3C: rs1142345, c.719A>G

TPMT\*4: rs1800584, c.626-1G>A

NUDT15 \*2 or \*3: rs116855232, c.415C>T

NUDT15\*4: rs147390019, c.416G>A

CLINICAL SENSITIVITY: 95 percent.

METHODOLOGY: Polymerase chain reaction (PCR) and fluorescence monitoring.

ANALYTICAL SENSITIVITY AND SPECIFICITY: 99 percent.

LIMITATIONS: Only the targeted TPMT and NUDT15 variants will be detected by this test. Because the complex TPMT\*3A allele contains the variants found in the \*3B and \*3C alleles, this test cannot distinguish the 3A/Negative genotype (intermediate enzyme activity) from the rare \*3B/\*3C genotype (no or low enzyme activity). Genotyping may reflect donor status in patients who have received allogenic stem cell or bone marrow transplants within 2 weeks of specimen collection. Actual enzyme activity and expression and risk for adverse reactions to thiopurines may be affected by additional genetic and non-genetic factors not evaluated by this test. Diagnostic errors can occur due to rare sequence variations. Genotyping does not replace the need for therapeutic drug monitoring and clinical observation.

Please note the information contained in this report does not contain medication recommendations, and should not be interpreted as recommending any specific medications. Any dosage adjustments or other changes to medications should be evaluated in consultation with a medical provider.

This test was developed and its performance characteristics determined by ARUP Laboratories. It has not been cleared or approved by the US Food and Drug Administration. This test was performed in a CLIA certified laboratory and is intended for clinical purposes.

Counseling and informed consent are recommended for genetic testing. Consent forms are available online.



**Test Information**

The following tables list the available gene-drug pairs and genotype-based dosing published by the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the FDA table of pharmacogenomic biomarkers in drug labeling.

**Published CPIC guidelines**

<b>GUIDELINES</b>	<b>DRUGS</b>	<b>GENES</b>
CYP2B6 and efavirenz	efavirenz	CYP2B6
CYP2C19 and Clopidogrel	clopidogrel	CYP2C19
CYP2C19 and Proton Pump Inhibitors	dexlansoprazole	CYP2C19
	esomeprazole	
	lansoprazole	
	omeprazole	
	pantoprazole	
	rabeprazole	
CYP2C19 and Voriconazole	voriconazole	CYP2C19
CYP2C9 and NSAIDs	aceclofenac	CYP2C9
	celecoxib	
	diclofenac	
	flurbiprofen	
	ibuprofen	
	indomethacin	
	lornoxicam	
	lumiracoxib	
	meloxicam	
	metamizole	
	nabumetone	
	naproxen	
	piroxicam	
tenoxicam		
CYP2C9, VKORC1, CYP4F2 and Warfarin	warfarin	CYP2C9, CYP4F2, VKORC1
CYP2D6 and Atomoxetine	atomoxetine	CYP2D6
CYP2D6 and Ondansetron and Tropisetron	ondansetron	CYP2D6
	tropisetron	
CYP2D6 and Tamoxifen	tamoxifen	CYP2D6
	citalopram	
	escitalopram	



CYP2D6, CYP2C19 and Selective Serotonin Reuptake Inhibitors	fluvoxamine	CYP2C19, CYP2D6
	paroxetine	
	sertraline	
CYP2D6, CYP2C19 and Tricyclic Antidepressants	amitriptyline	CYP2C19, CYP2D6
	clomipramine	
	desipramine	
	doxepin	
	imipramine	
	nortriptyline	
	trimipramine	
CYP2D6, OPRM1, COMT, and Opioids	alfentanil	COMT, CYP2D6, OPRM1
	buprenorphine	
	codeine	
	fentanyl	
	hydrocodone	
	hydromorphone	
	levomethadone	
	methadone	
	morphine	
	naltrexone	
	oxycodone	
	remifentanil	
	sufentanil	
tramadol		
CYP3A5 and Tacrolimus	tacrolimus	CYP3A5
DPYD and Fluoropyrimidines	capecitabine	DPYD
	fluorouracil	
	tegafur	
SLCO1B1, ABCG2, CYP2C9, and Statins	atorvastatin	ABCG2, CYP2C9, SLCO1B1
	fluvastatin	
	lovastatin	
	pitavastatin	
	pravastatin	
	rosuvastatin	
	simvastatin	
	azathioprine	



