BSC_CON_2.12	Genetic Testing: Pharmacogenetics		
Original Policy Date:	February 1, 2024	**Effective Date:**	March 1, 2024
Section:	2.0 Medicine	**Page:**	Page 1 of 36

Example Test Table

The tests and associated laboratories and CPT codes contained within this document serve only as examples to help users navigate claims and corresponding coverage criteria; as such, they are not comprehensive and are not a guarantee of coverage or non-coverage. Please see the Concert Genetics Platform for a comprehensive list of registered tests.

Policy Statement Sections	Example Tests (Labs)	Common CPT Codes
Pharmacogenetic Panel Tests	GeneSight Psychotropic (Myriad Genetics)	0345U
	Professional PGX (formerly Genecept Assay) (Genomind)	81418
	PGxOne (Admera Health)	
	Genomind Professional PGX Express CORE	0175U
	Cytochrome P450 Genotyping Panel (ARUP Laboratories)	81418
	OneOme RightMed Pharmacogenomic Test (OneOme)	0347U, 0348U, 0349U, 0350U
	Focused Pharmacogenomics Panel (Mayo Clinic Laboratories)	0029U
	Warfarin Response Genotype (Mayo Medical Laboratories)	0030U
	Psych HealthPGx Panel, (RPRD Diagnostics)	0173U
	PersonalisedRX (Lab Genomics LLC)	0380U
	Serotonin Receptor Genotype (HTR2A and HTR2C), (Mayo Medical Laboratories)	0033U
Pharmacogenetic Single Gene Tests		
BCHE Variant Analysis	BCHE Single Gene Test (Blueprint Genetics)	81479
CYP2C9 Variant Analysis	Cytochrome P450 2C9 Genotype (Quest Diagnostics)	81227
CYP2C19 Variant Analysis	CYP2C19 Single Gene Test (Blueprint Genetics)	81225
CYP2D6 Variant Analysis	CYP2D6 (ARUP Laboratories)	81226
	CYP2D6 Common Variants and Copy Number (Mayo Clinic Laboratories)	0070U
	CYP2D6 Full Gene Sequencing (Mayo Clinic Laboratories)	0071U
	CYP2D6-2D7 Hybrid Gene Targeted Sequence Analysis (Mayo Clinic Laboratories)	0072U
	CYP2D7-2D6 Hybrid Gene Targeted Sequence	0073U

Policy Statement Sections	Example Tests (Labs)	Common CPT Codes
	Analysis (Mayo Clinic Laboratories)	
	CYP2D6 CYP2D6 Nonduplicated Gene Analysis (Mayo Clinic Laboratories)	0074U
	CYP2D6 5′ gene duplication/multiplication targeted sequence analysis (Mayo Clinic Laboratories)	0075U
	CYP2D6 3′ gene duplication/multiplication targeted sequence analysis (Mayo Clinic Laboratories)	0076U
CYP3A5 Variant Analysis	CYP3A5 single gene test (Blueprint Genetics)	81231
CYP4F2 Variant Analysis	CYP4F2 Single Gene Test (Blueprint Genetics)	81479
DPYD Variant Analysis	DPD 5-Fluorouracil Toxicity (Labcorp)	81232
*HLA-B**15:02 Variant Analysis	HLA-B*15:02, Carbamazepine Sensitivity (Labcorp)	81381
*HLA-B**57:01 Variant Analysis	HLA B*57:01 Abacavir Hypersensitivity (Labcorp)	81381
NAT2 Variant Analysis	NAT2 single gene test (Blueprint Genetics)	81479
TPMT and *NUDT15* Variant Analysis	Thiopurine S-Methyltransferase (*TPMT*) Genotype (Quest Diagnostics)	81335
	TPMT and *NUDT15* (ARUP Laboratories)	81335, 81306
	Thiopurine Methyltransferase (*TPMT*) and Nudix Hydrolase (*NUDT15*) Genotyping (Mayo Clinic Laboratories)	0034U
	NT (*NUDT15* and *TPMT*) genotyping panel (RPRD Diagnostics)	0169U
UGT1A1 Variant Analysis	UGT1A1 Irinotecan Toxicity (Labcorp)	81350
UGT2B17 Variant Analysis	UGT2B17 Single Gene (Fulgent Genetics)	81479
VKORC1 Variant Analysis	VKORC1 Single Gene Test (Blueprint Genetics)	81355
Other Single Gene Variant Analysis	Catechol-O-Methyltransferase (COMT) Genotype (Mayo Clinic Laboratories)	0032U
	COMT single gene test (Blueprint Genetics)	81479
	Cytochrome P450 1A2 Genotype (Mayo Clinic Laboratories)	0031U
	CYP1A2 single gene test (Blueprint Genetics)	81479
	Cardio IQ KIF6 Genotype (Quest Diagnostics)	81479

Policy Statement Sections	Example Tests (Labs)	Common CPT Codes
	Opioid Receptor, mu OPRM1 Genotype, 1 Variant (ARUP Laboratories)	81479
	SLCO1B1, 1 Variant (ARUP Laboratories)	81328
	TYMS Single Gene (Sequencing & Deletion/Duplication) (Fulgent Genetics)	81479

Policy Statement

PHARMACOGENETIC PANEL TESTS

I. The use of pharmacogenetic testing panels (81418, 0029U, 0030U, 0033U, 0173U, 0345U, 0347U, 0348U, 0349U, 0350U, 0380U) is considered **investigational*** for all indications.

