blue of california

Medical Policy

Pharmacogenomics	
Type: Medical Necessity and Investigational / Experimental	**Policy Specific Section:** Laboratory/Pathology
Original Policy Date: October 1, 2010	**Effective Date:** April 4, 2014

Definitions of Decision Determinations

Medically Necessary: A treatment, procedure or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

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.

Description

Drug efficacy and toxicity vary substantially across individuals. Various factors may influence the variability of drug effects, including age, liver function, concomitant diseases, nutrition, smoking, and drug-drug interactions. Inherited deoxyribonucleic acid (DNA) sequence variation, polymorphisms, gene coding for drug metabolizing enzymes, drug receptors, drug transporters,

and molecules involved in signal transduction pathways also may have major effects on the activity of those molecules and thus on the efficacy or toxicity of a drug.

Pharmacogenomics is the study of how an individual's genetic inheritance affects the body's response to drugs. It may be possible to predict therapeutic failures or severe adverse drug reactions in individual patients. Potentially, test results could be used to optimize drug choice and/or dose for more effective therapy, avoid serious adverse effects, and decrease medical costs.

The cytochrome P450 family is a major subset of all drug-metabolizing enzymes.

Policy

Genotyping to determine cytochrome P450 genetic polymorphisms is considered **medically necessary** in patients with cardiovascular disease undergoing treatment with clopidogrel (Plavix®).

Genotyping to determine cytochrome P450 genetic polymorphisms is considered **investigational** for all other indications, including, but not limited to the following:

- Warfarin management and dosing
- Tamoxifen management for women at high risk for or with breast cancer
- Helicobacter pyloris infection management
- Selective serotonin reuptake inhibitor selection or dosing
- Selective norepinephrine reuptake inhibitors (SNRIs) selection or dosing
- Selection and dosing of tricyclic antidepressants
- Antipsychotic drugs selection or dosing
- Codeine for nursing mothers
- Atomoxetine hydrochloride dosing
- Efavirenz dosing (common component of highly active antiretroviral therapy for HIV [human immunodeficiency virus] infection)
- Immunosuppressant dosing for organ transplantation
- Beta blocker (e.g., metoprolol) selection or dosing
- Dosing and management of antituberculosis medications

Genotyping to determine vitamin K epoxide reductase subunit C1 (VKORC1) genetic polymorphism is considered **investigational** for warfarin management and dosing.

Policy Guideline

Coding:

Cytochrome P450 genotyping (i.e., clopidogrel, helicobacter pyloris, antipsychotic drugs, immunosuppressant dosing)

- 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)

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Determining cytochrome p450 2C9 (CYP2C9) and vitamin K epoxide reductase subunit C1 (VKORC1) for the management of the administration and dosing of warfarin:

- 81227: CYP2C9 (cytochrome P450, family 2, subfamily C, polypeptide 9) (e.g., drug metabolism), gene analysis, common variants (e.g., *2, *3, *5, *6)
- 81355: VKORC1 (vitamin K epoxide reductase complex, subunit 1) (e.g., warfarin metabolism), gene analysis, common variants (e.g., -1639/3673)

The Centers for Medicare and Medicaid Services (CMS) issues a HCPCS code to facilitate adminstration of their new national coverage decision on warfarin responsiveness testing:

- G9143: Warfarin responsiveness testing by genetic technique using any method, any number of specimen(s)

Determining cytochrome p450 (CYP2D6) genetic polymorphisms for managing treatment with tamoxifen:

- 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)

There are also Tier 2 CPT codes that include cytochrome P450 testing:

- 81401: Molecular pathology procedure, Level 2 (eg, 2-10 SNPs, 1 methylated variant, or 1 somatic variant [typically using nonsequencing target variant analysis], or detection of a dynamic mutation disorder/triplet repeat) includes –
    - *CYP3A4 (cytochrome P450, family 3, subfamily A, polypeptide 4)* (eg, drug metabolism), common variants (eg, *2, *3, *4, *5, *6)
    - *CYP3A5 (cytochrome P450, family 3, subfamily A, polypeptide 5)* (eg, drug metabolism), common variants (eg, *2, *3, *4, *5, *6)
- 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 congenital glaucoma), full gene sequence

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- 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

Indications for warfarin therapy include, but are not limited to, the following conditions:

- Artificial heart valves
- Deep vein thrombosis
- Pulmonary embolism
- Cardioembolic stroke
- Atrial fibrillation
- Following major orthopedic surgery (total hip or knee arthroplasty, long bone fractures)

Internal Information

There is an MD Determination Form for this Medical Policy. It can be found on the following Web page:
http://myworkpath.com/healthcareservices/MedicalOperations/PSR_Determination_Pages.htm

Documentation Required for Clinical Review
• Referring MD's history and physical and/or consultation notes • Office notes indicating specific test requested and reason for testing • Current medication records

The materials provided to you are guidelines used by this plan to authorize, modify, or deny care for persons with similar illness or conditions. Specific care and treatment may vary depending on individual need and the benefits covered under your contract. These Policies are subject to change as new information becomes available

Click here to view the appendix for this policy

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