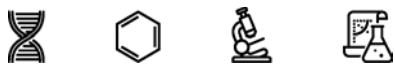
# TPMT and NUDT15



TPMT, NUDT15 and Thiopurines

mercaptopurine
thioguanine

NUDT15, TPMT



**FDA Table of Pharmacogenomic Biomarkers in Drug Labeling**

Drug	Therapeutic Area*	Biomarker†	Labeling Sections
Abrocitinib	Dermatology	CYP2C19	Dosage and Administration, Use in Specific Populations, Clinical Pharmacology
Amitriptyline	Psychiatry	CYP2D6	Precautions
Amoxapine	Psychiatry	CYP2D6	Precautions
Amphetamine	Psychiatry	CYP2D6	Clinical Pharmacology
Arformoterol	Pulmonary	CYP2D6	Clinical Pharmacology
Aripiprazole	Psychiatry	CYP2D6	Dosage and Administration, Use in Specific Populations, Clinical Pharmacology
Aripiprazole Lauroxil	Psychiatry	CYP2D6	Dosage and Administration, Use in Specific Populations, Clinical Pharmacology
Atomoxetine	Psychiatry	CYP2D6	Dosage and Administration, Warnings and Precautions, Adverse Reactions, Drug Interactions, Use in Specific Populations, Clinical Pharmacology
Avatrombopag	Hematology	CYP2C9	Clinical Pharmacology
Azathioprine	Rheumatology	TPMT	Dosage and Administration, Warnings, Precautions, Drug Interactions, Adverse Reactions, Clinical Pharmacology
Azathioprine	Rheumatology	NUDT15	Dosage and Administration, Warnings, Precautions, Adverse Reactions, Clinical Pharmacology
Belzutifan	Oncology	CYP2C19	Warnings and Precautions, Drug Interactions, Use in Specific Populations, Clinical Pharmacology
Brexpiprazole	Psychiatry	CYP2D6	Dosage and Administration, Use in Specific Populations, Clinical Pharmacology
Brivaracetam	Neurology	CYP2C19	Clinical Pharmacology
Bupropion	Psychiatry	CYP2D6	Clinical Pharmacology
Capecitabine	Oncology	DPYD	Warnings and Precautions, Clinical Pharmacology, Patient Counseling Information
Cariprazine	Psychiatry	CYP2D6	Clinical Pharmacology
Carisoprodol	Rheumatology	CYP2C19	Use in Specific Populations, Clinical Pharmacology
Carvedilol	Cardiology	CYP2D6	Drug Interactions, Clinical Pharmacology
Celecoxib	Rheumatology	CYP2C9	Dosage and Administration, Use in Specific Populations, Clinical Pharmacology
Cevimeline	Dental	CYP2D6	Precautions
Cisplatin	Oncology	TPMT	Adverse Reactions
Citalopram	Psychiatry	CYP2C19	Dosage and Administration, Warnings, Clinical Pharmacology



Citalopram	Psychiatry	CYP2D6	Clinical Pharmacology
Clobazam	Neurology	CYP2C19	Dosage and Administration, Use in Specific Populations, Clinical Pharmacology
Clomipramine	Psychiatry	CYP2D6	Precautions
Clopidogrel	Cardiology	CYP2C19	Boxed Warning, Warnings and Precautions, Clinical Pharmacology
Clozapine	Psychiatry	CYP2D6	Dosage and Administration, Use in Specific Populations, Clinical Pharmacology
Codeine	Anesthesiology	CYP2D6	Boxed Warning, Warnings and Precautions, Use in Specific Populations, Patient Counseling Information
Darifenacin	Urology	CYP2D6	Clinical Pharmacology
Desipramine	Psychiatry	CYP2D6	Precautions
Desvenlafaxine	Psychiatry	CYP2D6	Clinical Pharmacology
Deutetrabenazine	Neurology	CYP2D6	Dosage and Administration, Warnings and Precautions, Use in Specific Populations, Clinical Pharmacology
Dexlansoprazole	Gastroenterology	CYP2C19	Drug Interactions, Clinical Pharmacology
Dextromethorphan and Quinidine	Neurology	CYP2D6	Warnings and Precautions, Clinical Pharmacology
Diazepam	Neurology	CYP2C19	Clinical Pharmacology
Donepezil	Neurology	CYP2D6	Clinical Pharmacology
Doxepin	Psychiatry	CYP2D6	Clinical Pharmacology
Doxepin	Psychiatry	CYP2C19	Clinical Pharmacology
Dronabinol	Gastroenterology	CYP2C9	Use in Specific Populations, Clinical Pharmacology
Drospirenone and Ethinyl Estradiol	Gynecology	CYP2C19	Clinical Pharmacology
Duloxetine	Psychiatry	CYP2D6	Drug Interactions
Efavirenz	Infectious Diseases	CYP2B6	Clinical Pharmacology
Elagolix	Gynecology	SLCO1B1	Clinical Pharmacology
Eliglustat	Inborn Errors of Metabolism	CYP2D6	Indications and Usage, Dosage and Administration, Contraindications, Warnings and Precautions, Drug Interactions, Use in Specific Populations, Clinical Pharmacology, Clinical Studies
Erdafitinib	Oncology	CYP2C9	Use in Specific Populations, Clinical Pharmacology
Escitalopram	Psychiatry	CYP2D6	Drug Interactions
Escitalopram	Psychiatry	CYP2C19	Adverse Reactions
Esomeprazole	Gastroenterology	CYP2C19	Drug Interactions, Clinical Pharmacology



