Medica Central Coverage Policy

Policy Name:	**Genetic Testing - Specialty Testing: Toxicology and Pharmacogenomics MP9602**
Effective Date:	**01/01/2026**

Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica Central plans. Coverage is subject to requirements in applicable federal or state laws. Please refer to the member's plan document for other specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare, Medicaid, and other government programs, this policy will apply unless these programs require different coverage.

Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions may call the Provider Service Center. Please use the Quick Reference Guide on the Provider Communications page for the appropriate phone number. https://mo-central.medica.com/Providers/SSM-employee-health-plan-for-IL-MO-OK-providers

Medica Central coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care, and treatment.

OVERVIEW

This policy addresses the use of tests for drug and treatment response and toxicity testing. Test specifications/technology and sample type vary widely depending on the substance(s) of interest and the clinical question being asked.

For additional information see the Rationale and References section.

The tests, CPT codes, and ICD codes referenced in this policy are not comprehensive, and their inclusion does not represent a guarantee of coverage or non-coverage.

POLICY REFERENCE TABLE

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
Pharmacogenetic Panel Tests			
Pharmacogenetic Panel Tests	GeneSight Psychotropic - 0345U (Assurex Health, Inc.)	81418, 0029U, 0033U, 0078U, 0173U, 0175U, 0286U, 0345U, 0347U,	Rationale/ References

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
	Professional PGX (formerly Genecept Assay) - 0175U (Genomind)	0348U, 0349U, 0350U, 0392U, 0411U, 0419U, 0423U, 0434U, 0437U, 0438U, 0460U, 0461U, 0476U, 0477U, 0516U, 0533U, B20, C00.0-C96.9, D00.0-D49.9, E75.22, F01-F99, G10, G71.14, G89.0-G89.4, I20.0, I21.01-I22.9, I24.1, I25.110, I26.01-I26.99, I48.0, I60.00-I66.99, I73, I82.210-I82.91, K50.00-K50.019, K51.00-K51.319, R52, R79.9, T46.6X1A-T46.6X6S, Z13.71-Z13.79, Z80.3, Z81.8, Z82.49, Z85.3, Z86.000, Z86.59, Z86.71-Z86.79	
	PGxOne (Admera Health)		
	Genomind Professional PGX Express CORE - 0175U (Genomind)		
	Cytochrome P450 Genotyping Panel (ARUP Laboratories)		
	RightMed PGx16 Test - 0347U (OneOme, LLC)		
	RightMed Comprehensive Test Exclude F2 and F5 - 0348U (OneOme, LLC)		
	RightMed Comprehensive Test - 0349U (OneOme, LLC)		
	RightMed Gene Report - 0350U (OneOme, LLC)		
	RightMed Oncology Gene Report - 0460U (OneOme, LLC)		
	RightMed Oncology Medication Report - 0461U (OneOme, LLC)		
	Focused Pharmacogenomics Panel - 0029U (Mayo Clinic Laboratories)		
	Psych HealthPGx Panel - 0173U (RPRD Diagnostics)		
	CNT Genotyping Panel - 0286U (RPRD Diagnostics)		
	Serotonin Receptor Genotype (HTR2A and HTR2C) - 0033U (Mayo		

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
	Clinic Laboratories)		
	EffectiveRX Comprehensive Panel - 0438U (RCA Laboratory Services LLC d/b/a GENETWORx)		
	RightMed Gene Test Exclude F2 and F5 - 0434U (OneOme LLC)		
	Genomind Pharmacogenetics Report - Full - 0423U (Genomind, Inc.)		
	Tempus nP - 0419U (Tempus)		
	IDgenetix - 0411U (Castle Biosciences)		
	Medication Management Neuropsychiatric Panel - 0392U (RCA Laboratory Services LLC d/b/a GENETWORx)		
	RightMed Mental Health Gene Report - 0476U (OneOme, LLC)		
	RightMed Mental Health Medication Report - 0477U (OneOme, LLC)		
	MyGenVar Pharmacogenomics Test - 0516U (Geisinger Medical Laboratories)		
	UCSF Pharmacogenomics Panel - 0533U (University of California San Francisco Genomic Medicine		

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
	Laboratory)		
	MindX Blood Test - Anxiety - 0437U (MindX Sciences)		
Pharmacogenetic Single Gene Tests			
BCHE Variant Analysis	BCHE Single Gene Test (Blueprint Genetics)	81479, Z01.81, Z01.810, Z01.811, Z01.818, Z01.89	Rationale/ References
CYP2C9 Variant Analysis	Cytochrome P450 2C9 Genotype (Quest Diagnostics)	81227, E78.00, E78.1, G35, I21.0-I22.9, I26.01-I26.99, I48.0, I60.00-I66.99, I82.210-I82.9, Z86.71-Z86.79	Rationale/ References
CYP2C19 Variant Analysis	AccuType CP, Clopidogrel CYP2C19 Genotype (Quest Diagnostics)	81225, C64, F32, I21.0-I22.9, I24.9, I26.01-I26.99, I48.0, I60.00-I66.99, I82.210-I82.9, K21.9, L20, Q85.83, R56.9, R68.82, Z86.71-Z86.79	Rationale/ References
CYP2D6 Variant Analysis	CYP2D6 (ARUP Laboratories)	81226, 0070U, 0071U, 0072U, 0073U, 0074U, 0075U, 0076U, C50.011-C50.92, C79.81, D05.00-D05.92, D07.30-D07.39, E11.9, E75.22, F11, F20.9, F31, F33, F84.0, F90, F95.2, G10, G24, G47.419, I10, I20.0, I21.01-I22.9, I24.1, I25.110, I48, I63.50-I63.549, I66.01- I66.9, I73, K21.9, R42, R52, T75.3, Z13.71-Z13.79, Z80.3, Z85.3, Z86.000	Rationale/ References
	CYP2D6 Common Variants and Copy Number - 0070U (Mayo Clinic Laboratories)		
	CYP2D6 Full Gene Sequencing - 0071U (Mayo Clinic Laboratories)		
	CYP2D6-2D7 Hybrid Gene Targeted Sequence Analysis - 0072U (Mayo Clinic Laboratories)		
	CYP2D7-2D6 Hybrid Gene Targeted Sequence Analysis - 0073U (Mayo Clinic Laboratories)		

