Pharmacogenetic testing

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Approved By:	Highmark Health Options – Market Leadership
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Products:	Medicaid
Application:	All participating hospitals and providers
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Disclaimer

Highmark Health Options medical policy is intended to serve only as a general reference resource regarding coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT

Highmark Health Options may provide coverage under medical surgical benefits of the Company's Medicaid products for pharmacogenetic testing.

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

The qualifications of the policy will meet the standards of the National Committee for Quality Assurance (NCQA) and the Delaware Department of Health and Social Services (DHSS) and all applicable state and federal regulations.

DEFINITIONS

Highmark Health Options (HHO) – Managed care organization serving vulnerable populations that have complex needs and qualify for Medicaid. Highmark Health Options members include individuals and families with low income, expecting mothers, children, and people with disabilities. Members pay nothing to very little for their health coverage. Highmark Health Options currently services Delaware Medicaid: Delaware Healthy Children Program (DHCP) and Diamond State Health Plan Plus members.

Pharmacogenetic testing (PGx) – The study of how an individual's genetic makeup influences the response to different medications. pharmacogenomic tests are performed to assess a person's response to therapy or risk for toxicity from drug treatment. Testing may be performed prior to treatment, in order to determine if the individual has genetic differences that could affect drug response and/or increase the risk for adverse drug reactions. Testing may also be performed during treatment, to assess whether an individual is having an adequate response or to investigate the cause of an unusual or adverse reaction.

Multigene panel testing – Genetic testing that uses next-generation sequencing to test multiple genes simultaneously and is also called multi-gene testing.

Allele – An alternative form of a gene that is located at a specific position on a specific chromosome. Humans inherit one allele from their mother and another allele from their father. The physical characteristics (e.g., eye color, hair color, skin color) of an individual depend on both of the alleles. If the alleles are different, the dominant allele will be expressed, while the effect of the other allele, called recessive, is masked. In the case of a recessive genetic disorder, an individual must inherit two copies of the mutated allele in order for the disease to be present.

PROCEDURES

1. Prior authorization is required.

2. Pharmacogenetic testing (PGx) for behavioral health is investigational and therefore, not medically necessary.

   PGx testing is not considered reasonable and necessary merely on the basis of a patient having a particular diagnosis. Unless the record reflects that the treating clinician has already considered nongenetic factors to make a preliminary drug selection, PGx testing is not considered reasonable and necessary (CMS, 2020).

   PGx testing is not covered when a treating clinician is not considering treatment with a medication that has an actionable drug-gene interaction, or when the use of a medication with a drug-gene interaction is not reasonable and necessary (CMS, 2020).

   Genes not identified as having actionable use are not considered reasonable and necessary. The algorithms employed in combinatorial testing are also not currently considered reasonable and necessary components of multi-gene testing (CMS, 2020).

   The clinical record must clearly show the use of or intent to prescribe a drug that has known drug-gene interactions that require a PGx test to be ordered to define the safe use of that drug in that patient (CMS, 2020).

   If a treating clinician orders a single gene test or a test for a particular allele(s), but as a matter of operational practicality, the laboratory tests that single gene or allele on a platform that looks for variants in other genes/alleles as well, that particular test done in that particular instance is considered a single gene/allele test for coverage purposes. In this scenario the provider may bill for the component of the test that was reasonable and necessary (in this example, the single gene test) (CMS, 2020).

   A multi-gene panel is considered reasonable and necessary if more than one single gene on that panel would be considered reasonable and necessary for safe use of the medication in question or if multiple drugs are being considered (each fulfilling the criteria of actionable gene-drug interactions identified above) that have different relevant genes. Additionally, a gene panel must contain at a minimum all the necessary relevant gene/allele content required for their indicated use to meet clinical utility requirements. Such minimum criteria are determined by experts including relevant associations such as the Association for Molecular Pathology and are considered during the technical assessment. A multi-gene panel is not considered reasonable and necessary if only a single gene on the panel is considered reasonable and necessary (CMS, 2020).

   If two or more single genes are tested, rather than a multi-gene panel, then the record must reflect that a clinician individually ordered each gene, and each single gene must individually be reasonable and necessary at the time they are ordered (CMS, 2020).