Fesoterodine	Urology	CYP2D6	Drug Interactions, Clinical Pharmacology
Fosphenytoin	Neurology	CYP2C9	Warnings and Precautions, Use in Specific Populations, Clinical Pharmacology
Flibanserin	Gynecology	CYP2C9	Clinical Pharmacology
Flibanserin	Gynecology	CYP2C19	Adverse Reactions, Use in Specific Populations, Clinical Pharmacology
Flibanserin	Gynecology	CYP2D6	Clinical Pharmacology
Fluorouracil	Dermatology	DPYD	Contraindications, Warnings
Fluorouracil	Oncology	DPYD	Warnings and Precautions, Patient Counseling Information
Fluoxetine	Psychiatry	CYP2D6	Precautions, Clinical Pharmacology
Flurbiprofen	Rheumatology	CYP2C9	Clinical Pharmacology
Fluvoxamine	Psychiatry	CYP2D6	Drug Interactions
Formoterol	Pulmonary	CYP2D6	Clinical Pharmacology
Formoterol	Pulmonary	CYP2C19	Clinical Pharmacology
Galantamine	Neurology	CYP2D6	Clinical Pharmacology
Gefitinib	Oncology	CYP2D6	Clinical Pharmacology
Iloperidone	Psychiatry	CYP2D6	Dosage and Administration, Warnings and Precautions, Drug Interactions, Clinical Pharmacology
Imipramine	Psychiatry	CYP2D6	Precautions
Lacosamide	Neurology	CYP2C19	Clinical Pharmacology
Lansoprazole	Gastroenterology	CYP2C19	Drug Interactions, Clinical Pharmacology
Lesinurad	Rheumatology	CYP2C9	Drug Interactions, Clinical Pharmacology
Lofexidine	Anesthesiology	CYP2D6	Use in Specific Populations
Mavacamten	Cardiology	CYP2C19	Dosage and Administration, Clinical Pharmacology
Meclizine	Neurology	CYP2D6	Warnings and Precautions
Meloxicam	Anesthesiology	CYP2C9	Use in Specific Populations, Clinical Pharmacology
Mercaptopurine	Oncology	TPMT	Dosage and Administration, Warnings and Precautions, Adverse Reactions, Clinical Pharmacology
Mercaptopurine	Oncology	NUDT15	Dosage and Administration, Warnings and Precautions, Clinical Pharmacology
Metoclopramide	Gastroenterology	CYP2D6	Dosage and Administration, Use in Specific Populations, Clinical Pharmacology
Metoprolol	Cardiology	CYP2D6	Clinical Pharmacology
Mirabegron	Urology	CYP2D6	Clinical Pharmacology
Modafinil	Psychiatry	CYP2D6	Clinical Pharmacology