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
	CYP2D6 Nonduplicated Gene Analysis - 0074U (Mayo Clinic Laboratories)		
	CYP2D6 5' gene duplication/multiplication targeted sequence analysis - 0075U (Mayo Clinic Laboratories)		
	CYP2D6 3' gene duplication/multiplication targeted sequence analysis - 0076U (Mayo Clinic Laboratories)		
CYP3A5 Variant Analysis	Cytochrome P450 3A5 Genotype, Varies (Mayo Clinic Laboratories)	81231, T86, Z79.6, Z94	Rationale/ References
CYP4F2 Variant Analysis	PGX CYP4F2 Genotyping (Indiana University Molecular Genetics Diagnostic Laboratory)	81479, I21.0-I22.9, I26.01-I26.99, I48.0, I60.00-I66.99, I82.210-I82.91, Z86.71-Z86.79	Rationale/ References
DPYD Variant Analysis	DPYD Genotyping (LabCorp)	81232, C18, C50	Rationale/ References
*HLA-A**02:01 Variant Analysis	HLA A 02:01 Determination (Quest Diagnostics)	81379, 81380, 81381, C69, C69.4	Rationale/ References
	HLA-A*02:01-Specific (LabCorp)		
	HLA-A*02:01 Determination (Versiti)		
*HLA-B**15:02 Variant Analysis	HLA-B*15:02, Carbamazepine Sensitivity (LabCorp)	81381, G40	Rationale/ References
*HLA-B**57:01 Variant Analysis	HLA B*57:01 Abacavir Hypersensitivity (LabCorp)	81381, B20, Z21	Rationale/ References
NAT2 Variant Analysis	N-Acetyltransferase 2 (NAT2) Genotype, Varies (Mayo Clinic Laboratories)	81479, G73, M35.9	Rationale/ References

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
TPMT and *NUDT15* Variant Analysis	Thiopurine S-Methyltransferase (TPMT) Genotype (Quest Diagnostics)	81306, 81335, 0034U, 0169U, C91.0, K50.00-K50.90, K51.00-K51.319, M35.9, M05-M06.9, C85.90	Rationale/ References
	TPMT and NUDT15 (ARUP Laboratories)		
	Thiopurine Methyltransferase (TPMT) and Nudix Hydrolase (NUDT15) Genotyping - 0034U (Mayo Clinic Laboratories)		
	NT (NUDT15 and TPMT) genotyping panel - 0169U (RPRD Diagnostics)		
UGT1A1 Variant Analysis	UGT1A1 Irinotecan Toxicity (LabCorp)	81350, B20, C18, C19, C20, C50, C84, E80.4	Rationale/ References
UGT2B17 Variant Analysis	UGT2B17 Single Gene (Fulgent Genetics)	81479, C25, C64, C71, C72, Q85.83	Rationale/ References
VKORC1 Variant Analysis	VKORC1 Targeted Variant - Single Test (GeneDx)	81355, I21.0-I22.9, I26.01-I26.99, I48.0, I60.00-I66.99, I82.210-I82.91, Z86.71-Z86.79	Rationale/ References
Warfarin Sensitivity Panel Tests			
Warfarin Sensitivity Analysis Panels	Warfarin Response Genotype - 0030U (Mayo Clinic Laboratories)	81227, 81355, 0030U, I21, I26, I48	Rationale/ References
	AccuType Warfarin (Quest Diagnostics)		
Other Pharmacogenetic Single Gene Variant Tests			
81479, 0031U, 0032U	Rationale/ References		

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
	Cytochrome P450 1A2 Genotype - 0031U (Mayo Clinic Laboratories)		
	Cardio IQ KIF6 Genotype (Quest Diagnostics)		
	Opioid Receptor, mu OPRM1 Genotype, 1 Variant (ARUP Laboratories)		
	TYMS Single Gene (Sequencing & Deletion/Duplication) (Fulgent Genetics)		

RELATED POLICIES

This policy document provides coverage criteria for testing related to toxicology and pharmacogenetics. Please refer to:

- ***Oncology Testing: Solid Tumor Molecular Diagnostics*** for coverage criteria related to molecular profiling of a known or suspected cancer (e.g. broad molecular profiling, including Minimal Residual Disease (MRD) Testing, Tumor Mutational Burden (TMB), and cytogenetic / fusion testing).
- ***Specialty Testing: Hematology*** for coverage criteria related to diagnostic tests for benign (non-cancerous) hematologic conditions including sickle cell disease, inherited anemias, and hemophilias.
- ***Specialty Testing: Respiratory*** for coverage criteria related to diagnostic testing for cystic fibrosis and related therapies.
- ***Specialty Testing: Nutrition and Metabolism*** for coverage criteria related to diagnostic and serum biomarker tests for nutritional status and biochemical disorders.
- ***General Approach to Laboratory Testing*** or coverage criteria related to toxicology and pharmacology that is not specifically discussed in this or another non-general policy.

back to top

COVERAGE CRITERIA

PHARMACOGENETIC PANEL TESTS

Pharmacogenetic Panel Tests[1]

I. Pharmacogenetic panel tests are considered **medically necessary** when:

A. The member is age 18 years or older, **AND**

B. The member is being considered for, or is already being treated with, one or more specific medication(s) related to their diagnosis that is known to have a gene-drug interaction, **AND**

C. The pharmacogenetic panel test being considered has proven clinical validity[2], as demonstrated through independent evaluation from a recognized third-party source, including but not limited to MolDx, ECRI, Hayes, Optum Genomics or FDA, **AND**

D. The member has a diagnosis of any of the following for which a treatment is being considered:

1. Major depressive disorder, **OR**

2. Generalized anxiety disorder.

II. Pharmacogenetic panel tests are considered **investigational** for all other indications, including:

A. As an initial screening test for medication selection.

[1]Validated Tests

- GeneSight (Assurex Health): 0345U
- Neuropharmagen (Precision Molecular Solutions) 81418
- PGXPSYCH (PHD Laboratory LLC): 81418
- Psychotropic Pharmacogenomics Gene Panel (Mayo): 81418
- Focused Pharm Panel (Mayo): 0029U
- IDgenetix (Castle): 0411U
- Tempus nP (Tempus): 0419U
- Mental Health Panel (Exceltox Laboratories LLC): 81418
- PGX (PHD Laboratory LLC): 81418
- PGS SHORT COMP (PHD Laboratory LLC): 81418
- Sinochips PGx Comprehensive (Sinochips Kansas LLC): 81418
- Carolina Comprehensive PGx (Carolina Diagnostics Lab): 81418
- COR120 - Comprehensive Pharmacogenetic Test (Quantigen LLC): 81418
- PCL PGX+ Comprehensive Report (Patients Choice Laboratories of Indiana, LLC): 81418
- PharmGx Comprehensive PGx Panel (Dxome Clia Laboratory, Inc): 81418
- PsychPainMakers Panel (Genemarkers): 81418
- PredictScript Poly (Phenomics Health Inc): 81418
- PredictScriptCNS (Phenomics Health Inc): 81418