The ordering provider of a PGx test is restricted to providers who have the licensure, qualifications, and necessary experience/training to both diagnose the condition being treated and also to prescribe medications (the provider must be able to do both) for the condition either independently or in an arrangement as required by all the applicable state laws (CMS, 2020).

Pharmacogenetic testing of CYP2C9 or VKORC1 alleles to predict warfarin responsiveness is covered only when provided to members who are candidates for anticoagulation therapy with warfarin who:

- Have not been previously tested for CYP2C9 or VKORC1 alleles; and
- Have received fewer than five days of warfarin in the anticoagulation regimen for which the testing is ordered: and
- Are enrolled in a prospective, randomized, controlled clinical study when that study meets the standards specified in the decision memorandum (DM).

Once-per-lifetime genotyping for cytochrome P450 polymorphisms is clinically proven and, therefore, medically necessary for members with acute coronary syndrome undergoing percutaneous coronary intervention, in which clopidogrel (Plavix) is a treatment option (Scott, 2013).

In order for services to be covered, the patients' medical record must clearly reflect the following:

- The patient has a diagnosis for which pharmacologic therapy is reasonable and necessary, and the drug or drugs that the clinician is considering using must be reasonable and necessary for the treatment of the patient's diagnosis.
- The clinician has made an initial personalized decision for the patient based on the patient's diagnosis, the patient's other medical conditions, other medications the patient is taking, professional judgement, clinical science and basic science pertinent to the drug (e.g., mechanism of action, side effects), the patient's past medical history and when pertinent family history and the patient's preferences and values.
- The provider performing the service must have a record of what drug(s) is/are being considered and for what indication(s) to ensure the test performed is reasonable and necessary (CMS, 2020).

3. Post-payment Audit Statement

   The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Health Options at any time pursuant to the terms of your provider agreement.

4. Place of Service

   The place of service for laboratory testing is outpatient.

CODING REQUIREMENTS

CPT Code	Description
81232	DPYD Gene Analysis Common Variants.
81346	TYMS Gene Analysis Common Variants.
81230	CYP3A4 Gene Analysis Common Variants.
81231	CYP3A5 Gene Analysis Common Variants.

81283	IFNL3 Gene Analysis RS12979860 Variant.
81335	TPMT Gene Analysis Common Variants.
81247	G6PD Gene Analysis Common Variants.
81328	SLCO1B1 Gene Analysis Common Variants.
81220	CFTR Gene Analysis Common Variants.
84431	Thromboxane Metabolite(s), including Thromboxane if Performed, Urine.
82955	Glucose-6-phosphate Dehydrogenase (g6pd); Quantitative
88360	Morphometric Analysis, Tumor Immunohistochemistry (eg, Her-2/neu, Estrogen Receptor/progesterone Receptor), Quantitative or Semiquantitative, Per Specimen, Each Single Antibody Stain Procedure; Manual.

REIMBURSEMENT

Participating facilities will be reimbursed per their Highmark Health Options contract.

References

Centers for Medicare and Medicaid Services. (2009). Decision Memorandum for Pharmacogenetic Testing to Predict Warfarin Responsiveness. https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=224

Centers for Medicare and Medicaid Services. (2020). Local Coverage Determination (LCD): MolDX: Pharmacogenomics Testing. https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=38337

Penn Medicine. (2021). Pharmacogenetic Testing. https://www.pennmedicine.org/for-patients-and-visitors/find-a-program-or-service/translational-medicine-and-human-genetics/pharmacogenetics

Scott, S. A., Sangkuhl, K., Stein, C. M., Hulot, J. S., Mega, J. L., Roden, D. M., Klein, T. E., Sabatine, M. S., Johnson, J. A., Shuldiner, A. R., & Clinical Pharmacogenetics Implementation Consortium (2013). Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update. *Clinical pharmacology and therapeutics*, *94*(3), 317–323. https://doi.org/10.1038/clpt.2013.105

POLICY UPDATE HISTORY

08/19/2021	Medical Policy Committee approved
01/27/2022	Annual review, approved in Medical Policy Committee
02/2022	Approved in QI/UM
02/22/2023	Annual review, approved in Medical Policy Committee
02/28/2023	Approved in QI/UM