Nateglinide	Endocrinology	CYP2C9	Drug Interactions
Nebivolol	Cardiology	CYP2D6	Dosage and Administration, Clinical Pharmacology
Nefazodone	Psychiatry	CYP2D6	Precautions
Nortriptyline	Psychiatry	CYP2D6	Precautions
Oliceridine	Anesthesiology	CYP2D6	Warnings and Precautions, Drug Interactions, Use in Specific Populations, Clinical Pharmacology
Omeprazole	Gastroenterology	CYP2C19	Drug Interactions, Clinical Pharmacology
Ondansetron	Gastroenterology	CYP2D6	Clinical Pharmacology
Ospemifene	Gynecology	CYP2C9	Clinical Pharmacology
Ospemifene	Gynecology	CYP2B6	Clinical Pharmacology
Paliperidone	Psychiatry	CYP2D6	Clinical Pharmacology
Palonosetron	Gastroenterology	CYP2D6	Clinical Pharmacology
Pantoprazole	Gastroenterology	CYP2C19	Clinical Pharmacology
Paroxetine	Psychiatry	CYP2D6	Drug Interactions, Clinical Pharmacology
Perphenazine	Psychiatry	CYP2D6	Precautions, Clinical Pharmacology
Phenytoin	Neurology	CYP2C9	Warnings and Precautions, Use in Specific Populations, Clinical Pharmacology
Phenytoin	Neurology	CYP2C19	Clinical Pharmacology
Pimozide	Psychiatry	CYP2D6	Dosage and Administration, Precautions
Piroxicam	Rheumatology	CYP2C9	Clinical Pharmacology
Pitolisant	Psychiatry	CYP2D6	Dosage and Administration, Use in Specific Populations, Clinical Pharmacology
Prasugrel	Cardiology	CYP2C19	Use in Specific Populations, Clinical Pharmacology, Clinical Studies
Prasugrel	Cardiology	CYP2C9	Use in Specific Populations, Clinical Pharmacology, Clinical Studies
Prasugrel	Cardiology	CYP3A5	Use in Specific Populations, Clinical Pharmacology, Clinical Studies
Prasugrel	Cardiology	CYP2B6	Use in Specific Populations, Clinical Pharmacology, Clinical Studies
Propafenone	Cardiology	CYP2D6	Dosage and Administration, Warnings and Precautions, Drug Interactions, Clinical Pharmacology
Propranolol	Cardiology	CYP2D6	Clinical Pharmacology
Protriptyline	Psychiatry	CYP2D6	Precautions
Quinidine	Cardiology	CYP2D6	Precautions
Quinine Sulfate	Infectious Diseases	CYP2D6	Drug Interactions



Rabeprazole	Gastroenterology	CYP2C19	Drug Interactions, Clinical Pharmacology
Rimegepant	Neurology	CYP2C9	Clinical Pharmacology
Risperidone	Psychiatry	CYP2D6	Clinical Pharmacology
Rosuvastatin	Endocrinology	SLCO1B1	Clinical Pharmacology
Rucaparib (2)	Oncology	CYP2D6	Clinical Pharmacology
Siponimod	Neurology	CYP2C9	Dosage and Administration, Contraindications, Drug Interactions, Use in Specific Populations, Clinical Pharmacology
Tamoxifen	Oncology	CYP2D6	Clinical Pharmacology
Tamsulosin	Urology	CYP2D6	Warnings and Precautions, Adverse Interactions, Clinical Pharmacology
Tetrabenazine	Neurology	CYP2D6	Dosage and Administration, Warnings and Precautions, Use in Specific Populations, Clinical Pharmacology
Thioguanine	Oncology	TPMT	Dosage and Administration, Warnings, Precautions, Clinical Pharmacology
Thioguanine	Oncology	NUDT15	Dosage and Administration, Warnings, Precautions, Clinical Pharmacology
Thioridazine	Psychiatry	CYP2D6	Contraindications, Warnings, Precautions
Ticagrelor	Cardiology	CYP2C19	Clinical Pharmacology
Tolterodine	Urology	CYP2D6	Warnings and Precautions, Drug Interactions, Clinical Pharmacology
Tramadol	Anesthesiology	CYP2D6	Boxed Warning, Warnings and Precautions, Use in Specific Populations, Clinical Pharmacology, Patient Counseling Information
Trimipramine	Psychiatry	CYP2D6	Precautions
Umeclidinium	Pulmonary	CYP2D6	Clinical Pharmacology
Upadacitinib	Rheumatology	CYP2D6	Clinical Pharmacology
Valbenazine	Neurology	CYP2D6	Dosage and Administration, Warnings and Precautions, Use in Specific Populations, Clinical Pharmacology
Venlafaxine	Psychiatry	CYP2D6	Drug Interactions, Use in Specific Populations, Clinical Pharmacology
Viloxazine	Psychiatry	CYP2D6	Clinical Pharmacology
Viloxazine	Psychiatry	SLCO1B1	Clinical Pharmacology
Voriconazole	Infectious Diseases	CYP2C19	Clinical Pharmacology
Vortioxetine	Psychiatry	CYP2D6	Dosage and Administration, Clinical Pharmacology
Warfarin	Hematology	CYP2C9	Dosage and Administration, Drug Interactions, Clinical Pharmacology





Warfarin	Hematology	VKORC1	Dosage and Administration, Clinical Pharmacology
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\* Therapeutic areas do not necessarily reflect the CDER review division.

† Representative biomarkers are listed based on standard nomenclature as per the Human Genome Organization (HUGO) symbol and/or simplified descriptors using other common conventions. Listed biomarkers do not necessarily reflect the terminology used in labeling. The term "Nonspecific" is provided when labeling does not explicitly identify the specific biomarker(s) or when the biomarker is represented by a molecular phenotype or gene signature, and in some cases the biomarker was inferred based on the labeling language.

