Policy Number: PA.204.MPC
Last Review Date: 08/26/2021
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# PA.204.MPC – Genetic Testing – Whole Genome-Exome Sequencing

Maryland Physicians Care considers **Whole Genome-Exome Sequencing (WGS/WES) Genetic Testing** medically necessary for the following indications provided that the results could have a direct influence on clinical management:

A. The phenotype or family history data strongly implicate a genetic etiology, but the phenotype does not identify with any specific disorder for which clinical diagnostic testing or specific gene testing is available on a clinical basis
B. A member presents with indications of a likely genetic disorder but the available clinical diagnostic testing and available specific genetic testing for that phenotype have failed to arrive at a diagnosis
C. A member presents with a defined genetic disorder that demonstrates a high degree of genetic heterogeneity, making WGS/WES or targeted exome sequencing to test multiple genes simultaneously a more practical approach provided the specific gene testing can't be identified
D. A fetus with a likely genetic disorder but specific genetic tests available for that phenotype have failed to arrive at a diagnosis

And

WGS/WES including targeted exome and Next Generation Sequencing (NGS) testing is only considered medically necessary and covered when ALL of the following criteria are met:

1. Three generation pedigree, or documentation that insufficient familial information exists to complete prior to ordering WGS/WES or targeted exome.
2. The signs, symptoms, and any diagnostic testing of the member does not suggest a classic condition or genetic disorder for which there is ma validated specific test (genetic or other).
3. Informed consent must be obtained and kept on file prior to testing.
4. Pre-testing and post-testing consultation with a BC/BE genetic counselor or medical geneticist with documentation to discuss any the following issues:
    a. Possibility of incidental findings (i.e. misattributed paternity, etc.)
    b. Consanguinity
    c. Variants of uncertain significance
    d. Possible positive, negative or unclear results
    e. Adult-onset disease
5. Financial consult or counseling as appropriate.

6. The results of the WGS/WES, targeted exome, or molecular/genetic test will specifically determine medication, treatment, and/or clinical management of the patient, or family member covered by [client health plan].

### A. Limitations

WGS/WES is not considered medically necessary and is not covered for any of the following:

A. Screenings of individuals suspected to have a genetic disorder but are currently asymptomatic.
B. Evaluation of first and second trimester pregnancy losses without congenital anomalies.
C. WGS/WES including targeted exome and NGS done for an indication or criteria not listed under indications.
D. Members without documentation of informed consent completed prior to testing.
E. Members who have not participated in counseling with a BC/BE genetics counselor or a medical geneticist pre and post testing.
F. Members who present with signs and/or symptoms classic for a specific condition (a specific test should be ordered in lieu of WGS/WES including targeted exome).

**Background**

The American College of Medical Genetics and Genomics (ACMG) defines whole genome sequencing (WGS) as the determination of the sequence of most of the DNA content comprising the entire genome of an individual. However, ACMG notes that there may be components of the genome that are not included in a present-day “whole genome sequence.”

ACMG defines exome as the component of the genome that predominantly encodes protein, these segments are referred to as “exons” and can include noncoding exons. ACMG states that Whole exome sequencing involves determination of the DNA sequence of most of these protein-encoding exons and may include some DNA regions that encode RNA molecules that are not involved in protein synthesis. Whole exome sequencing offers lower cost analysis than whole genome sequencing. It is possible that some clinically significant mutations may be missed by this approach due to inefficient capture of certain exons. In some cases, exome testing or analysis may be targeted to particular genes of clinical interest for a given application

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**Codes:**

| CPT HCPCS Codes | |
|---|---|
| Code | Description |
| 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) (List separately in addition to code for primary procedure) |
| 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) |
| 81425 | Genome (e.g. unexplained constitutional or heritable disorders or syndrome); sequence analysis |
| 81426 | Genome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator genome (eg, parents, siblings) (List separately in addition to code for primary procedure) |
| 81427 | Genome (e.g., unexplained constitutional or heritable disorder or syndrome); re-evaluation of previously obtained genome sequence (e.g., updated knowledge or unrelated condition/syndrome) |
| 81479 | Unlisted molecular pathology procedure – This code should only be used when all of the components of the code descriptor are not performed. |

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**Disclaimer:**