*See *HLA-B**15:02 and *HLA-A**31:01 Variant Analysis and *TPMT* and *NUDT15* Variant Analysis below for coverage criteria. These tests involve analysis of more than one gene, but are not considered experimental/investigational as a panel ("panel" defined as a genetic test analyzing more than one gene)

PHARMACOGENETIC SINGLE GENE TESTS

BCHE Variant Analysis

II. *BCHE* variant analysis (81479) to determine drug metabolizer status may be considered **medically necessary** when **EITHER** of the following criteria are met:
   A. The member is being considered for or is currently undergoing treatment with mivacurium[1] (e.g., Mivacron)
   B. The member is being considered for or is currently undergoing treatment with succinylcholine[1] (e.g., Anectine, Suxamethonium)

III. *BCHE* variant analysis (81479) to determine drug metabolizer status is considered **investigational** for all other indications.

1 Commonly used as a muscle relaxant during surgery or intubation

CYP2C9 Variant Analysis

IV. *CYP2C9* variant analysis (81227) to determine drug metabolizer status may be considered **medically necessary** when **ANY** of the following criteria are met:
   A. The member is being considered for or is currently undergoing treatment with siponimod[1] (e.g., Mayzent)
   B. The member is being considered for or is currently undergoing treatment with celecoxib[2] (e.g., Celebrex, Elyxyb)
   C. The member is being considered for or is currently undergoing treatment with dronabinol[3] (e.g., Marinol, Syndros)
   D. The member is being considered for or is currently undergoing treatment with erdafitinib[4] (e.g., Balversa)
   E. The member is being considered for or is currently undergoing treatment with flurbiprofen[5] (e.g., Ansaid)
   F. The member is being considered for or is currently undergoing treatment with fosphenytoin[6] (e.g., Cerebyx, Sesquient)
   G. The member is being considered for or is currently undergoing treatment with meloxicam[7] (e.g., Anjeso, Mobic, Vivlodex, Qmiiz ODT)

H. The member is being considered for or is currently undergoing treatment with nateglinide[8] (e.g., Starlix)
I. The member is being considered for or is currently undergoing treatment with phenytoin[9] (e.g., Dilantin, Phenytek)
J. The member is being considered for or is currently undergoing treatment with piroxicam[10] (e.g., Feldene)
K. The member is being considered for or is currently undergoing treatment with warfarin[11] (e.g., Coumadin, Jantoven)

V. *CYP2C9* variant analysis (81227) 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

CYP2C19 Variant Analysis

VI. *CYP2C19* variant analysis (81225) to determine drug metabolizer status may be considered **medically necessary** when **ANY** of the following criteria are met:
A. The member meets **BOTH** of the following criteria:
1. The member is being considered for or is currently undergoing treatment with clopidogrel[1] (e.g., Plavix)
2. The member meets **all** of the following:
a. Will be undergoing percutaneous coronary intervention (PCI)
b. Has acute coronary syndromes (ACS)
c. Is at high risk for poor outcomes (e.g., urgent PCI for an ACS event, elective PCI for unprotected left main disease or last patent coronary artery)
B. The member is being considered for or is currently undergoing treatment with abrocitinib[2] (e.g., Cibinqo)
C. The member is being considered for or is currently undergoing treatment with belzutifan[3] (e.g., Welireg)
D. The member is being considered for or is currently undergoing treatment with brivaracetam[4] (e.g., Briviact, Brivajoy)
E. The member is being considered for or is currently undergoing treatment with citalopram[5] (e.g., Celexa)
F. The member is being considered for or is currently undergoing treatment with clobazam[6] (e.g., Onfi)
G. The member is being considered for or is currently undergoing treatment with flibanserin[7] (e.g., Addyi)
H. The member is being considered for or is currently undergoing treatment with pantoprazole[8] (e.g., Protonix)

VII. *CYP2C19* variant analysis (81225) to determine drug metabolizer status is considered **investigational** for all other indications.

1 Commonly prescribed after a 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

CYP2D6 Variant Analysis

VIII. *CYP2D6* variant analysis (81226, 0070U, 0071U, 0072U, 0073U, 0074U, 0075U, 0076U) to determine drug metabolizer status may be considered **medically necessary** when **ANY** of the following criteria are met:

