Maryland
DEPARTMENT OF HEALTH

Whole Genome Sequencing (WGS) Clinical Criteria (CPT 81425, 81426, 81427)

Whole genome sequencing (WGS) is the strategy of using next-generation technology to sequence the entire genetic code of a genome. Whole-genome sequencing (WGS), in contrast to (WES), may detect larger deletions or duplications, triple repeat expansions, and pathogenic variants in deep intronic regions; regulatory regions that are outside of the coding regions; and untranslated gene regions.

I. Criteria for Initial Approval

Whole GENOME Sequencing (WGS) – (Requires Prior Authorization)

- 81425 Genome (e.g., unexplained constitutional or heritable disorder or syndrome;) sequence analysis.
- 81426 Genome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator genome (eg, parents, siblings.)
- 81427 Genome (e.g., unexplained constitutional or heritable disorder or syndrome); re-evaluation of the previously obtained genome sequence (e.g., updated knowledge or unrelated condition/syndrome.)

CPT 81425 - Whole genome sequencing may be considered medically necessary for the evaluation of unexplained congenital anomalies or neurodevelopmental disorders in newborns when all the following criteria are met with supporting medical documentation:

- Approved for patients aged less than 1 year of life and currently admitted to or recently discharged from a Neonatal Intensive Care Unit (NICU).
- 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:
    - Neonatologist or neurologist 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.

- Clinical indications:
  - A definitive diagnosis cannot be made based on standard clinical workup.
  - The patient's phenotype does not clearly identify a specific disease with an established single gene or multi-gene panel, or the patient has phenotypic characteristics outside of, or in addition to, what has been established for the disease.
  - 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.)
  - No other causative circumstances (e.g., environmental exposures, injury, infection) can explain the symptoms.

- Clinical utility: A definitive diagnosis will have clinical utility (improvement in net health outcomes.) For example:
  - WGS results have a reasonable potential to directly impact patient management and clinical outcome for the individual being tested.
  - WGS is more practical than the separate single gene tests or panels that would be recommended based on the differential diagnosis.
  - Establishing the diagnosis by genetic testing will end or minimize the clinical workup for other disorders.
  - WGS results may preclude the need for multiple and/or invasive procedures.

CPT 81426 - Comparator genome sequence analysis is considered medically necessary when the above criteria for WGS (CPT 81425) have been met and WGS is being performed concurrently or has been previously performed.

CPT 81427 - Whole genome reanalysis of previously obtained uninformative whole exome sequence is medically necessary when one 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 Genome Sequencing NOT A COVERED BENEFIT?

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

WGS is not covered in, but is not limited to, the following scenarios.

- WGS is not covered for Uncomplicated Autism Spectrum Disorder, developmental delay, or mild to moderate global developmental delay.
- WGS is not covered when environmental exposures, injury, or infection may reasonably explain the patient's constellation of symptoms.
- WGS 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.

III. Billing Code/Information

Bill CPT code as appropriate (81425, 81426, 81427)

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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