DEFINITIONS

1. **[2]Clinical validity,** according to the National Institutes of Health-Department of Energy

(NIH-DOE) Task Force on Genetic Testing, describes the accuracy with which a test identifies a particular clinical condition. The components of measuring clinical validity are:

a. **Sensitivity**: among people with a specific condition, the proportion who have a positive test result

b. **Specificity**: among people who do not have the condition, the proportion who have a negative test result

c. **Positive predictive value**: among people with a positive test result, the proportion of people who have the condition

d. **Negative predictive value**: among people with a negative test result, the proportion who do not have the condition

view rationale
back to top

PHARMACOGENETIC SINGLE GENE TESTS

BCHE Variant Analysis

I. *BCHE* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

A. The member is being considered for or is currently undergoing treatment with either of the following:

1. Mivacurium[1] (e.g., Mivacron), **OR**

2. Succinylcholine[1] (e.g., Anectine, Suxamethonium).

II. *BCHE* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly used as a muscle relaxant during surgery or intubation.

view rationale
back to top

CYP2C9 Variant Analysis

I. *CYP2C9* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

A. The member is being considered for or is currently undergoing treatment with any of the following:

1. Siponimod[1] (e.g., Mayzent), **OR**
2. Celecoxib[2] (e.g., Celebrex, Elyxyb), **OR**
3. Dronabinol[3] (e.g., Marinol, Syndros), **OR**
4. Erdafitinib[4] (e.g., Balversa), **OR**

5. Flurbiprofen[5] (e.g., Ansaid), **OR**
6. Fosphenytoin[6] (e.g., Cerebyx, Sesquient), **OR**
7. Meloxicam[7] (e.g., Anjeso, Mobic, Vivlodex, Qmiiz ODT), **OR**
8. Nateglinide[8] (e.g., Starlix), **OR**
9. Phenytoin[9] (e.g., Dilantin, Phenytek), **OR**
10. Piroxicam[10] (e.g., Feldene), **OR**
11. Warfarin[11] (e.g., Coumadin, Jantoven).

II. *CYP2C9* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly prescribed for individuals diagnosed with multiple sclerosis
[2] Commonly prescribed for treating pain or inflammation
[3] Commonly prescribed for treating loss of appetite and severe nausea and vomiting
[4] Commonly prescribed for treatment of bladder cancer
[5] Commonly prescribed for treatment of pain or inflammation
[6] Commonly prescribed for preventing or controlling seizures
[7] Commonly prescribed for treating pain, inflammation, or severe pain
[8] Commonly prescribed for blood sugar control in individuals with type II diabetes
[9] Commonly prescribed for treatment of seizures
[10] Commonly prescribed to treat pain or inflammation
[11] Commonly prescribed to reduce the formation of blood clots

view rationale
back to top

CYP2C19 Variant Analysis

I. *CYP2C19* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

A. The member is being considered for or is currently undergoing treatment with any of the following:

1. Clopidogrel[1] (e.g., Plavix), **OR**
2. Abrocitinib[2] (e.g., Cibinqo), **OR**
3. Belzutifan[3] (e.g., Welireg), **OR**
4. Brivaracetam[4] (e.g., Briviact, Brivajoy), **OR**
5. Citalopram[5] (e.g., Celexa), **OR**
6. Clobazam[6] (e.g., Onfi), **OR**
7. Flibanserin[7] (e.g., Addyi), **OR**
8. Pantoprazole[8] (e.g., Protonix).

II. *CYP2C19* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly prescribed after an angina or cardiac arrest to lower risk of stroke and blood clots
[2] Commonly prescribed for eczema
[3] Commonly prescribed to treat tumors in individuals with Von Hippel-Lindau syndrome

[4] Commonly prescribed to treat seizures

[5] Commonly prescribed for treatment of depression and major depressive disorder

[6] Commonly prescribed for treatment of seizures caused by Lennox-Gastaut syndrome

[7] Commonly prescribed for low libido in pre-menopausal women

[8] Commonly prescribed for treatment of erosive esophagitis caused by GERD, and Zollinger-Ellison syndrome

view rationale
back to top

CYP2D6 Variant Analysis

I. *CYP2D6* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

A. The member is being considered for or is currently undergoing treatment with any of the following:

1. Eliglustat[1] (e.g., Cerdelga), **OR**
2. Tetrabenazine[2] (e.g., Xenazine), **OR**
3. Amphetamine[3] (e.g., Adzenys, Dyanavel, Evekeo), **OR**
4. Aripiprazole[4] (e.g., Abilify, Abilify Maintena), **OR**
5. Aripiprazole lauroxil[5] (e.g., Aristada), **OR**
6. Atomoxetine[6] (e.g., Strattera), **OR**
7. Brexpiprazole[7] (e.g., Rexulti), **OR**
8. Clozapine[8] (e.g., Versacloz, FazaClo, Clozaril), **OR**
9. Deutetrabenazine[9] (e.g., Austedo), **OR**
10. Gefitinib[10] (e.g., Iressa), **OR**
11. Iloperidone[11] (e.g., Fanapt), **OR**
12. Lofexidine[12] (e.g., Lucemyra), **OR**
13. Meclizine[13] (e.g., Antivert, Bonine, Dramamine, Verticalm, Zentrip), **OR**
14. Metoclopramide[14] (e.g., Reglan, Metozolv), **OR**
15. Oliceridine[15] (e.g., Olinvyk), **OR**
16. Pimozide[16] (e.g., Orap), **OR**
17. Pitolisant[17] (e.g., Wakix), **OR**
18. Propafenone[18] (e.g., Rythmol), **OR**
19. Thioridazine[19] (e.g., Mellaril), **OR**
20. Tramadol[20] (e.g., ConZip, Ultram), **OR**
21. Valbenazine[21] (e.g., Ingrezza), **OR**
22. Venlafaxine[22] (e.g., Effexor), **OR**
23. Vortioxetine[23] (e.g., Trintellix, Brintellix), **OR**
24. Codeine[24].

