Medical Policy Bulletin

Title:

Pharmacogenetic Testing to Determine Drug Sensitivity (AmeriHealth Administrators)

Policy #:

06.02.30f

Policy

Coverage is subject to the terms, conditions, and limitations of the member's contract.

This policy only applies to members for whom AmeriHealth Administrators serves as the claims administrator and whose group has not enrolled in the UM vendor program. For those groups who have been given the option to enroll in the UM vendor program, this policy is no longer applicable upon their renewal effective date. Individual member benefits must be verified before/prior to providing services.

The intent of this policy is to communicate the coverage positions for certain pharmacogenetic tests to determine various drug sensitivities.

Please see each individual attachment for more comprehensive information, medical necessity criteria, and specific CPT, HCPCS, and ICD-10 codes on each topic.

- **Attachment A:** CYP450 phenotyping for CYP2C19 prior to initiation of clopidogrel (Plavix®)
- **Attachment B:** Pharmacogenomic testing (CYP2C9 or VKORC1 alleles) for predicting warfarin response
- **Attachment C:** Genetic testing to determine cytochrome p450 (CYP2C19) genetic polymorphisms for treatment management of *H. pylori* infection
- **Attachment D:** Genetic testing to determine cytochrome p450 (CYP2D6) genetic polymorphisms for management of tamoxifen treatment for women with, or at high risk for, breast cancer
- **Attachment E:** Genetic testing for BRAF mutation analysis in metastatic colorectal cancer to predict nonresponse to anti-EGFR monoclonal antibodies, cetuximab and pantimumab
- **Attachment F:** Genetic testing for predicting cardiovascular risk and/or effectiveness of statin therapy by KIF6 genotyping
- **Attachment G:** Genetic testing for somatic mutations by KRAS mutation analysis in non-small cell lung cancer technique to predict treatment response to erlotinib (Tarceva®)
- **Attachment H:** Genetic testing for epidermal growth factor receptor (EGFR) mutation in individuals with non-small cell lung cancer (NSCLC) as a technique to predict treatment response to erlotinib (Tarceva®)
- **Attachment I:** Testing for the BRAF (V600E) mutation in tumor tissue for select individuals for treatment with vemurafenib (Zelboraf®)
- **Attachment J:** BCR-ABL Testing for Monitoring of Individuals with Chronic Myelogenous Leukemia or Acute Myelogenous Leukemia, who are Receiving Imatinib Mesylate (Gleevec®) Therapy

REQUIRED DOCUMENTATION

The individual's medical record must reflect the medical necessity for the care provided. These medical records may include, but are not limited to: records from the professional provider's office, hospital, nursing home, home health agencies, therapies, and test reports.

The Company may conduct reviews and audits of services to our members, regardless of the participation status of the provider. All documentation is to be available to the Company upon request. Failure to produce the requested information may result in a denial for the service.

Guidelines

BENEFIT APPLICATION

Medically Necessary
Subject to the terms and conditions of the applicable benefit contract, certain pharmacogenetic testing to determine drug sensitivity is covered under the medical benefits of the Company's products when the medical necessity criteria and the technical requirements listed in this medical policy are met.

Experimental/Investigational
Subject to the terms and conditions of the applicable benefit contract, certain pharmacogenetic testing to determine drug sensitivity listed in this policy is not eligible for payment under the medical benefits of the Company's products because the service is considered experimental/investigational and, therefore, not covered.

MEDICARE

There are no Medicare coverage criteria addressing most of the pharmacogenetic services listed in this policy; therefore, the Company policy is applicable for all services without a Medicare coverage determination.

This policy is consistent with Medicare's coverage determination for Pharmacogenetic Testing for Warfarin Response. The Company's payment methodology may differ from Medicare.

For preferred provider organization (PPO) members to receive the highest level of benefits, cytochrome p450 genotyping for assessment of individuals using clopidogrel bisulfate (Plavix®) should always be performed by a participating provider. Health maintenance organization (HMO) members must go to a capitated site to receive benefits, as cytochrome p450 genotyping for assessment of individuals using clopidogrel bisulfate (Plavix®) is included in capitation.

US FOOD AND DRUG ADMINISTRATION STATUS

Genetic testing is a laboratory procedure and is historically not regulated by the US Food and Drug Administration (FDA). Clinical Laboratory Improvement Amendments (CLIA) establishes quality standards for all laboratory testing. However, recently, the FDA is reported to be involved in the evaluation of the

service of genetic testing.

Description

Pharmacogenomics describes the relationship between variations in the human genome (ie, differences in DNA sequence, copy number, or transcriptional perturbations) and individual variations in response to drug therapy, including adverse effects of drug therapy.

According to the National Center for Biologic Information (NCBI), pharmacogenetics and pharmacogenomics are defined as follows:

- *Pharmacogenomics* refers to the general study of all of the many different genes that determine drug behavior.
- *Pharmacogenetics* refers to the study of inherited differences (variation) in drug metabolism and response.

While there is a distinction between the two terms, they are often used interchangeably in the scientific community.