A. The member is being considered for or is currently undergoing treatment with eliglustat[1] (e.g., Cerdelga)
B. The member is being considered for or is currently undergoing treatment with tetrabenazine[2] (e.g., Xenazine)
C. The member is being considered for or is currently undergoing treatment with amphetamine[3] (e.g., Adzenys, Dyanavel, Evekeo)
D. The member is being considered for or is currently undergoing treatment with aripiprazole[4] (e.g., Abilify, Abilify Maintena)
E. The member is being considered for or is currently undergoing treatment with aripiprazole lauroxil[5] (e.g., Aristada)
F. The member is being considered for or is currently undergoing treatment with atomoxetine[6] (e.g., Strattera)
G. The member is being considered for or is currently undergoing treatment with brexpiprazole[7] (e.g., Rexulti)
H. The member is being considered for or is currently undergoing treatment with clozapine[8] (e.g., Versacloz, FazaClo, Clozaril)
I. The member is being considered for or is currently undergoing treatment with deutetrabenazine[9] (e.g., Austedo)
J. The member is being considered for or is currently undergoing treatment with gefitinib[10] (e.g., Iressa)
K. The member is being considered for or is currently undergoing treatment with iloperidone[11] (e.g., Fanapt)
L. The member is being considered for or is currently undergoing treatment with lofexidine[12] (e.g., Lucemyra)
M. The member is being considered for or is currently undergoing treatment with meclizine[13] (e.g., Antivert, Bonine, Dramamine, Verticalm, Zentrip)
N. The member is being considered for or is currently undergoing treatment with metoclopramide[14] (e.g., Reglan)
O. The member is being considered for or is currently undergoing treatment with oliceridine[15] (e.g., Olinvyk)
P. The member is being considered for or is currently undergoing treatment with pimozide[16] (e.g., Orap)
Q. The member is being considered for or is currently undergoing treatment with pitolisant[17] (e.g., Wakix)
R. The member is being considered for or is currently undergoing treatment with propafenone[18] (e.g., Rythmol)
S. The member is being considered for or is currently undergoing treatment with thioridazine[19] (e.g., Mellaril)
T. The member is being considered for or is currently undergoing treatment with tramadol[20] (e.g., ConZip, Ultram)
U. The member is being considered for or is currently undergoing treatment with valbenazine[21] (e.g., Ingrezza)

V. The member is being considered for or is currently undergoing treatment with venlafaxine[22] (e.g., Effexor)
W. The member is being considered for or is currently undergoing treatment with vortioxetine[23] (e.g., Trintellix, Brintellix)
X. The member is being considered for or is currently undergoing treatment with codeine[24].

IX. *CYP2D6* variant analysis (81226, 0070U, 0071U, 0072U, 0073U, 0074U, 0075U, 0076U) 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

CYP3A5 Variant Analysis

X. *CYP3A5* variant analysis (81231) to determine drug metabolizer status may be 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)

XI. *CYP3A5* variant analysis (81231) 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

CYP4F2 Variant Analysis

XII. *CYP4F2* variant analysis (81479) to determine drug metabolizer status may be considered **medically necessary** when:
A. The member is being considered for or is currently undergoing treatment with warfarin[1] (e.g., Coumadin, Jantoven)

XIII. *CYP4F2* variant analysis (81479) to determine drug metabolizer status is considered **investigational** for all other indications

1 Commonly prescribed to reduce the formation of blood clots

DPYD Variant Analysis

XIV. *DPYD* variant analysis (81232) to determine drug metabolizer status may be considered **medically necessary** when **EITHER** of the following criteria are met:
- A. The member is being considered for or is currently undergoing treatment with fluorouracil[1] (e.g., Adrucil)
- B. The member is being considered for or is currently undergoing treatment with capecitabine[1] (e.g., Xeloda)

XV. *DPYD* variant analysis (81232) 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

*HLA-B*15:02* Variant Analysis

XVI. *HLA-B*15:02* variant analysis (81381) to determine drug metabolizer status may be considered **medically necessary** when **ANY** of the following criteria are met:
- A. The member is being considered for or is currently undergoing treatment with any carbamazepine containing therapy[1] (e.g., Tegretol, Carbatrol, Epitol, Equetro)
- B. The member is being considered for or is currently undergoing treatment with phenytoin[2] (e.g., Dilantin, Phenytek)
- C. The member is being considered for or is currently undergoing treatment with fosphenytoin[2] (e.g., Cerebyx, Sesquient)

XVII. *HLA-B*15:02* variant analysis (81381) 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

*HLA-B*57:01* Variant Analysis

XVIII. *HLA-B*57:01* variant analysis (81381) to determine drug metabolizer status may be considered **medically necessary** when:
- A. The member is being considered for or is currently undergoing treatment with abacavir[1] (e.g., Ziagen).

XIX. *HLA-B*57:01* variant analysis (81381) to determine drug metabolizer status is considered **investigational** for all other indications.

1 Commonly prescribed for individuals with HIV

NAT2 Variant Analysis

XX. *NAT2* variant analysis (81479) to determine drug metabolizer status may be 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)

XXI. *NAT2* variant analysis (81479) to determine drug metabolizer status is considered **investigational** for all other indications.

1 Commonly prescribed for treatment of Lambert-Eaton myasthenic syndrome

TPMT and *NUDT15* Variant Analysis

XXII. *TMPT* and *NUDT15* variant analysis (81306, 81335, 0034U, 0169U) to determine drug metabolizer status may be considered **medically necessary** when **ANY** of the following criteria are met:
- A. The member is being considered for or is currently undergoing treatment with azathioprine[1] (e.g., Imuran and Azasan)
- B. The member is being considered for or is currently undergoing treatment with mercaptopurine[2] (e.g., Purinethol and Purixan)
- C. The member is being considered for or is currently undergoing treatment with thioguanine[3] (e.g., Tabloid)
- D. The member is on thiopurine therapy and has had abnormal complete blood count results that do not respond to dose reduction.

XXIII. *TPMT* and *NUDT15* variant analysis (81306, 81335, 0034U, 0169U) 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

UGT1A1 Variant Analysis

XXIV. *UGT1A1* variant analysis (81350) to determine drug metabolizer status may be considered **medically necessary** when **ANY** of the following criteria are met:
- A. The member is being considered for or is currently undergoing treatment with irinotecan[1] (e.g., Onivyde, Camptosar)
- B. The member is being considered for or is currently undergoing treatment with belinostat[2] (e.g., Beleodaq)
- C. The member is being considered for or is currently undergoing treatment with sacituzumab govitecan-hziy[3] (e.g., Trodelvy)

XXV. *UGT1A1* variant analysis (81350) to determine drug metabolizer status is considered **investigational** for all other indications.

