November 2023

SONIC HEALTHCARE USA

Client Communication

Medicare Local Coverage Determination Policy: CGS

Coverage Policy

L38394 - MolDX: Pharmacogenomics Testing

CPT: 81220, 81225, 81226, 81227, 81231, 81232, 81247, 81283, 81306, 81328, 81335, 81350, 81355, 81374, 81377, 81381, 81383, 81406, 81479, 0029U, 0030U, 0034U, 0070U, 0071U, 0072U, 0073U, 0074U, 0075U, 0076U, 0286U

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Coverage Indications, Limitations, and/or Medical Necessity

This is a limited coverage policy for pharmacogenomics testing (PGx) including single gene, multi-gene panels, and combinatorial tests. These tests are generally covered (with a few exceptions) as described in further detail below to improve safety in the use of specific medications by avoiding potentially harmful medications, doses and/or adverse reactions known to occur with certain genotypes.

PGx testing is considered reasonable and necessary in limited circumstances as described below as an adjunctive personalized medical decision-making tool once a treating clinician has narrowed treatment possibilities to specific medications under consideration for use, or is already using a specified medication, based on other clinical considerations including the patient's diagnosis, the patient's other medical conditions, other medications, professional judgment, clinical science and basic science pertinent to the drug, and the patient's preferences and values.[1]

PGx tests must demonstrate analytical validity, clinical validity, and clinical utility to be considered reasonable and necessary for coverage. This is demonstrated through a required technical assessment of the test. PGx tests are considered germline tests and must adhere to other relevant germline testing policies published by this contractor.

It is understood that some panel/combinatorial tests may include content that has demonstrated clinical utility and some that has not. In such circumstances, this contractor may provide coverage for the components of tests that have demonstrated clinical utility when used in the proper clinical context described below.

Clinical Indications

PGx tests are indicated when medications are being considered for use (or already being administered) that are medically necessary, appropriate, and approved for use in the patient's condition and are known to have a gene(s)-drug interaction that has been demonstrated to be clinically actionable as defined by the FDA (PGx information

required for safe drug administration) or Clinical Pharmacogenetic Implementation Consortium (CPIC) guidelines (category A and B).

The selection of the medications in question must be derived from clinical factors/necessity rather than from a PGx test. Once the putative therapeutic agents are selected, and those agents are known to have gene-drug interactions as identified above, then a PGx test may be considered reasonable and necessary when the result of that test is necessary for the physician's decision-making process regarding safely administering or dosing the drug.

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 non-genetic factors to make a preliminary drug selection, PGx testing is not considered reasonable and necessary.

This LCD does not address (provides neither coverage nor non-coverage criteria) PGx testing for anticoagulation dosing, which is addressed by the National Coverage Determination (NCD) 90.1.

Definitions

For the purpose of this LCD, the following terms are defined as follows:

Gene – the term "gene" in this document will be used as a term to encapsulate all of the following: gene, pseudogene, and genetic locus.

Single-gene test - a laboratory test to detect relevant genetic variants (alleles) of 1 gene. If two or more different single genes are ordered individually but simultaneously, this is not a panel but rather a couple of or multiple single gene tests.

Multi-gene panel – a laboratory test to detect genetic variants of at least 2 genes, wherein the clinician does not individually order genes, but orders a panel with a specified list of genes.

Combinatorial PGx test – a type of multi-gene panel that requires a proprietary algorithm to evaluate pharmacokinetic or pharmacodynamic relationships resulting in drug recommendations or warnings.

Actionable use – A test is considered to have an actionable use when the genotype information may lead to selection of or avoidance of a specific therapy or modification of dosage of a therapy. The selection, avoidance, or dose change must be based on the FDA-label for the drug, an FDA warning or safety concern, or a CPIC level A or B gene-drug interaction. An intended change in therapy based on the result of a genotyping test that is not supported by one of these sources is not considered an actionable use for the purposes of this LCD.

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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.

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).

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.

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.

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.

Test components that are not reasonable and necessary

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.

Technical requirements

The treating clinician receiving the laboratory report must be able to use the genetic information presented to guide treatment. To accomplish this, the laboratory must clearly report the clinical significance of the resultant genotype, based on empirical data or validated methodologies, as an annotation or interpretation. For clarity, the report should document the specific genotype-drug interaction that lead to the resultant interpretation.

A lab may test for a reference allele as a matter of exclusion (e.g. report that a patient has a reference allele when alternate alleles are not found). However, in such cases, the report must identify which allele is the reference allele and that the reference allele is reported as a matter of exclusion.

Noncovered Indications

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.

Special Documentation Requirements

In order for any of the above services to be covered, the patient's medical record must clearly reflect the following:

1. 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.
2. 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, pertinent family history, and the patient's preferences and values.
3. 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.

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The ICD10 codes listed below are the top 40 diagnosis codes Sonic most commonly receives from ordering physicians for this limited-coverage test. Medicare supports provider utilization of all the diagnosis codes listed below, except those notated in bold. If you are providing a diagnosis code that is bolded below, please submit a valid ABN form with the order. To view the complete policy and the full list of medically supported diagnosis codes, please refer to the CMS website for guidance: https://www.cms.gov/medicare-coverage-database/search.aspx

Code	Description
Z79.899	**Other long term (current) drug therapy**
M32.10	Systemic lupus erythematosus, organ or system involvement unspecified
Z79.52	Long term (current) use of systemic steroids
M06.09	Rheumatoid arthritis without rheumatoid factor, multiple sites
M81.0	Age-Related Osteoporosis without Current Pathological Fracture
G62.9	Polyneuropathy, unspecified
M19.90	Unspecified osteoarthritis, unspecified site
I48.91	Unspecified atrial fibrillation
M54.9	Dorsalgia, unspecified
K74.60	Unspecified cirrhosis of liver
I10	Essential (primary) hypertension
K76.0	Fatty (change of) liver, not elsewhere classified
M25.50	Pain in the Unspecified Joint
L40.59	Other psoriatic arthropathy
M54.2	Cervicalgia
M05.79	Rheumatoid arthritis with rheumatoid factor of multiple sites without organ or systems involvement
M79.7	Fibromyalgia
Z79.891	Long term (current) use of opiate analgesic
T50.905D	Adverse effect of unspecified drugs, medicaments and biological substances, subsequent encounter
D64.9	Anemia, Unspecified
I25.10	Atherosclerotic heart disease of native coronary artery without angina pectoris
M15.4	Erosive (osteo)arthritis

D50.0	Iron deficiency anaemia secondary to blood loss (chronic)
M15.0	Primary generalized (osteo)arthritis
R53.83	Other Fatigue
E03.8	Other specified hypothyroidism
E78.2	Mixed Hyperlipidemia
R79.82	Elevated C-reactive protein (CRP)
E29.1	Testicular hypofunction
R94.4	Abnormal results of kidney function studies
E72.11	Homocystinuria