CLINICAL MEDICAL POLICY	
Policy Name:	Pharmacogenetic Testing
Policy Number:	MP-126-MD-PA
Responsible Department(s):	Medical Management
Provider Notice/Issue Date:	10/01/2023
Effective Date:	11/01/2023
Next Annual Review:	07/2024
Implementation Date:	07/19/2023
Products:	Highmark Wholecare℠ Medicaid
Application:	All participating hospitals and providers
Page Number(s):	1 of 5

Policy History

Date	Action
11/01/2023	Provider Effective date
08/31/2023	PARP Approval
07/19/2023	QI/UM Committee review
07/19/2023	Policy initially developed

Disclaimer

Highmark Wholecare℠ 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 Wholecare℠ may provide coverage under the medical-surgical benefits of the Company's Medicaid products for medically necessary 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.

(Current applicable Pennsylvania HealthChoices Agreement Section V. Program Requirements, B. Prior Authorization of Services, 1. General Prior Authorization Requirements.)

Definitions

Prior Authorization Review Panel (PARP) – A panel of representatives from within the PA Department of Human Services who have been assigned organizational responsibility for the review, approval and denial of all PH-MCO Prior Authorization policies and procedures.

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. A multi-gene panel is considered medically necessary if more than one (1) single gene on that panel would be considered medically 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 below) 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 medically necessary if only a single gene on that panel is considered medically necessary.

2. If two (2) 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 must individually be medically necessary at the time they are ordered.

3. The ordering physician 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.

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

5. The patient's medical record must clearly reflect the ALL of the following information:
    A. The patient has a diagnosis for which pharmacologic therapy is medically necessary, and the drug(s) that the clinician is considering using must be medically necessary for the treatment of the patient's diagnosis; AND
    B. 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; AND
    C. 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 medically necessary.

    Note: 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.

6. When the pharmacogenetic testing services are not considered medically necessary
    - PGx for behavioral health is considered experimental/investigational, and therefore not medically necessary.
    - PGx testing is not considered reasonable or 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 or necessary.
    - PGx testing is considered not medically necessary 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 or necessary.
    - Genes not identified as having actionable use are considered not medically necessary. The algorithms employed in combinatorial testing are also not currently considered medically necessary components of multi-gene testing.

7. Post-payment Audit Statement
    The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Highmark Wholecare℠ at any time pursuant to the terms of your provider agreement.

8. Place of Service
    The proper place of service for pharmacogenetic testing is outpatient.

9. Related Policies
    - MP-063-MD-PA Genetic Testing for Warfarin and Clopidogrel Therapy
    - MP-071-MD-PA Non-Oncologic Genetic Testing Panels

Governing Bodies Approval

FDA

The Food & Drug Administration (FDA) considers pharmacogenetic tests for clinical use to be mostly those that are intended to provide information that may aid in selection of certain therapeutics. When sufficient clinical information is available, they may also aid in dosage selection of the therapeutic. Therefore, a pharmacogenetic test target population will typically be composed of candidates for a particular therapeutic.

CLIA

Pharmacogenetic tests are offered as laboratory-developed tests under Clinical Laboratory Improvement Amendments (CLIA) licensed laboratories. Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratories offering such tests as a clinical service must meet general regulatory standards of CLIA and must be licensed by CLIA for high complexity testing.

Coding Requirements

Procedure Codes

CPT Code	Description
81479	Unlisted molecular pathology procedure
81232	DPYD (dihydropyrimidine dehydrogenase) (eg, 5-fluorouracil/5-FU and capecitabine drug metabolism), gene analysis, common variant(s) (eg, *2A, *4, *5, *6)
81346	TYMS (thymidylate synthetase) (eg, 5-fluorouracil/5-FU drug metabolism), gene analysis, common variant(s) (eg, tandem repeat variant)
81230	CYP3A4 (cytochrome P450 family 3 subfamily A member 4) (eg, drug metabolism), gene analysis, common variant(s) (eg, *2, *22)
81231	CYP3A5 (cytochrome P450 family 3 subfamily A member 5) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3, *4, *5, *6, *7)
81283	IFNL3 (interferon, lambda 3) (eg, drug response), gene analysis, rs12979860 variant
81335	TPMT (thiopurine S-methyltransferase) (eg, drug metabolism), gene analysis, common variants (eg, *2, *3)
84999	Unlisted chemistry procedure
81247	G6PD (glucose-6-phosphate dehydrogenase) (eg, hemolytic anemia, jaundice), gene analysis; common variant(s) (eg, A, A-)
81328	SLCO1B1 (solute carrier organic anion transporter family, member 1B1) (eg, adverse drug reaction), gene analysis, common variant(s) (eg, *5)
81220	CFTR (cystic fibrosis transmembrane conductance regulator) (eg, cystic fibrosis) gene analysis; common variants (eg, ACMG/ACOG guidelines)
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
87999	Unlisted microbiology procedure

Reimbursement

Participating facilities will be reimbursed per their Highmark Wholecare℠ contract.

Reference Sources

The Food & Drug Administration (FDA). Guidance for Industry and FDA Staff Pharmacogenetic Tests and Genetic Tests for Heritable Markers. June 19, 2007. Accessed on June 13, 2023.

The Centers for Medicare and Medicaid Services (CMS). National Coverage Analysis (NCA) Pharmacogenomic Testing for Warfarin Response. August 3, 2009. Accessed on June 13, 2023.

The Centers for Medicare and Medicaid Services (CMS). Local Coverage Determination (LCD) MolDX: Pharmacogenomics Testing. Original Effective date August 17, 2020. Accessed on June 13, 2023.

Penn Medicine. Pharmacogenetic Testing. 2023. June 13, 2023.

Scott SA, Sangkuhl K, Stein CM, Hulot JS, et. al. Clinical Pharmacogenetics Implementation Consortium. Clinical Pharmacogenetics Implementation Consortium guidelines for CYP2C19 genotype and clopidogrel therapy: 2013 update. May 22, 2013. Accessed on June 13, 2023.