Health Plans

Manual: IU Health Plans
Department: Utilization Management
Policy # MP033
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Medicare Advantage **X Commercial**

Genetic Testing – Whole Genome-Exome Sequencing Policy

I. Purpose

Indiana University Health Plans (IU Health Plans) considers clinical indications when making a medical necessity determination for Genetic Testing – Whole Genome-Exome Sequencing.

II. Scope

This policy applies to all Utilization Management staff having decision- making responsibilities where authorization is required for Fully-insured commercial plans.

III. Exceptions

Whole Genome Sequencing (WGS) and Whole Exome Sequencing (WES) are **not considered medically necessary** and are **not covered for any of the following**:

1. Screenings of individuals suspected to have a genetic disorder but are currently asymptomatic.
2. Evaluation of first and second trimester pregnancy losses without congenital anomalies.
3. WGS/WES including targeted exome and NGS done for an indication or criteria not listed under indications.
4. Members without documentation of informed consent completed prior to testing.
5. Members who have not participated in counseling with a BC/BE genetics counselor or a medical geneticist pre and post testing.
6. 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).

IV. Definitions

Whole Genome Sequencing- 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."

Whole Exome Sequencing- 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."

V. Policy Statements

IU Health Plans considers:

1. **Whole Genome-Exome Sequencing (WGS/WES) Genetic Testing** medically necessary when **ONE or more of the following** indications must be met:
    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
2. **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:
    a. Three generation pedigree, or documentation that insufficient familial information exists to complete prior to ordering WGS/WES or targeted exome.
    b. The signs, symptoms, and any diagnostic testing of the member does not suggest a classic condition or genetic disorder for which there is a validated specific test (genetic or other).
    c. Informed consent must be obtained and kept on file prior to testing.
    d. Pre-testing and post-testing consultation with a BC/BE genetic counselor or medical geneticist with documentation to discuss any the following issues:
        i. Possibility of incidental findings (i.e. misattributed paternity, etc.)
        ii. Consanguinity
        iii. Variants of uncertain significance
        iv. Possible positive, negative or unclear results
        v. Adult-onset disease
        vi. Financial consult or counseling as appropriate.
    e. The results of the WGS/WES, targeted exome, or molecular/genetic test will specifically determine medication, treatment, and/or clinical management of the member.

Codes:

Code	Description
0094U	Genome, rapid sequence analysis
0212U	Rare disease genetic DNA analysis, proband
0213U	Rare diseases (constitutional/heritable disorders), whole genome 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 genome (e.g., parent, sibling)
0214U	Rare disease exome and mitochondrial DNA analysis proband
0215U	Rare disease exome DNA analysis each comparator
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.

VI. Procedures

None

VII. References/Citations

1. Centers for Medicare and Medicaid Services (CMS). National Coverage Determination (NCD) Next Generation Sequencing (NGS). 90.2. Effective date 1/27/2020. NCD - Next Generation Sequencing (NGS) (90.2) (cms.gov)
2. National Institute of Health Intramural Sequencing Center. (2018, October 22). Whole Genome Sequencing. FAQ whole genome_FINAL3 (nih.gov)
3. Miller, D. T., Lee, K., Gordon, A. S., Amendola, L. M., Adelman, K., Bale, S. J., Chung, W. K., Gollob, M. H., Harrison, S. M., Herman, G. E., Hershberger, R. E., Klein, T. E., McKelvey, K.,

Richards, C. S., Vlangos, C. N., Stewart, D. R., Watson, M. S., Martin, C. L., & ACMG Secondary Findings Working Group (2021). Recommendations for reporting of secondary findings in clinical exome and genome sequencing, 2021 update: a policy statement of the American College of Medical Genetics and Genomics (ACMG). *Genetics in medicine : official journal of the American College of Medical Genetics*, *23*(8), 1391–1398. https://doi.org/10.1038/s41436-021-01171-4

4. Zhao, E. Y., Jones, M., & Jones, S. J. M. (2019). Whole-Genome Sequencing in Cancer. *Cold Spring Harbor perspectives in medicine*, *9*(3), a034579. https://doi.org/10.1101/cshperspect.a034579

VIII. Forms/Appendices

None

IX. Responsibility

Medical Director