The goal of pharmacogenetic research is the development of personalized medicine. Personalized medicine takes into account an individual's characteristics, such as genetic makeup and other specific biomarkers in order to provide patient-specific care. Once specific genetic information is known that allows for the ability to detect key genetic variations in individuals, it will permit the health care provider to determine the most effective treatment response and/or avoid severe adverse reactions. Currently, the optimal drug doses are defined by averages from data in clinical trials with large populations. If an individual can be identified who may have a high propensity for a severe reaction to a particular drug, this personalized approach can allow for the consideration of an alternate dosage of a drug or a completely alternative treatment. This proactive treatment approach would help to avoid extended monitoring and the intensive medical support required for severe toxicity reactions. Moreover, this new approach to individualized therapy can assist in the early selection of the most appropriate drug or drug dose where it is known that the response to the specific agent is variable depending on the person's genetic architecture.

The Centers for Disease Control and Prevention (CDC) Office of Public Health Genomics helped to establish and support the ACCE Model Project, which has become the standard for evaluating scientific data on new genetic tests. The ACCE Model System* for Collecting, Analyzing and Disseminating Information on Genetic Tests provides an evaluation framework that is applicable to a variety of genetic tests. The Evaluation of Genomic Applications in Practice and Prevention (EGAPP) used the ACCE framework and established this process as a way of evaluating an evidence-based method for assessing genetic tests and other types of genomic technology as it has transitioned from the research arena to the practice arena. The ACCE evaluation framework examines:

- **Analytical validity:** Measures the specific genotypic test performance characteristics and whether the test accurately and reliably detects the gene marker(s) of interest. This refers to how well a test performs in the laboratory and how well the test measures the property or characteristic it is intended to measure. If the test does what its makers claim, it must produce the same results repeatedly and in different laboratories given the same set of procedures.
- **Clinical validity:** Refers to the associations of the test result(s) with patient outcomes of interest; may be expressed as clinical sensitivity, specificity, and predictive value for the outcome. Evidence is usually retrospective. This component refers to the accuracy with which a test predicts the presence or absence of a clinical condition or predisposition. Initially, the test has to be conducted on individuals who are known to have the condition (as well as those who do not) to determine its success rate.
- **Clinical utility:** Determines whether the use of genetic testing to modify management decisions improves patient outcomes. Best evidence is prospective, from randomized clinical trials of standard management procedures vs. genetic test-directed management. Evidence may also be derived by using banked samples from already completed clinical trials or by constructing an indirect chain of evidence linking test result to clinical outcome. This refers to the usefulness of the test and the value of information to the person being tested. If a test has utility, it means that the results, positive or negative, provide information that is of value to the person being tested because he or she can use that information to seek an effective treatment or preventive strategy. Even if no interventions are available to treat or prevent disease, there may be benefits associated with knowledge of a result.
- **Ethical, Legal, and Social Implications:** Determines what, if any, ethical, legal, or social implications may arise from the use of this test and its results.
  *From: Haddow JE, Palomaki GE. ACCE: A Model Process for Evaluating Data on Emerging Genetic Tests. In: *Human Genome Epidemiology: A Scientific Foundation for Using Genetic Information to Improve Health and Prevent Disease.* Khoury M, Little J, Burke W (eds.), Oxford University Press, pp. 217-233, 2003.

References

Centers for Disease Control and Prevention. Office of Public Health Genomics. Evaluation of Genomic Testing. ACCE Model for Evaluating Genetic Tests. [Office of Public Health Genomics Web Site] January 3, 2011. Available at: http://www.cdc.gov/genomics/gtesting/ACCE/index.htm. Accessed July 31, 2013.

Centers for Disease Control and Prevention. Office of Public Health Genomics. Public Health Genomics. Genetic Testing. [Office of Public Health Genomics Web Site]. December 14, 2010. Available at:.http://www.cdc.gov/genomics/gtesting/index.htm Accessed July 31, 2013.

Centers for Disease Control and Prevention. Public Health Genomics. Genomic Testing. ACCE Model for Evaluating Genetic Testing. Available at: http://www.cdc.gov/genomics/gtesting/ACCE/index.htm. Accessed July 31, 2013.

Centers for Disease Control and Prevention. Public Helath Genomics. Genomic Testing. ACCE Model list of 44 targeted questions aimed at a comprehensive review of genetic testing. [Office of Public Helath Genomic Web Site]. December 12, 2010. Available at: http://www.cdc.gov/genomics/gtesting/ACCE/acce_proj.htm#wheel. Accessed July 31, 2013.

Center for Genetics Education. Pharmacogenetics/Pharmacogenomics. Fact Sheet 25. Available at: http://www.genetics.com.au/pdf/factsheets/fs25.pdf. Accessed July 31, 2013.

Genomics.Energy.gov. Human Genomic Project Information. Available at:http://www.ornl.gov/sci/techresources/Human_Genome/home.shtml. Accessed July 31, 2013.

Gudgeon JM, McClain MR, Palomaki GE, Williams MS. Rapid ACCE: experience with a rapid and structured approach for evaluating gene-based testing. *Genet Med.* 2007;9:473-478.

Guttmacher AE, Feero WG, Collins FS. The genome gets personal--almost. *JAMA.* 2008;299(11):1351-1352.

