Clinical Policy: Whole Exome Sequencing

Reference Number: WA.CP.MP.528
Date of Last Revision: 08/21
Effective Date: 09/01/21

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
This policy describes the medical necessity guidelines for whole exome sequencing (WES). Most genetic mutations that cause disease occur in the pieces of DNA that provide rules for making proteins, called exons. All exons together are called the exome. WES is a DNA analysis technique that looks at all of the exons in a person at one time, rather than looking at individual genes one at a time.

Policy/Criteria
I. It is the policy of Coordinated Care of Washington, Inc., in accordance with the Health Care Authority Health Technology Assessment and Billing Guidelines, that whole exome sequencing is considered medically necessary for the evaluation of unexplained congenital or neurodevelopmental disorders in a phenotypically affected individual when all of the following criteria are met:

   A. A board-certified or board-eligible medical geneticist, or an advanced practice nurse in genetic (APGN) credentialed by either the Genetic Nursing Credentialing Commission (GNCC) or the American Nurses Credentialing Center (ANCC), who is not employed by a commercial genetic testing laboratory, has evaluated the patient and family history and recommends or orders, or both, the test.

   B. A genetic etiology is considered the most likely explanation for the phenotype, based on either of the following:

      1. Multiple abnormalities affecting unrelated organ systems (e.g., multiple congenital anomalies), or

      2. Two of the following:

         ▪ Significant abnormality affecting at a minimum a single organ system
         ▪ Profound global developmental delay (member age 5 or younger) or intellectual disability (member older than 5 years)
         ▪ Family history strongly suggestive of a genetic etiology, including consanguinity
         ▪ Period of unexplained developmental regression (unrelated to autism or epilepsy)
         ▪ Biochemical findings suggestive of an inborn error of metabolism were targeted testing is not available

   C. Other circumstances (e.g., environmental exposures, injury, infection, etc.) do not reasonably explain the constellation of symptoms

   D. Clinical presentation does not fit a well-described syndrome for which single-gene or targeted panel testing (e.g., comparative genomic hybridization [CGH]/chromosomal microarray analysis [CMA]) is available
E. The differential diagnosis list or phenotype warrant testing, or both, of multiple genes and one of the following:
   1. WES is more efficient and economical than the separate single-gene tests or panels that would be recommended based on the differential diagnosis (e.g., genetic conditions that demonstrate a high degree of genetic heterogeneity)
   2. WES results may preclude the need for multiple invasive procedures or screening that would be recommended in the absence of testing (e.g., muscle biopsy).
F. A standard clinical work-up has been conducted and did not lead to a diagnosis
G. Results will impact clinical decisions-making for the individual being tested
H. Pre- and post-test counseling is performed by an American Board of Medical Genetics-certified or American Board of Genetic Counseling-certified genetic counselor

II. It is the policy of Coordinated Care of Washington, Inc., in accordance with the Health Care Authority Billing Guidelines, that whole exome sequencing is considered **not medically necessary** for any of the following:
   A. Uncomplicated autism spectrum disorder, developmental delay, or mild to moderate global developmental delay
   B. Other circumstances (e.g., environmental exposures, injury, infection, etc.) that reasonably explain the constellation of symptoms
   C. Carrier testing for “at risk” relatives
   D. Prenatal or pre-implantation testing

**Background**
This policy is based entirely on Washington State Health Care Authority (HCA) Billing Guidelines.

**Coding Implications**
This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2019, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

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<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
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<tr>
<td>0036U</td>
<td>Exome (i.e., somatic mutations), paired formalin-fixed paraffin-embedded tumor tissue and normal specimen, sequence analyses</td>
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<tr>
<td>0214U</td>
<td>Rare diseases (constitutional/heritable disorder), whole exome and mitochondrial DNA sequence analysis, including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants, proband</td>
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CPT® Codes | Description
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0215U | Rare diseases (constitutional/heritable disorder), whole exome and mitochondrial DNA sequence analysis, including small sequence changes, deletions, duplications, short tandem repeat gene expansions, and variants in non-uniquely mappable regions, blood or saliva, identification and categorization of genetic variants, each comparator exome (e.g., parent, sibling)
81415 | Exome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis
81416 | Exome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator exome (e.g., parents, siblings)
81417 | Exome (e.g., unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained exome sequence (e.g., updated knowledge or unrelated condition/syndrome)

Reviews, Revisions, and Approvals

| Reviews Date | Approval Date |
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Policy developed. | 08/21 | 09/21 |

References


Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and
limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

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This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members/enrollees. This clinical policy is not intended to recommend treatment for members/enrollees. Members/Enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

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**Note: For Medicaid members/enrollees,** when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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