Pharmacogenomic Testing for Drug Toxicity and Response

Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

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<thead>
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<th>Procedures addressed by this guideline</th>
<th>Procedure codes</th>
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<tr>
<td>5-Fluorouracil (5-FU) Toxicity and Chemotherapeutic Response</td>
<td>81232, 81346</td>
</tr>
<tr>
<td>Catechol-O-Methyltransferase (COMT) Genotype</td>
<td>0032U</td>
</tr>
<tr>
<td>CYP3A4</td>
<td>81230</td>
</tr>
<tr>
<td>CYP3A5</td>
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<tr>
<td>Cytochrome P450 1A2 Genotype</td>
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<td>IFNL3 rs12979860 gene variant</td>
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<td>INFINITI Neural Response Panel</td>
<td>0078U</td>
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<td>NT (NUDT15 and TPMT) Genotyping Panel</td>
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<td>Serotonin Receptor Genotype (HTR2A and HTR2C)</td>
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<tr>
<td>Investigational and experimental tests that make use of molecular and genomic technologies</td>
<td>81479, 84999, 81599, and Others</td>
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</table>
What are pharmacogenomic tests

Definition

For the purposes of this guideline, pharmacogenomic tests are those germline tests performed to predict or assess an individual’s response to therapy as well as the risk of toxicity from drug treatment. Testing may be performed prior to treatment in order to determine if the individual has genetic variants 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 investigate the cause of an unexpected or adverse reaction.

Companion Diagnostics

Companion diagnostics are assays that help determine whether a drug may be safe or effective for a particular patient. Companion assays are evaluated as part of the Food & Drug Administration’s (FDA’s) development and approval process for the new drug. According to the FDA, “A companion diagnostic is a medical device, often an in vitro device, which provides information that is essential for the safe and effective use of a corresponding drug or biological product. The test helps a health care professional determine whether a particular therapeutic product’s benefits to patients will outweigh any potential serious side effects or risks.” 1 Although specific companion diagnostic tests may be identified in the FDA label for a new drug approval, similar laboratory-developed tests (LDTs) performed by a CLIA-certified laboratory are generally accepted as alternatives that can typically provide the required information.

Complementary Diagnostics

Complementary diagnostics are assays that were developed and in use prior to the FDA’s approval of a new drug. They are not evaluated through the FDA’s development and approval process for new drugs. Complementary diagnostics are used to help provide additional information about how a drug might be used, or whether someone should receive a certain class of drugs. These tests are not specifically required for the safe and effective use of a drug, which is part of what differentiates them from companion diagnostics. As with companion diagnostics, LDTs that are similar to the defined complementary diagnostic, when performed by a CLIA-certified laboratory, are able to provide the same information.2

Criteria

Criteria: General Coverage Guidance

Pharmacogenomic tests may be indicated when ALL of the following conditions are met:
• The individual is currently taking or considering treatment with a drug potentially affected by a known mutation that can be detected by a corresponding test.

• Technical and clinical validity: The test must be accurate, sensitive, and specific, based on sufficient, quality scientific evidence to support the claims of the test.

• Clinical utility: Healthcare providers can use the test results to guide changes in drug therapy management that will improve patient outcomes.

• Reasonable use: The usefulness of the test is not significantly offset by negative factors, such as expense, clinical risk, or social, or ethical challenges.

Criteria: Companion or Complementary Diagnostic Testing

Testing for purposes of medication usage will be approved when the following criteria are met:

• Testing is being performed in a CLIA-certified laboratory, AND

• Testing of the requested gene has not previously been performed, AND

• A medication’s FDA label requires results from the genetic test to effectively or safely use the therapy in question, AND

• Healthcare providers can use the test results to directly impact medical care for the individual, OR

• The member meets all criteria in a test-specific guideline, if available

Criteria: Investigational and/or Experimental Single Gene Tests

Single Gene Tests: The following pharmacogenomic tests and indications are considered investigational and/or experimental and, therefore, not eligible for reimbursement. This list is not intended to be all inclusive.*