II. *CYP2D6* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications, including:

A. For the purpose of managing treatment with tamoxifen for women at high risk for or with breast cancer.

[1] Commonly prescribed for treatment of Gaucher disease

[2] Commonly prescribed for treatment of involuntary movements (chorea) caused by Huntington

disease

[3] Commonly prescribed for treatment of hyperactivity, impulse control, and attention deficit hyperactivity disorder (ADHD)

[4] Commonly prescribed for schizophrenia, bipolar I disorder, and major depressive disorder

[5] Commonly prescribed for schizophrenia

[6] Commonly prescribed for treatment of attention deficit hyperactivity disorder (ADHD)

[7] Commonly prescribed for treatment of schizophrenia and major depressive disorder

[8] Commonly prescribed for treatment of schizophrenia

[9] Commonly prescribed for treatment of involuntary muscle movements (chorea) caused by Huntington disease, and tardive dyskinesia

[10] Commonly prescribed for treatment of non-small cell lung cancer

[11] Commonly prescribed for treatment of schizophrenia

[12] Commonly prescribed for treatment of opioid withdrawal symptoms

[13] Commonly prescribed for treatment of motion sickness and vertigo

[14] Commonly prescribed for treatment of heartburn caused by GERD, gastroparesis, nausea and vomiting, and to aid in certain medical procedures involving the stomach or intestines

[15] Commonly prescribed for treatment of severe pain

[16] Commonly prescribed for treatment of Tourette's syndrome

[17] Commonly prescribed for treatment of excessive daytime sleepiness or sudden loss of muscle strength (cataplexy) related to narcolepsy

[18] Commonly prescribed for treatment of heart rhythm disorders

[19] Commonly prescribed for treatment of schizophrenia

[20] Commonly prescribed for treatment of moderate to severe pain

[21] Commonly prescribed for treatment of tardive dyskinesia

[22] Commonly prescribed for treatment of major depressive disorder, anxiety, and panic disorder

[23] Commonly prescribed for treatment of major depressive disorder

[24] Commonly prescribed for treatment of mild to moderately severe pain, and to help reduce coughing

view rationale
back to top

CYP3A5 Variant Analysis

I. *CYP3A5* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

   A. The member is being considered for or is currently undergoing treatment with tacrolimus[1] (e.g., Protopic, Envarsus, Astagraf, Prograf).

II. *CYP3A5* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly prescribed to individuals who have undergone a heart, kidney, liver, or lung transplant

view rationale
back to top

CYP4F2 Variant Analysis

I. *CYP4F2* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

   A. The member is being considered for or is currently undergoing treatment with warfarin[1] (e.g., Coumadin, Jantoven).

II. *CYP4F2* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly prescribed to reduce the formation of blood clots

view rationale
back to top

DPYD Variant Analysis

I. *DPYD* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

   A. The member is being considered for or is currently undergoing treatment with either of the following:

      1. Fluorouracil[1] (e.g., Carac, Efudex, Tolak, Fluoroplex), **OR**
      2. Capecitabine[1] (e.g., Xeloda).

II. *DPYD* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly prescribed for individuals diagnosed with colorectal, breast, and aerodigestive tract tumors

view rationale
back to top

*HLA-A*02:01* Variant Analysis

I. *HLA-A*02:01* variant analysis is considered **medically necessary** when the member meets the following:

   A. The member is age 18 or older, **AND**

   B. The member has a diagnosis of one of the following:

      1. Metastatic uveal melanoma, **OR**
      2. Unresectable uveal melanoma.

II. *HLA-A*02:01* variant analysis is considered **investigational** for all other indications.

view rationale
back to top

*HLA-B**15:02 Variant Analysis

I. *HLA-B*15:02* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

   A. The member is being considered for or is currently undergoing treatment with any of the following:

      1. Carbamazepine containing therapy[1] (e.g., Tegretol, Carbatrol, Epitol, Equetro), **OR**
      2. Phenytoin[2] (e.g., Dilantin, Phenytek), **OR**
      3. Fosphenytoin[2] (e.g., Cerebyx, Sesquient).

II. *HLA-B*15:02* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly prescribed for individuals with epilepsy, trigeminal neuralgia, or bipolar disorder

[2] Commonly prescribed for treatment of seizures

view rationale
back to top

*HLA-B**57:01 Variant Analysis

I. *HLA-B*57:01* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

   A. The member is being considered for or is currently undergoing treatment with abacavir[1] (e.g., Ziagen).

II. *HLA-B*57:01* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly prescribed for individuals with HIV

view rationale
back to top

NAT2 Variant Analysis

I. *NAT2* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

   A. The member is being considered for or is currently undergoing treatment with amifampridine/amifampridine phosphate[1] (e.g., Firdapse, Ruzurgi).

II. *NAT2* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly prescribed for treatment of Lambert-Eaton myasthenic syndrome

view rationale
back to top

TPMT and *NUDT15* Variant Analysis

I. *TPMT* and *NUDT15* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

A. The member is being considered for or is currently undergoing treatment with any of the following:

1. Azathioprine[1] (e.g., Imuran and Azasan), **OR**
2. Mercaptopurine[2] (e.g., Purinethol and Purixan), **OR**
3. Thioguanine[3] (e.g., Tabloid), **OR**

B. The member is on thiopurine therapy, **AND**

1. The member has had abnormal complete blood count results.

II. *TPMT* and *NUDT15* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly prescribed for treatment of avoiding rejection of a transplanted organ, and rheumatoid arthritis

[2] Commonly prescribed for treatment of acute lymphoblastic or lymphocytic leukemia

[3] Commonly prescribed for treatment of acute nonlymphocytic leukemia

view rationale
back to top

UGT1A1 Variant Analysis

I. *UGT1A1* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

A. The member is being considered for or is currently undergoing treatment with any of the following:

1. Irinotecan[1] (e.g., Onivyde, Camptosar), **OR**
2. Belinostat[2] (e.g., Beleodaq), **OR**
3. Sacituzumab govitecan-hziy[3] (e.g., Trodelvy).

II. *UGT1A1* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly prescribed for treatment of colon, rectal and pancreatic cancers

[2] Commonly prescribed for treatment of peripheral T-cell lymphoma

[3] Commonly prescribed for treatment of breast and urothelial cancers

view rationale
back to top

UGT2B17 Variant Analysis

I. *UGT2B17* variant analysis to determine drug metabolizer status is **medically necessary** when:

   A. The member is being considered for or is currently undergoing treatment with belzutifan[1] (e.g., Welireg).

II. *UGT2B17* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly prescribed to treat tumors in individuals with Von Hippel-Lindau syndrome

view rationale
back to top

VKORC1 Variant Analysis

I. *VKORC1* variant analysis to determine drug metabolizer status is considered **medically necessary** when:

   A. The member is being considered for or is currently undergoing treatment with warfarin[1] (e.g., Coumadin, Jantoven).

II. *VKORC1* variant analysis to determine drug metabolizer status is considered **investigational** for all other indications.