1 Commonly prescribed for treatment of colon and rectal cancers

2 Commonly prescribed for treatment of peripheral T-cell lymphoma

3 Commonly prescribed for treatment of breast and urothelial cancers

UGT2B17 Variant Analysis

XXVI. *UGT2B17* variant analysis (81479) to determine drug metabolizer status may be considered **medically necessary** when:
- A. The member is being considered for or is currently undergoing treatment with belzutifan[1] (e.g., Welireg)

XXVII. *UGT2B17* variant analysis (81479) 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

VKORC1 Variant Analysis

XXVIII. *VKORC1* variant analysis (81355) to determine drug metabolizer status may be considered **medically necessary** when:

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

XXIX. *VKORC1* variant analysis (81355) to determine drug metabolizer status is considered **investigational** for all other indications

1 Commonly prescribed to reduce the formation of blood clots

Other Single Gene Variant Analysis

XXX. Variant analysis of all other genes for drug metabolizer status is considered **investigational**, including but not limited to **ANY** of the following:
A. *COMT* (0032U, 81479)
B. *CYP1A2* (0031U, 81479)
C. *KIF6* (81479)
D. *OPRM1* (81479)
E. *SLCO1B1* (81328)
F. *TYMS* (81479)

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

- N/A

Description

Pharmacogenetic tests are germline genetic tests that are developed to aid in assessing an individual's response to a drug treatment or to predict the risk of toxicity from a specific drug treatment. Testing may be performed prior to initiation of treatment to identify if an individual has genetic variants that could either affect response to a particular drug and/or increase the risk of adverse drug reactions. Testing may also be performed during treatment to assess an individual who has had an adverse drug reaction or to assess response to treatment. Test methodology includes genotyping and single nucleotide variant testing.

Related Policies

This policy document provides coverage for tests that determine the dosage of or the selection of a specific drug based on pharmacogenetic testing. For other related testing, please refer to:

- ***Oncology: Molecular Analysis of Solid Tumors and Hematologic Malignancies*** for coverage criteria related to DNA testing of a solid tumor or a blood cancer.
- ***Genetic Testing: Hematologic Conditions (non-cancerous)*** for coverage criteria related to diagnostic testing for non-cancerous genetic blood disorders *(to be published)*
- ***Genetic Testing: Multisystem Inherited Disorders, Intellectual Disability, and Developmental Delay*** for coverage criteria related to diagnostic testing for cystic fibrosis, and related therapies *(to be published)*
- ***Genetic Testing: Metabolic, Endocrine, and Mitochondrial Disorders*** for coverage criteria related to *MTHFR* testing. *(to be published)*
- ***Genetic Testing: General Approach to Genetic and Molecular Testing*** for coverage criteria related to pharmacogenetic testing that are not specifically discussed in this or other specific policies.

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

- N/A

Rationale

BACKGROUND AND RATIONALE

Pharmacogenetic Panel Testing

There are no professional society guidelines that address the clinical utility of large pharmacogenetic testing panels for the general population or for a specific population. The US Food and Drug Administration (FDA) also does not address the usage of pharmacogenetic panels.

There are several recent studies that investigated the usefulness of pharmacogenetic panels [for example, Greden et al (2019), Perlis et al (2020), Shan et al (2019), Tiwari et al (2022), Oslin (2022)]. However, these studies had different designs and often conflicting results regarding clinical utility, making it difficult to determine whether there is clinical utility for these types of tests.

A rapid review and meta-analysis by Bunka et al (2023) of 10 randomized controlled trials to evaluate pharmacogenomic-guided care for major depression showed that, while there is likely beneficial effects to adults with moderate to severe major depressive disorder utilizing pharmacogenomic panels, there is "very low certainty in the magnitude of effect." (p. 1) This analysis also noted the "high risk of bias and inconsistency between trials." (p. 1)

There are several single gene pharmacogenetic tests in which the FDA describes the clinical utility of the test results for a given gene/drug/testing indication. These are outlined below.

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

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
			administer test dose to assess sensitivity and administer cautiously via slow infusion.

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 metabolizers)	May result in higher systemic 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 an alternative to carbamazepine in patients who are CYP2C9*3 carriers. Genotyping

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
			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.

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 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.
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.

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
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.

CYP2D6 Variant Analysis

National Comprehensive Cancer Network (NCCN)

NCCN breast cancer guidelines (4.2023) recommend against *CYP2D6* genotype testing for women being considered for tamoxifen treatment. (p. DCIS-2 and p. BINV-K)

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 lower starting dosage or use 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.
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.

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
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).
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 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.
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.

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
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.

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.

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.

DPYD 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 *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

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
			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.

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 vigilance and patient management.

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.

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.
Amifampridine Phosphate	NAT2	poor metabolizers	Results in higher systemic concentrations. Use lowest recommended starting dosage (15 mg/day) and monitor for adverse reactions.

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 (myelosuppression). Initial dosages should be reduced in poor metabolizers; poor metabolizers generally tolerate 10% or less of the recommended

Drug	Gene	Affected Subgroups	Description of Gene-Drug Interaction
			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.

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.

