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# Cytochrome P450 Genotype-Guided Treatment Strategy Corporate Medical Policy

File Name: Cytochrome P450 Genotype-Guided Treatment Strategy
File Code: UM.SPSVC.25
Origination: 05/2019 New Policy
Last Review: 05/2019
Next Review: 05/2020
Effective Date: 10/01/2019

## Description/Summary

The cytochrome P450 (CYP450) family is involved in the metabolism of many currently administered drugs, and genetic variants in cytochrome P450 are associated with altered metabolism of many drugs. Testing for cytochrome P450 variants may assist in selecting and dosing drugs affected by these genetic variants.

## Policy

### Coding Information
### Click the links below for attachments, coding tables & instructions.
Attachment I

### When a service may be considered medically necessary

*CYP2D6* genotyping to determine drug metabolizer status may be considered **medically necessary** for patients:

- With Gaucher disease being considered for treatment with eliglustat; OR
- With Huntington disease being considered for treatment with tetrabenazine in a dosage greater than 50 mg per day.

### When a service is considered investigational

*CYP450* genotyping for the purpose of aiding in the choice of drug or dose to increase efficacy and/or avoid toxicity for the following drugs is considered **investigational**, for all other indications. Investigational uses include the following:

- selection or dosage of codeine
- dosing of efavirenz and other antiretroviral therapies for HIV infection
- dosing of immunosuppressants for organ transplantation
- selection or dosing of ß-blockers (eg, metoprolol)
- dosing and management of antitubercular medications.
- Dosing and managing warfarin
- Management of tamoxifen for women at high risk for, or with breast cancer
- Dosing and management of medication for treatment of mental health conditions

*CYP450* genotyping for the purpose of aiding in the choice of clopidogrel vs alternative antiplatelet agents, or in decisions on the optimal dosing for clopidogrel, is considered **investigational**.

The use of genetic testing panels that include multiple *CYP450* variants is considered **investigational**.

CYP450 genotyping is considered **investigational** for all other indications

**Coding**

There is specific CPT coding for this testing:

81225 *CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19)* (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17)

81226 *CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6)* (eg, drug metabolism), gene analysis, common variants (eg, *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)* (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *5, *6).
There are also tier 2 CPT codes that include cytochrome P450 testing:

81230 CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis, common variant(s) (eg, *2, *22) (effective 01/01/18)

81231 CYP3A5 (cytochrome P450, family 3, subfamily A member 5) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *7) (effective 01/01/18)

81402 Molecular pathology procedure, Level 3 (eg, >10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants of 1 exon, loss of heterozygosity [LOH], uniparental disomy [UPD]) includes - *CYP21A2 (cytochrome P450, family 21, subfamily A, polypeptide 2)* (eg, congenital adrenal hyperplasia, 21-hydroxylase deficiency), common variants (eg, IVS2-13G, P30L, I172N, exon 6 mutation cluster [I235N, V236E, M238K], V281L, L307FfsX6, Q318X, R356W, P453S, G110VfsX21, 30- kb deletion variant)

81404 Molecular pathology procedure, Level 5 (eg, analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat bySouthern blot analysis) includes - *CYP1B1 (cytochrome P450, family 1, subfamily B, polypeptide 1)* (eg, primary congenital glaucoma), full gene sequence

81405 Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons, regionally targeted cytogenomic array analysis) includes - *CYP11B1 (cytochrome P450, family 11, subfamily B, polypeptide 1)* (eg, congenital adrenal hyperplasia), full gene sequence *CYP17A1 (cytochrome P450, family 17, subfamily A, polypeptide 1)* (eg, congenital adrenal hyperplasia), full gene sequence *CYP21A2 (cytochrome P450, family 21, subfamily A, polypeptide 2)* (eg, steroid 21-hydroxylase isoform, congenital adrenal hyperplasia), full gene sequence.

PLA code effective January 1, 2018 include:

0029U Drug metabolism (adverse drug reactions and drug response), targeted sequence analysis (ie, CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, SLCO1B1, VKORC1 and rs12777823) (Focused Pharmacogenomics Panel)

0031U CYP1A2 (cytochrome P450 family 1, subfamily A, member 2)(eg, drug metabolism) gene analysis, common variants (ie, *1F, *1K, *6, *7) (Cytochrome P450 1A2 Genotype).