[1] Commonly prescribed to reduce the formation of blood clots

view rationale
back to top

WARFARIN SENSITIVITY PANEL TESTS

Warfarin Sensitivity Analysis Panels

I. Multigene panel analysis to determine drug metabolizer status for warfarin[1] sensitivity is considered **medically necessary** when:

   A. The member is being considered for or is undergoing treatment with warfarin, **AND**

      1. The member has not reached a therapeutic dose, **AND**

   B. The member is undergoing prophylaxis and treatment of venous thrombosis or pulmonary embolism, **OR**

   C. The member is undergoing prophylaxis and treatment of thromboembolic complications associated with atrial fibrillation and/or cardiac valve replacement, **OR**

   D. The member has a history of previous myocardial infarction.

II. Multigene panel analysis to confirm drug metabolizer status for warfarin[1] sensitivity is considered **investigational** for all other indications.

[1] Commonly prescribed to reduce the formation of blood clots

view rationale
back to top

OTHER PHARMACOGENETIC SINGLE GENE VARIANT TESTS

Other Pharmacogenetic Single Gene Variant Analysis

I. Variant analysis of all other genes for drug metabolizer status is considered **investigational**, including but not limited to:

A. *COMT* (0032U, 81479)

B. *CYP1A2* (0031U, 81479)

C. *KIF6* (81479)

D. *OPRM1* (81479)

E. *TYMS* (81479).

view rationale

RATIONALE AND REFERENCES

Pharmacogenetic Panel Tests

Centers for Medicare and Medicaid Services (CMS)

The CMS local coverage determination (LCD) entitled “MolDX: Pharmacogenomics Testing” states the following: “PGx tests are indicated when medications are being considered for use (or already being administered) that are medically necessary, appropriate, and approved for use in the patient’s condition and are known to have a gene(s)-drug interaction that has been demonstrated to be clinically actionable…”

Centers for Medicare & Medicaid Services. Medicare Coverage Database: Local Coverage Determination. MolDX: Phenotypic Biomarker Detection in Circulating Tumor Cells (L38294). Revision Effective August 24, 2023. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=38294&ver=19&

Bunka, et al.

In their 2023 rapid review and meta-analysis, Bunka, et al. discuss the age of patients who have participated in studies related to the use of pharmacogenetic panels. The authors note that there is currently insufficient evidence to support ordering PGx tests for adolescents as a part of their treatment for depression (p. 5).

Bunka M, Wong G, Kim D, et al. Evaluating treatment outcomes in pharmacogenomic-guided care for major depression: A rapid review and meta-analysis. Psychiatry Res. 2023;321:115102. doi:10.1016/j.psychres.2023.115102

Concert Note
Without clear guidance from professional society guidelines or other comparable resources, Concert maintains the position of coverage for this testing contingent on the member failing at least one medication in keeping with mainstream clinical practice and the practical realities of needing to treat patients prior to return of test results.

back to top

BCHE Variant Analysis

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations, which details possible gene-drug interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, lists the following recommendations for *BCHE*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Mivacurium	BCHE	intermediate or poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk (prolonged neuromuscular blockade). Avoid use in poor metabolizers.
Succinylcholine	BCHE	intermediate or poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk (prolonged neuromuscular blockade). Avoid use in poor metabolizers. May administer a test dose to assess sensitivity and administer cautiously via slow infusion.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

back to top

CYP2C9 Variant Analysis

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations which details possible gene-drug interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, list the following recommendations for *CYP2C9*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Celecoxib	CYP2C9	poor metabolizers or *3 carriers	Results in higher systemic concentrations. Reduce starting dose to half of the lowest recommended dose in poor metabolizers. Consider alternative therapy in poor metabolizers with juvenile rheumatoid arthritis.
Dronabinol	CYP2C9	intermediate or poor metabolizers	May result in higher systemic concentrations and higher adverse reaction risk. Monitor for adverse reactions.
Erdafitinib	CYP2C9	*3/*3 (poor	May result in higher systemic

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
		metabolizers)	concentrations and higher adverse reaction risk. Monitor for adverse reactions.
Flurbiprofen	CYP2C9	poor metabolizers or *3 carriers	Results in higher systemic concentrations. Use a reduced dosage in poor metabolizers.
Fosphenytoin	CYP2C9	intermediate or poor metabolizers	May result in higher systemic concentrations and higher adverse reaction risk (central nervous system toxicity). Consider starting at the lower end of the dosage range and monitor serum concentrations. Refer to FDA labeling for specific dosing recommendations. Carriers of CYP2C9*3 alleles may be at increased risk of severe cutaneous adverse reactions. Consider avoiding fosphenytoin as an alternative to carbamazepine in patients who are CYP2C9*3 carriers. Genotyping is not a substitute for clinical vigilance and patient management.
Meloxicam	CYP2C9	poor metabolizers or *3 carriers	Results in higher systemic concentrations. Consider dose reductions in poor metabolizers. Monitor patients for adverse reactions.
Nateglinide	CYP2C9	poor metabolizers	Results in higher systemic concentrations and may result in higher adverse reaction risk (hypoglycemia). Dosage reduction is recommended. Increase monitoring frequency for adverse reactions. Refer to FDA labeling for specific dosing recommendations.
Phenytoin	CYP2C9	intermediate or poor metabolizers	May result in higher systemic concentrations and higher adverse reaction risk (central nervous system toxicity). Refer to FDA labeling for specific dosing recommendations. Carriers of CYP2C9*3 alleles may be at increased risk of severe cutaneous adverse reactions. Consider avoiding phenytoin as

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
			an alternative to carbamazepine in patients who are CYP2C9*3 carriers. Genotyping is not a substitute for clinical vigilance and patient management.
Piroxicam	CYP2C9	intermediate or poor metabolizers	Results in higher systemic concentrations. Consider reducing dosage in poor metabolizers.
Siponimod	CYP2C9	intermediate or poor metabolizers	Results in higher systemic concentrations. Adjust dosage based on genotype. Do not use in patients with CYP2C9 *3/*3 genotype. Refer to FDA labeling for specific dosing recommendations.
Warfarin	CYP2C9	intermediate or poor metabolizers	Alters systemic concentrations and dosage requirements. Select initial dosage, taking into account clinical and genetic factors. Monitor and adjust dosages based on INR.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations.

back to top

CYP2C19 Variant Analysis

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations which details possible gene-drug interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, list the following recommendations for *CYP2C19*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Abrocitinib	CYP2C19	poor metabolizers	Results in higher systemic concentrations and may result in higher adverse reaction risk. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations.
Belzutifan	CYP2C19 and/or	poor metabolizers	Results in higher systemic concentrations and may result in

