Maryland
DEPARTMENT OF HEALTH

Whole Exome Sequencing (WES) Clinical Criteria (CPT 81415, 81416, 81417)

Whole Exome Sequencing (WES) refers to the sequencing of the exome, or coding, regions of a genome. WES is powerful genetic technology that is used for the diagnosis of children with multiple anomalies, intellectual disabilities, and/or seizures. WES analyzes the exons or coding regions of approximately 19,000 to 20,000 genes simultaneously using next-generation sequencing techniques. This test can be valuable for uncovering changes in Mendelian genes (single genes) responsible for medical disorders. By sequencing the exome of a patient and comparing it with the normal reference sequence, variations in an individual's DNA sequence can be identified and related back to the individual's medical concerns in an effort to discover the cause of the medical disorder.

Whole Exome Sequencing (WES) – (Requires Prior Authorization)

- 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); reevaluation of previously obtained exome sequence (e.g., updated knowledge or unrelated condition/syndrome.)

I. Criteria for Initial Approval

WES will be considered for coverage when **all** of the criteria below are met, and confirmed with supporting medical documentation.

CPT 81415 - Whole exome sequencing may be considered medically necessary for the evaluation of unexplained congenital anomalies or neurodevelopmental disorders in children when all the following criteria are met:

- Test is ordered by **one** of the following provider types, who has evaluated the patient and family history, and recommends and/or orders the test:
  - Neurologist in collaboration with a medical geneticist or certified genetic counselor.
  - Developmental pediatrician in collaboration with a medical geneticist or certified genetic counselor.

    - Psychiatrist in collaboration with a medical geneticist or certified genetic counselor.
- The patient has been evaluated by a board-certified clinician with expertise in clinical genetics and counseled about the potential risks of genetic testing.
    - Pre- and post-test counseling is performed by an American Board of Medical Genetics or American Board of Genetic Counseling certified genetic counselor.
- The patient and/or parents/legal guardians (if applicable) have been appropriately counseled about the testing by a qualified professional (same or similar to ordering providers) who is involved in the member's care.
- The patient has <u>one</u> of the following:
    - Profound global developmental delay or intellectual disability.
    - Family history strongly suggests a genetic etiology, including consanguinity.
    - Period of unexplained developmental regression (unrelated to autism or epilepsy).
- Clinical presentation does not fit a well-described syndrome for which single-gene or targeted panel testing (e.g., comparative genomic hybridization/chromosomal microarray analysis) is available.
- A genetic etiology is the most likely explanation for the phenotype or clinical scenario despite previous genetic testing (e.g., chromosomal microarray analysis and/or targeted single gene testing), OR when previous genetic testing has failed to yield a diagnosis and the affected individual is faced with invasive procedures or testing as the next diagnostic step (e.g., muscle biopsy).
    - WES is more practical than the separate single gene tests or panels that would be recommended based on the differential diagnosis.
    - WES results may preclude the need for multiple and/or invasive procedures.
- No other causative circumstances (e.g. environmental exposures, injury, or infection) can explain the symptoms.
- WES results have a reasonable potential to directly impact patient management and clinical outcome for the individual being tested.

<u>CPT 81416</u> - Comparator exome sequence analysis is considered medically necessary when the above criteria for WES (CPT 81415) have been met and WES is being performed concurrently or has been previously performed.

<u>CPT 81417</u> - Whole exome reanalysis of previously obtained uninformative whole exome sequence is medically necessary when **<u>one</u>** of the following criteria is met:

- There has been an onset of additional symptoms that broadens the phenotype assessed during the original exome evaluation.
- There has been the birth or diagnosis of a similarly affected first-degree relative that has expanded the clinical picture.

II. Exclusions from Coverage

When is Whole Exome Sequencing NOT A COVERED BENEFIT?

The use of WES for indications other than those listed above is considered experimental, investigational, or unproven.

WES is not covered in the following scenarios*.

- WES is not covered for uncomplicated Autism Spectrum Disorder, developmental delay, and mild to moderate global developmental delay.
- WES is not covered when environmental exposures, injury, or infection may reasonably explain the patient's constellation of symptoms.
- WES is considered investigational for:
    - Prenatal screening for fetal diagnosis.
    - Preimplantation testing of an embryo.
    - Purpose of genetic carrier screening.
    - Genetic disorders in all other situations.

*This list is not an exhaustive list of all scenarios where WES may not be considered a covered benefit.

III. Length of Authorization

WES will be authorized for 3 months when the criteria for initial approval are met.

IV. Billing Code/Information

Bill CPT code as appropriate (81415, 81416, 81417).

Prior authorization of benefits is not the practice of medicine nor the substitute for the independent medical judgment of a treating medical provider. The materials provided are a component used to assist in making coverage decisions and administering benefits. Prior authorization does not constitute a contract or guarantee regarding member eligibility or payment. Prior authorization criteria are established based on a collaborative effort using input from the current medical literature and based on evidence available at the time.

Approved by MDH Clinical Criteria Committee: 12/2021
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