Mayo Clinic. Pharmacogenomics: When drug treatment becomes personalized medicine. [June 27, 2008]. Available at:http://www.mayoclinic.com/health/personalized-medicine/CA00078. Accessed July 31, 2013.

National Center for Biologic Information. A Science Primer: Just the Facts: A Basic Introduction to the Science Underlying NCBI Resources. One Size Does Not Fit All: The Promise of Pharmacogenetics. [National Center for Biologic Information Web Site]. Last Revised 3/31/2004. Available at: http://www.ncbi.nlm.nih.gov/About/primer/pharm.html. Accessed July 31, 2013.

Coding

CPT Procedure Code Number(s)

PLEASE REVIEW THE SPECIFIC INDIVIDUAL ATTACHMENTS FOR CODING INFORMATION ON EACH TOPIC LISTED IN THIS MEDICAL

POLICY.

ICD - 10 Procedure Code Number(s)

N/A

ICD - 10 Diagnosis Code Number(s)

N/A

HCPCS Level II Code Number(s)

PLEASE REVIEW THE SPECIFIC INDIVIDUAL ATTACHMENTS FOR CODING INFORMATION ON EACH TOPIC LISTED IN THIS MEDICAL POLICY.

Revenue Code Number(s)

N/A

Cross Reference

Attachment A: Pharmacogenetic Testing to Determine Drug Sensitivity (AmeriHealth Administrators)
Description: Cytochrome p450 Genotyping for Assessment of Individuals Prior to Initiation of Clopidogrel Bisulfate (Plavix®)
Attachment B: Pharmacogenetic Testing to Determine Drug Sensitivity (AmeriHealth Administrators)
Description: Genetic Testing for Warfarin (Coumadin®) Dose
Attachment C: Pharmacogenetic Testing to Determine Drug Sensitivity (AmeriHealth Administrators)
Description: Genetic Testing for Helicobacter pylori treatment
Attachment D: Pharmacogenetic Testing to Determine Drug Sensitivity (AmeriHealth Administrators)
Description: Genetic Testing for Tamoxifen Treatment
Attachment E: Pharmacogenetic Testing to Determine Drug Sensitivity (AmeriHealth Administrators)
Description: KRAS and BRAF Mutation Analysis in Metastatic Colorectal Cancer prior to use of cetuximab (Erbitux®) and pantiumumab (Vectibix®)
Attachment F: Pharmacogenetic Testing to Determine Drug Sensitivity (AmeriHealth Administrators)
Description: KIF6 Genotyping for Predicting Cardiovascular Risk and/or Effectiveness of Statin Therapy
Attachment G: Pharmacogenetic Testing to Determine Drug Sensitivity (AmeriHealth Administrators)
Description: KRAS mutation analylsis to predict treatment response to elotinib (Tarceva®) in non-small cell lung cancer (NSCLC)
Attachment H: Pharmacogenetic Testing to Determine Drug Sensitivity (AmeriHealth Administrators)
Description: Epidermal Growth Factor (EGFR) Mutation Analysis for individuals with non-small cell lung cancer
Attachment I: Pharmacogenetic Testing to Determine Drug Sensitivity (AmeriHealth Administrators)
Description: BRAF for melanoma
Attachment J: Pharmacogenetic Testing to Determine Drug Sensitivity (AmeriHealth Administrators)
Description: BCR-ABL Testing for Monitoring of Individuals with Chronic Myelogenous Leukemia or Acute Myelogenous Leukemia, who are Receiving Imatinib Mesylate (Gleevec®) Therapy

Policy History

Revisions From 06.02.30f:

04/17/2024	**This policy has been reissued in accordance with the Company's annual review process.**
05/03/2023	This policy has been reissued in accordance with the Company's annual review process.
01/01/2023	This version of the policy communicating the Company's continuing position on Pharmacogenetic Testing to Determine Drug Sensitivity will be reissued effective 01/01/2023.

Revisions From 06.02.30e:

07/01/2022	**This policy has been reissued in accordance with the Company's annual review process.** **The following disclaimer language…:** ***This policy only applies to members for whom AmeriHealth Administrators serves as the claims administrator and whose group has not enrolled in the UM vendor program. For those groups who have been given the option to enroll in the UM vendor program, this policy is no longer applicable upon their renewal effective date. Individual member benefits must be verified before/prior to providing services.*** **… is replacing this disclaimer language…:** ***This policy only applies to members for whom AmeriHealth Administrators serves as the claims administrator. For all other Independence members, refer to the policy entitled eviCore Lab Management Program.***
06/02/2021	This policy has been reissued in accordance with the Company's annual review process.
10/09/2019	This policy has been reissued in accordance with the Company's annual review process.
10/09/2019	This policy has been reissued in accordance with the Company's annual review process.
11/21/2018	This policy has been reissued in accordance with the Company's annual review process.
11/22/2017	This policy has been reissued in accordance with the Company's annual review process.

Effective 10/05/2017 this policy has been updated to the new policy template format.

Version Effective Date: 01/01/2023

Version Issued Date: 12/30/2022

Version Reissued Date: 04/17/2024