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
	UGT2B17		higher adverse reaction risk (anemia, hypoxia). Monitor patients who are poor metabolizers for both genes for adverse reactions.
Brivaracetam	CYP2C19	intermediate or poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk. Consider dosage reductions in poor metabolizers.
Citalopram	CYP2C19	poor metabolizers	Results in higher systemic concentrations and adverse reaction risk (QT prolongation). The maximum recommended dose is 20 mg.
Clobazam	CYP2C19	intermediate or poor metabolizers	Results in higher systemic active metabolite concentrations. Poor metabolism results in higher adverse reaction risk. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations.
Clopidogrel	CYP2C19	intermediate or poor metabolizers	Results in lower systemic active metabolite concentrations, lower antiplatelet response, and may result in higher cardiovascular risk. Consider use of another platelet P2Y12 inhibitor.
Flibanserin	CYP2C19	poor metabolizers	May result in higher systemic concentrations and higher adverse reaction risk. Monitor patients for adverse reactions.
Pantoprazole	CYP2C19	intermediate or poor metabolizers	Results in higher systemic concentrations. Consider dosage reduction in children who are poor metabolizers. No dosage adjustment is needed for adult patients who are intermediate or poor metabolizers.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations.

Clinical Pharmacogenetics Implementation Consortium (CPIC)

In their 2023 guideline for dosing of Serotonin Reuptake Inhibitor Antidepressants (SSRIs) based

on *CYP2D6, CYP2C19, CYP2B6, SLC6A4,* and *HTR2A* genotypes, CPIC describes the likely pharmacokinetic effects of *CYP2C19* genotypes in SSRI metabolism and offers dosing considerations for individuals with a known genotype, but does not include a recommendation to perform *CYP2C19* genotyping prior to or during treatment with SSRIs (p. 9, p. 22 Table 3).

Bousman CA, Stevenson JM, Ramsey LB, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A genotypes and serotonin reuptake inhibitor antidepressants. Clin Pharmacol Ther. 2023;114(1):51-68. doi:10.1002/cpt.2903

back to top

CYP2D6 Variant Analysis

National Comprehensive Cancer Network (NCCN): Breast Cancer (4.2025)

This guideline recommends against *CYP2D6* genotype testing for women being considered for tamoxifen treatment (p. DCIS-2 and p. BINV-K 2 of 3).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer 4.2025 https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations which details possible gene-drug interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, list the following recommendations for *CYP2D6*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Amphetamine	CYP2D6	poor metabolizers	May affect systemic concentrations and adverse reaction risk. Consider a lower starting dosage or use an alternative agent.
Aripiprazole	CYP2D6	poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations.
Aripiprazole Lauroxil	CYP2D6	poor metabolizers	Results in higher systemic concentrations. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations.

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Atomoxetine	CYP2D6	poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk. Adjust titration interval and increase dosage if tolerated. Refer to FDA labeling for specific dosing recommendations.
Brexpiprazole	CYP2D6	poor metabolizers	Results in higher systemic concentrations. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations.
Clozapine	CYP2D6	poor metabolizers	Results in higher systemic concentrations. Dosage reductions may be necessary.
Codeine	CYP2D6	ultrarapid metabolizers	Results in higher systemic active metabolite concentrations and higher adverse reaction risk (life-threatening respiratory depression and death). Codeine is contraindicated in children under 12 years of age.
Deutetrabenazine	CYP2D6	poor metabolizers	Results in higher systemic concentrations and adverse reaction risk (QT prolongation). The maximum recommended dosage should not exceed 36 mg (maximum single dose of 18 mg).

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Eliglustat	CYP2D6	ultrarapid, normal, intermediate, or poor metabolizers	Alters systemic concentrations, effectiveness, and adverse reaction risk (QT prolongation). Indicated for normal, intermediate, and poor metabolizer patients. Ultrarapid metabolizers may not achieve adequate concentrations to achieve a therapeutic effect. The recommended dosages are based on CYP2D6 metabolizer status. Coadministration with strong CYP3A inhibitors is contraindicated in intermediate and poor CYP2D6 metabolizers. Refer to FDA labeling for specific dosing recommendations.
Gefitinib	CYP2D6	poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk. Monitor for adverse reactions.
Iloperidone	CYP2D6	poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk (QT prolongation). Reduce dosage by 50%.
Lofexidine	CYP2D6	poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk. Monitor for orthostatic hypotension and bradycardia.
Meclizine	CYP2D6	ultrarapid, intermediate, or poor metabolizers	May affect systemic concentrations. Monitor for adverse reactions and clinical effect.
Metoclopramide	CYP2D6	poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk. The recommended dosage is lower. Refer to FDA labeling for specific dosing recommendations.

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Oliceridine	CYP2D6	poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk (respiratory depression and sedation). May require less frequent dosing.
Pimozide	CYP2D6	poor metabolizers	Results in higher systemic concentrations. Dosages should not exceed 0.05 mg/kg in children or 4 mg/day in adults who are poor metabolizers and dosages should not be increased earlier than 14 days.
Pitolisant	CYP2D6	poor metabolizers	Results in higher systemic concentrations. Use the lowest recommended starting dosage. Refer to FDA labeling for specific dosing recommendations.
Propafenone	CYP2D6	poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk (arrhythmia). Avoid use in poor metabolizers taking a CYP3A4 inhibitor.
Tetrabenazine	CYP2D6	poor metabolizers	Results in higher systemic concentrations. The maximum recommended single dose is 25 mg and should not exceed 50 mg/day.
Thioridazine	CYP2D6	poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk (QT prolongation). Predicted effect based on experience with CYP2D6 inhibitors. Contraindicated in poor metabolizers.

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Tramadol	CYP2D6	Ultrarapid metabolizers	Results in higher systemic and breast milk active metabolite concentrations, which may result in respiratory depression and death. Contraindicated in children under 12 and in adolescents following tonsillectomy/adenoidectomy. Breastfeeding is not recommended during treatment.
Valbenazine	CYP2D6	poor metabolizers	Results in higher systemic active metabolite concentrations and higher adverse reaction risk (QT prolongation). Dosage reductions may be necessary.
Venlafaxine	CYP2D6	poor metabolizers	Alters systemic parent drug and metabolite concentrations. Consider dosage reductions.
Vortioxetine	CYP2D6	poor metabolizers	Results in higher systemic concentrations. The maximum recommended dose is 10 mg.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations.

