Cytochrome P450 Genotype-Guided Treatment Strategy
Corporate Medical Policy

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 β-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:


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),

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 by Southern blot analysis)
includes - CYP1B1 (cytochrome P450, family 1, subfamily B, polypeptide 1) (eg, primary
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

Reference Resources

   2018.

2. Food and Drug Administration. Highlights of Prescribing Information: Xenazine
   (tetrabenazine). 2015;
   https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/021894s010lbl.pdf.

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;
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
15. King J, Aberg JA. Clinical impact of patient population differences and genomic variation in efavirenz therapy. AIDS. Sep 12 2008;22(14):1709-1717. PMID 18753940

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

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

Joshua Plavin, MD, MPH, MBA
Chief Medical Officer

Kate McIntosh, MD, MBA, FAAP
Senior Medical Director

Attachment I

<table>
<thead>
<tr>
<th>Code Type</th>
<th>Number</th>
<th>Brief Description</th>
<th>Policy Instructions</th>
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<tr>
<td>CPT®</td>
<td>Code</td>
<td>Description</td>
<td>Required Action</td>
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<td>0029U</td>
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The following codes will be denied as Not Medically Necessary, Contract Exclusions or Investigational:

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<tr>
<td>0031U</td>
<td>CYP1A2 (cytochrome P450 family 1, subfamily A, member 2) (eg, drug metabolism) gene analysis, common variants (ie, *1F, *1K, *6, *7)</td>
<td>Investigational</td>
<td></td>
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