• 5HT2C (Serotonin Receptor) gene variants

• Ankyrin G gene variants

• COMT (Catechol Methyl Transferase) gene variants

• Catechol-O-Methyltransferase (COMT) Genotype from Mayo Clinic

• CYP450 gene variants (including, but not limited to CYP1A2, CYP2D6, CYP2C9, CYP2C19, CYP3A4, CYP3A5) for psychotherapeutic, cardiovascular, or general drug response

• Cytochrome P450 1A2 Genotype from Mayo Clinic

• CYP2C19 testing for the management of H. pylori

• DRD2 (Dopamine Receptor) gene variants

• DRD4 dopamine D4 receptor p450

• IFNL3 rs12979860 gene variant

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• KIF6 gene variants
• MTHFR gene variants
• NAT2 gene variants
• OPRM1 gene variants
• Serotonin Receptor Genotype (HTR2A and HTR2C) from Mayo Clinic
• SLC6A4 (5-HTTLPR) serotonin transporter variants
• Warfarin Response Genotype from Mayo Clinic

**Note** *Please note that some single gene tests may be coverable under a narrow set of indications. Please see test-specific guidelines or the companion or complementary diagnostic testing section above.

**Criteria: Investigational and/or Experimental Panel Tests**

Pharmacogenomic panels, regardless of how they are billed, are considered investigational and/or experimental and, therefore, are not eligible for reimbursement. The following are examples of panels that are considered investigational and/or experimental. This list is not intended to be all inclusive:

• 5-Fluorouracil (5-FU) Toxicity and Chemotherapeutic Response [Proprietary panel of DPYD and TYMS gene variants to assess risk of 5-fluorouracil toxicity from ARUP Laboratory]
• Focused Pharmacogenomics Panel from Mayo Clinic
• Genecept Assay [Proprietary panel of biomarker tests to predict response to different psychiatric treatments from Genomind]
• Mental Health DNA Insight [Proprietary test from Pathway Genomics]
• INFINITI® Neural Response Panel [Pain management (opioid-use disorder) genotyping panel, 16 common variants (ie, ABCB1, COMT, DAT1, DBH, DOR, DRD1, DRD2, DRD4, GABA, GAL, HTR2A, HTTLPR, MTHFR, MUOR, OPRK1, OPRM1), buccal swab or other germline tissue sample, algorithm reported as positive or negative risk of opioid-use disorder from PersonalizeDx Labs, AutoGenomics Inc]
• NT (NUDT15 and TPMT) Genotyping Panel from RPRD Diagnostics
• OneOme RightMed, [Drug metabolism (adverse drug reactions), DNA, 22 drug metabolism and transporter genes, real-time PCR, blood or buccal swab, genotype and metabolizer status for therapeutic decision support from OneOme, LLC]
• Thiopurine Methyltransferase (TPMT) and Nudix Hydrolase (NUDT15) Genotyping from Mayo Clinic
• Pain Medication DNA Insight [Proprietary test from Pathway Genomics]
Other Considerations

Testing will be covered only for the number of genes or tests necessary to establish drug response. When available and cost-efficient, a tiered approach to testing, with reflex to more detailed testing and/or different genes, is recommended.

For pharmacogenomic tests that look for changes in germline DNA (i.e., not tumor DNA or viral DNA), testing will be allowed once per lifetime per gene. Exceptions may be considered if technical advances in testing or the discovery of novel genetic variants demonstrate significant advantages that would support a medical need to retest.

Testing performed in a CLIA-certified laboratory will be considered for coverage. The use of a specific FDA approved companion diagnostic is not necessary for coverage to be considered.

Test-specific guidelines are available for some pharmacogenomic tests. Please see the guidelines manual for a list of test-specific guidelines. For tests without a specific guideline, use the General Coverage Guidance above.

For somatic mutation testing in solid tumor tissue, see the guideline *Somatic Mutation Testing - Solid Tumors*. For somatic mutation testing in hematological malignancies, see the guideline, *Somatic Mutation Testing - Hematological Malignancies*.

References

1. Companion diagnostics. U.S. Food & Drug Administration website. Available at: https://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/InVitroDiagnostics/ucm407297.htm