Clinical Pharmacogenetics Implementation Consortium (CPIC)

In their 2023 guideline for dosing of Serotonin Reuptake Inhibitor Antidepressants (SSRIs) based on *CYP2D6, CYP2C19, CYP2B6, SLC6A4,* and *HTR2A* genotypes, CPIC describes the likely pharmacokinetic effects of *CYP2D* genotypes in SSRI metabolism and offers dosing considerations for individuals with a known genotype, but does not include a recommendation to perform *CYP2D6* genotyping prior to or during treatment with SSRIs (p. 7, p. 19 Table 2).

Bousman CA, Stevenson JM, Ramsey LB, et al. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A genotypes and serotonin reuptake inhibitor antidepressants. Clin Pharmacol Ther. 2023;114(1):51-68. doi:10.1002/cpt.2903

back to top

CYP3A5 Variant Analysis

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations which details possible gene-drug

interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, lists the following recommendations for *CYP3A5*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Tacrolimus	CYP3A5	intermediate or normal metabolizers	Results in lower systemic concentrations, lower probability of achieving target concentrations and may result in higher rejection risk. Measure drug concentrations and adjust dosage based on trough whole blood tacrolimus concentrations.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

back to top

CYP4F2 Variant Analysis

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations which details possible gene-drug interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, list the following recommendations for *CYP4F2*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Warfarin	CYP4F2	V433M variant carriers	May affect dosage requirements. Monitor and adjust doses based on INR.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

back to top

DPYD Variant Analysis

National Comprehensive Cancer Network (NCCN): Colon Cancer (4.2025)

This guideline recommends that patients planning to undergo fluoropyrimidine therapy be offered *DPYD* testing with the caveat that patients understand the limitations of this testing including variability among platforms and the lack of variant-specific dosing recommendations for some results (p. COL-J 2 of 3, COL-2).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Colon Cancer 4.2025 https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations which details possible gene-drug interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, list the following recommendations for *DPYD*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Capecitabine	DPYD	intermediate or poor metabolizers	Results in higher adverse reaction risk (severe, life-threatening, or fatal toxicities). No dosage has proven safe in poor metabolizers, and insufficient data are available to recommend a dosage in intermediate metabolizers. Withhold or discontinue in the presence of early-onset or unusually severe toxicity.
Fluorouracil	DPYD	intermediate or poor metabolizer	Results in higher adverse reaction risk (severe, life-threatening, or fatal toxicities). No dosage has proven safe in poor metabolizers and insufficient data are available to recommend a dosage in intermediate metabolizers. Withhold or discontinue in the presence of early-onset or unusually severe toxicity.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

back to top

*HLA-A**02:01 Variant Analysis

Food and Drug Administration (FDA)

In the FDA's label for Kimmtrak, they state, "KIMMTRAK [(tebentafusp-tebn)] is a bispecific gp100 peptide-HLA-directed CD3 T cell engager indicated for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma" (p. 1).

U.S. Food and Drug Administration. KIMMTRAK (tebentafusp-tebn) prescribing information (label). Approved 2022. Revised June 2024. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761228s003lbl.pdf

Chen, et al.

"Tebentafusp…should be the preferred frontline agent for most HLA-A*0201 positive patients. However, patients with rapidly progressing disease or high tumor benefit may not derive the same benefit" (p. 1).
"In most cases, tebentafusp should be the preferred front-line agent for the treatment of metastatic

uveal melanoma. However, it is limited to patients with HLA-A2*0201 positivity and may not be the preferred upfront agent in patients with rapidly progressing disease or high tumor burden" (p. 17).

Chen LN, Carvajal RD. Tebentafusp for the treatment of HLA-A*02:01-positive adult patients with unresectable or metastatic uveal melanoma. Expert Rev Anticancer Ther. 2022;22(10):1017-1027. doi: 10.1080/14737140.2022.2124971

back to top

*HLA-B*15:02* Variant Analysis

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations which details possible gene-drug interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, list the following recommendations for *HLA-B*15:02*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Carbamazepine	HLA-B	*15:02 allele positive	Results in higher adverse reaction risk (severe skin reactions). Avoid use unless potential benefits outweigh risks and consider risks of alternative therapies. Patients positive for HLA-B*15:02 may be at increased risk of severe skin reactions with other drugs that are associated with a risk of Stevens Johnson Syndrome/Toxic Epidermal necrolysis (SJS/TEN). Genotyping is not a substitute for clinical vigilance.
Fosphenytoin	HLA-B	*15:02 allele positive	May result in higher adverse reaction risk (severe cutaneous reactions). Patients positive for HLA-B*15:02 may be at increased risk of Stevens Johnson Syndrome/Toxic Epidermal necrolysis (SJS/TEN). Consider avoiding fosphenytoin as an alternative to carbamazepine in patients who are positive for HLA-B*15:02. Genotyping is not a substitute for clinical vigilance and patient management.
Phenytoin	HLA-B	*15:02 allele positive	May result in higher adverse reaction risk (severe cutaneous reactions). Patients positive for HLA-B*15:02 may be at increased risk of Stevens Johnson Syndrome/Toxic Epidermal necrolysis (SJS/TEN). Consider avoiding phenytoin as an alternative to carbamazepine in patients who are positive for HLA-B*15:02. Genotyping is not a substitute for clinical

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
			vigilance and patient management.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations.

back to top

*HLA-B**57:01 Variant Analysis

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations which details possible gene-drug interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, list the following recommendations for *HLA-B*57:01*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Abacavir	HLA-B	*57:01 allele positive	Results in higher adverse reaction risk (hypersensitivity reactions). Do not use abacavir in patients positive for HLA-B*57:01.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations.

back to top

NAT2 Variant Analysis

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations, which details possible gene-drug interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, lists the following recommendations for *NAT2*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Amifampridine	NAT2	poor metabolizers	Results in higher systemic concentrations and higher adverse reaction risk. Use lowest recommended starting dosage and monitor for adverse reactions. Refer to FDA labeling for specific dosing recommendations.