## Reference Resources


1. Genzyme. Highlights of Prescribing Information: Cerdelga (eliglustat). 2014; http://www.cerdelga.com/pdf/cerdelga_prescribing_information.pdf. Accessed May 24, 2018.
2. Food and Drug Administration. Highlights of Prescribing Information: Xenazine (tetrabenazine). 2015; https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/021894s010lbl.pdf. Accessed May 24, 2018.
3. FDA statement from Douglas Throckmorton, M.D., deputy center director for regulatory programs, Center for Drug Evaluation and Research, on new warnings about the use of codeine and tramadol in children & nursing mothers. 2017;

https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm553285.htm. Accessed May 24, 2018.
4. BCBSA Medical Policy 2.04.38 Cytochrome P450 Genotype Guided Treatment Strategy. Last review June 2018
5. BCBSA Medical Policy 2.04.110 Genetic Testing for Diagnosis and Management of Mental Health Conditions. Last Review June 2018
6. BCBSA Medical Policy 2.04.51 Genotype-Guided Tamoxifen Treatment. Last review July 2018
7. BCBSA Medical Policy 2.04.48 Genotype-Guided Warfarin Dosing. Last review June 2018
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### Document Precedence

Blue Cross and Blue Shield of Vermont (BCBSVT) Medical Policies are developed to provide clinical guidance and are based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. The applicable group/individual contract and member certificate language, or employer's benefit plan if an ASO group, determines benefits that are in effect at the time of service. Since medical practices and knowledge are constantly evolving, BCBSVT reserves the right to review and revise its medical policies periodically. To the extent that there may be any conflict between medical policy and contract/employer benefit plan language, the member's contract/employer benefit plan language takes precedence.

### Audit Information

BCBSVT reserves the right to conduct audits on any provider and/or facility to ensure compliance with the guidelines stated in the medical policy. If an audit identifies instances of non-compliance with this medical policy, BCBSVT reserves the right to recoup all non-compliant payments.

## Administrative and Contractual Guidance

### Benefit Determination Guidance

Prior approval is required and benefits are subject to all terms, limitations and conditions of the subscriber contract.

Incomplete authorization requests may result in a delay of decision pending submission of missing information. To be considered compete, see policy guidelines above.

NEHP/ABNE members may have different benefits for services listed in this policy. To confirm benefits, please contact the customer service department at the member's health plan.

Federal Employee Program (FEP): Members may have different benefits that apply. For further information please contact FEP customer service or refer to the FEP Service Benefit Plan Brochure. It is important to verify the member's benefits prior to providing the service to determine if benefits are available or if there is a specific exclusion in the member's benefit.

Coverage varies according to the member's group or individual contract. Not all groups are required to follow the Vermont legislative mandates. Member Contract language takes precedence over medical policy when there is a conflict.

If the member receives benefits through an Administrative Services Only (ASO) group, benefits may vary or not apply. To verify benefit information, please refer to the member's employer benefit plan documents or contact the customer service department. Language in the employer benefit plan documents takes precedence over medical policy when there is a conflict.

## Policy Implementation/Update information

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| 05/2019 | New Policy. Prior authorization required for codes: 81226, 0028U, 0029U. |

## Eligible providers

Qualified healthcare professionals practicing within the scope of their license(s).

## Approved by BCBSVT Medical Directors — Date Approved

Joshua Plavin, MD, MPH, MBA
Chief Medical Officer

Kate McIntosh, MD, MBA, FAAP
Senior Medical Director

Attachment I

| Code Type | Number | Brief Description | Policy Instructions |
|---|---|---|---|
| **The following codes will be considered medically necessary if the above criteria is met.** | | | |

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|---|---|---|---|
| CPT® | 81226 | CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *9, *10, *17, *19, *29, *35, *41, *1XN, *2XN, *4XN) | Require Prior Authorization |
| CPT® | 0029U | Drug metabolism (adverse drug reactions and drug response), targeted sequence analysis (ie, CYP1A2, CYP2C19, CYP2C9, CYP2D6, CYP3A4, CYP3A5, CYP4F2, SLCO1B1, VKORC1 and rs12777823) | Require Prior Authorization |
| **The following codes will be denied as Not Medically Necessary, Contract Exclusions or Investigational** | | | |
| CPT® | 81225 | CYP2C19 (cytochrome P450, family 2, subfamily C, polypeptide 19) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *8, *17) | Investigational |
| CPT® | 81227 | CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *5, *6) | Investigational |
| CPT® | 81230 | CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis, common variant(s) (eg, *2, *22) | Investigational |
| CPT® | 81231 | CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *7) | Investigational |
| CPT® | 81402 | MOLECULAR PATHOLOGY PROCEDURE LEVEL 3 | Investigational |
| CPT® | 81404 | MOLECULAR PATHOLOGY PROCEDURE LEVEL 5 | Investigational |
| CPT® | 81405 | MOLECULAR PATHOLOGY PROCEDURE LEVEL 6 | Investigational |
| CPT® | 0031U | CYP1A2 (cytochrome P450 family 1, subfamily A, member 2) (eg, drug metabolism) gene analysis, common variants (ie, *1F, *1K, *6, *7) | Investigational |
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