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.

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.

Other Single Gene Variant Analysis

The Food and Drug Administration (FDA) does not list *COMT, CYP1A2, KIF6, OPRM1, SLCO1B1,* or *TYMS* in Section 1 of the Table of Pharmacogenetic Associations ("Pharmacogenetic Associations for which the Data Support Therapeutic Management Recommendations").

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2. Perlis RH, Dowd D,Fava M, Lencz T, Krause DS. Randomized,controlled, participant- and rater-blind trial of pharmacogenomic test-guided treatment versus treatment as usual for major depressive disorder. Depress Anxiety. 2020;37(9): 834-841. doi:10.1002/da.23029
3. Shan X, Zhao W, Qiu Y,et al. Preliminary clinical investigation of combinatorial pharmacogenomic testing for the optimized treatment of depression: a randomized single-blind study. Front Neurosci. 2019;13:960. doi:10.3389/fnins.2019.00960
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5. Oslin DW, Lynch KG, Shih MC, et al. Effect of Pharmacogenomic Testing for Drug-Gene Interactions on Medication Selection and Remission of Symptoms in Major Depressive Disorder: The PRIME Care Randomized Clinical Trial. JAMA. 2022;328(2):151-161. doi:10.1001/jama.2022.9805
6. 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.
7. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Breast Cancer. Version 4.2023. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf

8. Table of Pharmacogenetic Associations. (2022, October 26). FDA. https://www.fda.gov/medical-devices/precision-medicine/table-pharmacogenetic-associations. Accessed April 28, 2023.

Documentation for Clinical Review

Please provide the following documentation:

- Name of the test being requested or the Concert Genetics GTU identifier.
  The Concert Genetics GTU can be found at https://app.concertgenetics.com
- CPT codes to be billed for the particular genetic test (GTU required for unlisted codes)
- History and physical and/or consultation notes including:
  - Clinical findings:
    - Signs/symptoms leading to a suspicion of genetic condition
    - Family history if applicable
  - Prior evaluation/treatment:
    - Previous test results (i.e., imagining, lab work, etc.) related to reason for genetic testing
    - Family member's genetic test result, if applicable
  - Rationale
    - Reason for performing test
    - How test result will impact clinical decision making

Post Service (in addition to the above, please include the following):

- Results/reports of tests performed

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	81225	CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *8, *17)
	81226	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN)
	81227	CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *5, *6)
	81231	CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *4, *5, *6, *7)
	81232	DPYD (dihydropyrimidine dehydrogenase) (e.g., 5-fluorouracil/5-FU and capecitabine drug metabolism), gene analysis, common variant(s) (e.g., *2A, *4, *5, *6)

Type	Code	Description
	81306	NUDT15 (nudix hydrolase 15) (eg, drug metabolism) gene analysis, common variant(s) (e.g., *2, *3, *4, *5, *6)
	81328	SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (e.g., adverse drug reaction), gene analysis, common variant(s) (e.g., *5)
	81335	TPMT (thiopurine S-methyltransferase) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3)
	81350	UGT1A1 (UDP glucuronosyltransferase 1 family, polypeptide A1) (e.g., drug metabolism, hereditary unconjugated hyperbilirubinemia [Gilbert syndrome]) gene analysis, common variants (e.g., *28, *36, *37)
	81355	VKORC1 (vitamin K epoxide reductase complex, subunit 1) (e.g., warfarin metabolism), gene analysis, common variant(s) (e.g., -1639G>A, c.173+1000C>T)
	81381	HLA Class I typing, high resolution (i.e., alleles or allele groups); one allele or allele group (e.g., B*57:01P), each
	81418	Drug metabolism (e.g., pharmacogenomics) genomic sequence analysis panel, must include testing of at least 6 genes, including CYP2C19, CYP2D6, and CYP2D6 duplication/deletion analysis
	81479	Unlisted molecular pathology procedure
	0029U	Drug metabolism (adverse drug reactions and drug response), targeted sequence analysis (i.e., CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, SLCO1B1, VKORC1 and rs12777823)
	0030U	Drug metabolism (warfarin drug response), targeted sequence analysis (i.e., CYP2C9, CYP4F2, VKORC1, rs12777823)
	0031U	CYP1A2 (cytochrome P450 family 1, subfamily A, member 2)(e.g., drug metabolism) gene analysis, common variants (i.e., *1F, *1K, *6, *7)
	0032U	COMT (catechol-O-methyltransferase)(drug metabolism) gene analysis, c.472G>A (rs4680) variant
	0033U	HTR2A (5-hydroxytryptamine receptor 2A), HTR2C (5-hydroxytryptamine receptor 2C) (e.g., citalopram metabolism) gene analysis, common variants (i.e., HTR2A rs7997012 [c.614-2211T>C], HTR2C rs3813929 [c.-759C>T] and rs1414334 [c.551-3008C>G])
	0034U	TPMT (thiopurine S-methyltransferase), NUDT15 (nudix hydroxylase 15)(e.g., thiopurine metabolism), gene analysis, common variants (i.e., TPMT *2, *3A, *3B, *3C, *4, *5, *6, *8, *12; NUDT15 *3, *4, *5)
	0070U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism) gene analysis, common and select rare variants (i.e., *2, *3, *4, *4N, *5, *6, *7, *8, *9, *10, *11, *12, *13, *14A, *14B, *15, *17, *29, *35, *36, *41, *57, *61, *63, *68, *83, *xN)
	0071U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism) gene analysis, full gene sequence (List separately in addition to code for primary procedure)
	0072U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism) gene analysis, targeted sequence analysis (i.e., CYP2D6-2D7 hybrid gene) (List separately in addition to code for primary procedure)
	0073U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism) gene analysis, targeted sequence analysis (i.e., CYP2D7-2D6 hybrid gene) (List separately in addition to code for primary procedure)
	0074U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism) gene analysis, targeted sequence analysis (i.e., non-

Type	Code	Description
		duplicated gene when duplication/multiplication is trans) (List separately in addition to code for primary procedure)
	0075U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism) gene analysis, targeted sequence analysis (i.e., 5' gene duplication/multiplication) (List separately in addition to code for primary procedure)
	0076U	CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (e.g., drug metabolism) gene analysis, targeted sequence analysis (i.e., 3' gene duplication/ multiplication) (List separately in addition to code for primary procedure)
	0169U	NUDT15 (nudix hydrolase 15) and TPMT (thiopurine S-methyltransferase) (e.g., drug metabolism) gene analysis, common variants
	0173U	Psychiatry (i.e., depression, anxiety), genomic analysis panel, includes variant analysis of 14 genes
	0175U	Psychiatry (e.g., depression, anxiety), genomic analysis panel, variant analysis of 15 genes
	0345U	Psychiatry (e.g., depression, anxiety, attention deficit hyperactivity disorder [ADHD]), genomic analysis panel, variant analysis of 15 genes, including deletion/duplication analysis of CYP2D6
	0347U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 16 gene report, with variant analysis and reported phenotypes
	0348U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 25 gene report, with variant analysis and reported phenotypes
	0349U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 27 gene report, with variant analysis, including reported phenotypes and impacted gene-drug interactions
	0350U	Drug metabolism or processing (multiple conditions), whole blood or buccal specimen, DNA analysis, 27 gene report, with variant analysis and reported phenotypes
	0380U	Drug metabolism (adverse drug reactions and drug response), targeted sequence analysis, 20 gene variants and CYP2D6 deletion or duplication analysis with reported genotype and phenotype
	0423U	Psychiatry (e.g., depression, anxiety), genomic analysis panel, including variant analysis of 26 genes, buccal swab, report including metabolizer status and risk of drug toxicity by condition ***(Code effective 1/1/2024)***
	0434U	Drug metabolism (adverse drug reactions and drug response), genomic analysis panel, variant analysis of 25 genes with reported phenotypes ***(Code effective 1/1/2024)***
	0437U	Psychiatry (anxiety disorders), mRNA, gene expression profiling by RNA sequencing of 15 biomarkers, whole blood, algorithm reported as predictive risk score ***(Code effective 1/1/2024)***
	0438U	Drug metabolism (adverse drug reactions and drug response), buccal specimen, gene-drug interactions, variant analysis of 33 genes, including deletion/duplication analysis of CYP2D6, including reported phenotypes and impacted gene-drug interactions ***(Code effective 1/1/2024)***
HCPCS	None	

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
02/01/2024	New policy.
03/01/2024	Coding update.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local

standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE	**AFTER** Blue font: Verbiage Changes/Additions
New Policy **Policy Statement:** N/A	**Genetic Testing: Pharmacogenetics BSC_CON_2.12** **Policy Statement:** **PHARMACOGENETIC PANEL TESTS** I. The use of pharmacogenetic testing panels (81418, 0029U, 0030U, 0033U, 0173U, 0345U, 0347U, 0348U, 0349U, 0350U, 0380U) is considered **investigational*** for all indications. *See *HLA-B**15:02 and *HLA-A**31:01 Variant Analysis and *TPMT* and *NUDT15* Variant Analysis below for coverage criteria. These tests involve analysis of more than one gene, but are not considered experimental/investigational as a panel ("panel" defined as a genetic test analyzing more than one gene) **PHARMACOGENETIC SINGLE GENE TESTS** ***BCHE* Variant Analysis** II. *BCHE* variant analysis (81479) to determine drug metabolizer status may be considered **medically necessary** when **EITHER** of the following criteria are met: A. The member is being considered for or is currently undergoing treatment with mivacurium[1] (e.g., Mivacron) B. The member is being considered for or is currently undergoing treatment with succinylcholine[1] (e.g., Anectine, Suxamethonium) III. *BCHE* variant analysis (81479) to determine drug metabolizer status is considered **investigational** for all other indications. 1 Commonly used as a muscle relaxant during surgery or intubation

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	***CYP2C9* Variant Analysis** IV. *CYP2C9* variant analysis (81227) to determine drug metabolizer status may be considered **medically necessary** when **ANY** of the following criteria are met: A. The member is being considered for or is currently undergoing treatment with siponimod[1] (e.g., Mayzent) B. The member is being considered for or is currently undergoing treatment with celecoxib[2] (e.g., Celebrex, Elyxyb) C. The member is being considered for or is currently undergoing treatment with dronabinol[3] (e.g., Marinol, Syndros) D. The member is being considered for or is currently undergoing treatment with erdafitinib[4] (e.g., Balversa) E. The member is being considered for or is currently undergoing treatment with flurbiprofen[5] (e.g., Ansaid) F. The member is being considered for or is currently undergoing treatment with fosphenytoin[6] (e.g., Cerebyx, Sesquient) G. The member is being considered for or is currently undergoing treatment with meloxicam[7] (e.g., Anjeso, Mobic, Vivlodex, Qmiiz ODT) H. The member is being considered for or is currently undergoing treatment with nateglinide[8] (e.g., Starlix) I. The member is being considered for or is currently undergoing treatment with phenytoin[9] (e.g., Dilantin, Phenytek) J. The member is being considered for or is currently undergoing treatment with piroxicam[10] (e.g., Feldene) K. The member is being considered for or is currently undergoing treatment with warfarin[11] (e.g., Coumadin, Jantoven) V. *CYP2C9* variant analysis (81227) 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

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	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 ***CYP2C19* Variant Analysis** VI. *CYP2C19* variant analysis (81225) to determine drug metabolizer status may be considered **medically necessary** when **ANY** of the following criteria are met: A. The member meets **BOTH** of the following criteria: 1. The member is being considered for or is currently undergoing treatment with clopidogrel[1] (e.g., Plavix) 2. The member meets **all** of the following: a. Will be undergoing percutaneous coronary intervention (PCI) b. Has acute coronary syndromes (ACS) c. Is at high risk for poor outcomes (e.g., urgent PCI for an ACS event, elective PCI for unprotected left main disease or last patent coronary artery) B. The member is being considered for or is currently undergoing treatment with abrocitinib[2] (e.g., Cibinqo) C. The member is being considered for or is currently undergoing treatment with belzutifan[3] (e.g., Welireg) D. The member is being considered for or is currently undergoing treatment with brivaracetam[4] (e.g., Briviact, Brivajoy) E. The member is being considered for or is currently undergoing treatment with citalopram[5] (e.g., Celexa) F. The member is being considered for or is currently undergoing treatment with clobazam[6] (e.g., Onfi) G. The member is being considered for or is currently undergoing treatment with flibanserin[7] (e.g., Addyi) H. The member is being considered for or is currently undergoing treatment with pantoprazole[8] (e.g., Protonix)

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	VII. *CYP2C19* variant analysis (81225) to determine drug metabolizer status is considered **investigational** for all other indications. 1 Commonly prescribed after a 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 ***CYP2D6* Variant Analysis** VIII. *CYP2D6* variant analysis (81226, 0070U, 0071U, 0072U, 0073U, 0074U, 0075U, 0076U) to determine drug metabolizer status may be considered **medically necessary** when **ANY** of the following criteria are met: A. The member is being considered for or is currently undergoing treatment with eliglustat[1] (e.g., Cerdelga) B. The member is being considered for or is currently undergoing treatment with tetrabenazine[2] (e.g., Xenazine) C. The member is being considered for or is currently undergoing treatment with amphetamine[3] (e.g., Adzenys, Dyanavel, Evekeo) D. The member is being considered for or is currently undergoing treatment with aripiprazole[4] (e.g., Abilify, Abilify Maintena) E. The member is being considered for or is currently undergoing treatment with aripiprazole lauroxil[5] (e.g., Aristada) F. The member is being considered for or is currently undergoing treatment with atomoxetine[6] (e.g., Strattera) G. The member is being considered for or is currently undergoing treatment with brexpiprazole[7] (e.g., Rexulti) H. The member is being considered for or is currently undergoing treatment with clozapine[8] (e.g., Versacloz, FazaClo, Clozaril)

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	I. The member is being considered for or is currently undergoing treatment with deutetrabenazine[9] (e.g., Austedo) J. The member is being considered for or is currently undergoing treatment with gefitinib[10] (e.g., Iressa) K. The member is being considered for or is currently undergoing treatment with iloperidone[11] (e.g., Fanapt) L. The member is being considered for or is currently undergoing treatment with lofexidine[12] (e.g., Lucemyra) M. The member is being considered for or is currently undergoing treatment with meclizine[13] (e.g., Antivert, Bonine, Dramamine, Verticalm, Zentrip) N. The member is being considered for or is currently undergoing treatment with metoclopramide[14] (e.g., Reglan) O. The member is being considered for or is currently undergoing treatment with oliceridine[15] (e.g., Olinvyk) P. The member is being considered for or is currently undergoing treatment with pimozide[16] (e.g., Orap) Q. The member is being considered for or is currently undergoing treatment with pitolisant[17] (e.g., Wakix) R. The member is being considered for or is currently undergoing treatment with propafenone[18] (e.g., Rythmol) S. The member is being considered for or is currently undergoing treatment with thioridazine[19] (e.g., Mellaril) T. The member is being considered for or is currently undergoing treatment with tramadol[20] (e.g., ConZip, Ultram) U. The member is being considered for or is currently undergoing treatment with valbenazine[21] (e.g., Ingrezza) V. The member is being considered for or is currently undergoing treatment with venlafaxine[22] (e.g., Effexor) W. The member is being considered for or is currently undergoing treatment with vortioxetine[23] (e.g., Trintellix, Brintellix) X. The member is being considered for or is currently undergoing treatment with codeine[24].

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	IX. *CYP2D6* variant analysis (81226, 0070U, 0071U, 0072U, 0073U, 0074U, 0075U, 0076U) 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

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	***CYP3A5* Variant Analysis** X. *CYP3A5* variant analysis (81231) to determine drug metabolizer status may be 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) XI. *CYP3A5* variant analysis (81231) 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 ***CYP4F2* Variant Analysis** XII. *CYP4F2* variant analysis (81479) to determine drug metabolizer status may be considered **medically necessary** when: A. The member is being considered for or is currently undergoing treatment with warfarin[1] (e.g., Coumadin, Jantoven) XIII. *CYP4F2* variant analysis (81479) to determine drug metabolizer status is considered **investigational** for all other indications 1 Commonly prescribed to reduce the formation of blood clots ***DPYD* Variant Analysis** XIV. *DPYD* variant analysis (81232) to determine drug metabolizer status may be considered **medically necessary** when **EITHER** of the following criteria are met: A. The member is being considered for or is currently undergoing treatment with fluorouracil[1] (e.g., Adrucil) B. The member is being considered for or is currently undergoing treatment with capecitabine[1] (e.g., Xeloda) XV. *DPYD* variant analysis (81232) to determine drug metabolizer status is considered **investigational** for all other indications.

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	1 Commonly prescribed for individuals diagnosed with colorectal, breast, and aerodigestive tract tumors ***HLA-B*15:02* Variant Analysis** XVI. *HLA-B*15:02* variant analysis (81381) to determine drug metabolizer status may be considered **medically necessary** when **ANY** of the following criteria are met: A. The member is being considered for or is currently undergoing treatment with any carbamazepine containing therapy[1] (e.g., Tegretol, Carbatrol, Epitol, Equetro) B. The member is being considered for or is currently undergoing treatment with phenytoin[2] (e.g., Dilantin, Phenytek) C. The member is being considered for or is currently undergoing treatment with fosphenytoin[2] (e.g., Cerebyx, Sesquient) **XVII.** *HLA-B*15:02* variant analysis (81381) 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 ***HLA-B*57:01* Variant Analysis** XVIII. *HLA-B*57:01* variant analysis (81381) to determine drug metabolizer status may be considered **medically necessary** when: A. The member is being considered for or is currently undergoing treatment with abacavir[1] (e.g., Ziagen). XIX. *HLA-B*57:01* variant analysis (81381) to determine drug metabolizer status is considered **investigational** for all other indications. 1 Commonly prescribed for individuals with HIV ***NAT2* Variant Analysis** XX. *NAT2* variant analysis (81479) to determine drug metabolizer status may be considered **medically necessary** when:

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	A. The member is being considered for or is currently undergoing treatment with amifampridine/amifampridine phosphate[1] (e.g., Firdapse, Ruzurgi) XXI. *NAT2* variant analysis (81479) to determine drug metabolizer status is considered **investigational** for all other indications. 1 Commonly prescribed for treatment of Lambert-Eaton myasthenic syndrome ***TPMT* and *NUDT15* Variant Analysis** XXII. *TMPT* and *NUDT15* variant analysis (81306, 81335, 0034U, 0169U) to determine drug metabolizer status may be considered **medically necessary** when **ANY** of the following criteria are met: A. The member is being considered for or is currently undergoing treatment with azathioprine[1] (e.g., Imuran and Azasan) B. The member is being considered for or is currently undergoing treatment with mercaptopurine[2] (e.g., Purinethol and Purixan) C. The member is being considered for or is currently undergoing treatment with thioguanine[3] (e.g., Tabloid) D. The member is on thiopurine therapy and has had abnormal complete blood count results that do not respond to dose reduction. XXIII. *TPMT* and *NUDT15* variant analysis (81306, 81335, 0034U, 0169U) 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 ***UGT1A1* Variant Analysis** XXIV. *UGT1A1* variant analysis (81350) to determine drug metabolizer status may be considered **medically necessary** when **ANY** of the following criteria are met:

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	A. The member is being considered for or is currently undergoing treatment with irinotecan[1] (e.g., Onivyde, Camptosar) B. The member is being considered for or is currently undergoing treatment with belinostat[2] (e.g., Beleodaq) C. The member is being considered for or is currently undergoing treatment with sacituzumab govitecan-hziy[3] (e.g., Trodelvy) XXV. *UGT1A1* variant analysis (81350) to determine drug metabolizer status is considered **investigational** for all other indications. 1 Commonly prescribed for treatment of colon and rectal cancers 2 Commonly prescribed for treatment of peripheral T-cell lymphoma 3 Commonly prescribed for treatment of breast and urothelial cancers ***UGT2B17* Variant Analysis** XXVI. *UGT2B17* variant analysis (81479) to determine drug metabolizer status may be considered **medically necessary** when: A. The member is being considered for or is currently undergoing treatment with belzutifan[1] (e.g., Welireg) XXVII. *UGT2B17* variant analysis (81479) 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 ***VKORC1* Variant Analysis** XXVIII. *VKORC1* variant analysis (81355) to determine drug metabolizer status may be considered **medically necessary** when: A. The member is being considered for or is currently undergoing treatment with warfarin[1] (e.g., Coumadin, Jantoven) XXIX. *VKORC1* variant analysis (81355) to determine drug metabolizer status is considered **investigational** for all other indications 1 Commonly prescribed to reduce the formation of blood clots

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	Other Single Gene Variant Analysis XXX. Variant analysis of all other genes for drug metabolizer status is considered **investigational**, including but not limited to **ANY** of the following: A. *COMT* (0032U, 81479) B. *CYP1A2* (0031U, 81479) C. *KIF6* (81479) D. *OPRM1* (81479) E. *SLCO1B1* (81328) F. *TYMS* (81479)