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Amifampridine Phosphate	NAT2	poor metabolizers	Results in higher systemic concentrations. Use lowest recommended starting dosage (15 mg/day) and monitor for adverse reactions.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations.

back to top

TPMT and *NUDT15* Variant Analysis

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations which details possible gene-drug interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, list the following recommendations for *TPMT* and *NUDT15*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Azathioprine	TPMT and/or NUDT15	intermediate or poor metabolizers	Alters systemic active metabolite concentration and dosage requirements. Results in higher adverse reaction risk (myelosuppression). Consider alternative therapy in poor metabolizers. Dosage reduction is recommended in intermediate metabolizers for NUDT15 or TPMT. Intermediate metabolizers for both genes may require more substantial dosage reductions. Refer to FDA labeling for specific dosing recommendations.
Mercaptopurine	TPMT and/or NUDT15	intermediate or poor metabolizers	Alters systemic active metabolite concentration and dosage requirements. Results in higher adverse reaction risk

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
			(myelosuppression). Initial dosages should be reduced in poor metabolizers; poor metabolizers generally tolerate 10% or less of the recommended dosage. Intermediate metabolizers may require dosage reductions based on tolerability. Intermediate metabolizers for both genes may require more substantial dosage reductions. Refer to FDA labeling for specific dosing recommendations.
Thioguanine	TPMT and/or NUDT15	intermediate or poor metabolizers	Alters systemic active metabolite concentration and dosage requirements. Results in higher adverse reaction risk (myelosuppression). Initial dosages should be reduced in poor metabolizers; poor metabolizers generally tolerate 10% or less of the recommended dosage. Intermediate metabolizers may require dosage reductions based on tolerability. Intermediate metabolizers for both genes may require more substantial dosage reductions. Refer to FDA labeling for specific dosing recommendations.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations.

National Comprehensive Cancer Network (NCCN): Acute Lymphoblastic Leukemia (2.2025)

This guideline recommends that, for patients receiving treatment with 6-MP, testing for *TPMT* gene polymorphisms is recommended for patients who develop severe myelosuppression after starting 6-MP (p. ALL-D, MS-15, MS-29, MS-50, MS-51, MS-53).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/all.pdf

back to top

UGT1A1 Variant Analysis

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations which details possible gene-drug interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, list the following recommendations for *UGT1A1*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Belinostat	UGT1A1	*28/*28 (poor metabolizers)	May result in higher systemic concentrations and higher adverse reaction risk. Reduce starting dose to 750 mg/m2 in poor metabolizers.
Irinotecan	UGT1A1	*1/*6, *1/*28 (intermediate metabolizers) or *6/*6, *6/*28, *28/*28 (poor metabolizers)	Results in higher systemic active metabolite concentrations and higher adverse reaction risk (severe or life-threatening neutropenia, severe diarrhea). Closely monitor for neutropenia during and after treatment. Consider reducing the starting dosage by at least one level in poor metabolizers and modify the dosage based on individual patient tolerance. Refer to FDA labeling for specific dosing recommendations.
Sacituzumab Govitecan-hziy	UGT1A1	*28/*28 (poor metabolizers)	May result in higher systemic concentrations and adverse reaction risk (neutropenia). Monitor for adverse reactions and tolerance to treatment.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022.
https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

back to top

UGT2B17 Variant Analysis

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations, which details possible gene-drug interactions. Section 1, entitled Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations, lists the following recommendations for *UGT2B17*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Belzutifan	CYP2C19 and/or UGT2B17	poor metabolizers	Results in higher systemic concentrations and may result in higher adverse reaction risk (anemia, hypoxia). Monitor patients who are poor metabolizers for both genes for adverse reactions.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations.

back to top

VKORC1 Variant Analysis

Food and Drug Administration (FDA)

The FDA published a Table of Pharmacogenetic Associations which details possible gene-drug interactions. Section 1, entitled “Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations”, list the following recommendations for *VKORC1*:

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
Warfarin	VKORC1	-1639G>A variant carriers	Alters dosage requirements. Select initial dosage, taking into account clinical and genetic factors. Monitor and adjust dosages based on INR.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

back to top

Warfarin Sensitivity Analysis Panels

Food and Drug Administration (FDA)

Per the FDA label, the indications and usage for Warfarin include the following:

- Prophylaxis and treatment of venous thrombosis and its extension, pulmonary embolism
- Prophylaxis and treatment of thromboembolic complications associated with atrial fibrillation and/or cardiac valve replacement

- Reduction in the risk of death, recurrent myocardial infarction, and thromboembolic events such as stroke or systemic embolization after myocardial infarction

U.S. Food and Drug Administration. Labeling for Coumadin (warfarin sodium) (NDA No. 009218/S-127). FDA website. Approved June 8, 1954. Updated October 2011. https://www.accessdata.fda.gov/drugsatfda_docs/label/2011/009218s107lbl.pdf

The FDA published a "Table of Pharmacogenetic Associations", which details possible gene-drug interactions. Section 1, entitled "Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations", lists the following recommendations for *CYP2C9, CYP4F2* and *VKORC1*:

Warfarin	CYP2C9	intermediate or poor metabolizers	Alters systemic concentrations and dosage requirements. Select initial dosage, taking into account clinical and genetic factors. Monitor and adjust dosages based on INR.
	CYP4F2	V433M variant carriers	May affect dosage requirements. Monitor and adjust doses based on INR.
	VKORC1	-1639G>A variant carriers	Alters dosage requirements. Select initial dosage, taking into account clinical and genetic factors. Monitor and adjust dosages based on INR.

Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations

back to top

Other Pharmacogenetic Single Gene Variant Analysis

Food and Drug Administration (FDA)

The Food and Drug Administration (FDA) does not list *COMT, CYP1A2, KIF6, OPRM1,* or *TYMS* in Section 1 of the Table of Pharmacogenetic Associations ("Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations").
Table of Pharmacogenetic Associations. FDA website. Updated October 26, 2022. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations.

Concert Note

There is insufficient evidence of clinical utility to support the routine use of these tests in clinical care. A search for the genes listed above in Section 1 of the Table of Pharmacogenetic Associations ("Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations") was performed in April 2025, they were not present.

back to top

Medica Central Coverage Policy

Note: The Health Plan uses the genetic testing clinical criteria developed by Concert Genetics, an industry-leader in genetic testing technology assessment and policy development.

	Committee/Source	Date(s)
Document Created:	Medical Policy Committee/Health Services Division	November 16, 2022
Revised:	Medical Policy Committee/Health Services Division	February 15, 2023
	Medical Policy Committee/Health Services Division	March 15, 2023
	Medical Policy Committee/Health Services Division	August 16, 2023
	Medical Policy Committee/Health Services Division	March 20, 2024
Reviewed:	Medical Policy Committee/Health Services Division	February 15, 2023
	Medical Policy Committee/Health Services Division	March 15, 2023
	Medical Policy Committee/Health Services Division	August 16, 2023
	Medical Policy Committee/Health Services Division	March 20, 2024

Original Effective Date: 03/01/2023

Re-Review Date(s): 12/19/2024- Concert Genetics Effective Date: January 01, 2025 (V.1.2025)

06/18/2025 - Concert Genetics Effective Date: July 01, 2025 (V.2.2025)

12/16/2025 - Concert Genetics Effective Date: January 01, 2026 (V.1.2026)

Administrative Update: