Health Plans

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

Genetic Testing- Whole Genome, Exome, and Next Generation Sequencing Testing 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 and Next Generation Sequencing.

II. Scope

This policy applies to all IU Health Plans and Utilization Management staff having decision-making responsibilities where authorization is required for Fully-insured and Team Member commercial plans.

III. Exceptions

Whole Genome Sequencing (WGS) and Whole Exome Sequencing (WES) and Next Generation Sequencing (NGS) 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

Biomarker: The state of Indiana defines biomarker as a characteristic that is objectively measured and evaluated as an indicator of:

1. Normal biological processes
2. Pathogenic processes; or
3. Pharmacologic responses to a specific therapeutic intervention, including known gene-drug interactions for medications being considered for use or already being administered.

The term includes gene mutations, characteristics of genes, and protein expression.

Biomarker Testing: The state of Indiana defines Biomarker Testing as the analysis of a patient's tissue, blood, or other biospecimen for the presence of a biomarker.
The term includes:

1. single-analyte tests;
2. multiplex panel tests;
3. protein expression; and
4. whole exome, whole genome, and whole transcriptome sequencing.

Nationally Recognized Clinical Practice Guidelines: Nationally recognized clinical practice guidelines means evidence based clinical practice guidelines that were:

1. Developed by an independent organization or medical professional society with:
   a. Transparent methodology and reporting structure
   b. Conflict of interest policy.

2. Established standards of care informed by:
   a. Systemic review of evidence
   b. Assessment of benefit versus risk of alternative care options

3. Include recommendations intended to optimize patient care.

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. State of Indiana Biomarker Guidance

Indiana University Health Plans prioritizes following regulatory guidance in determining medical necessity and coverage of medical care. For a test to be approved it must meet ALL of the supporting criteria.

The state of Indiana has provided for coverage of biomarker testing under Indiana Code 27-8-14.3-10. (*As added by P.L.37-2024, SEC.2.*):

Sec. 10. (a) A health plan shall provide coverage for biomarker testing for the purposes of diagnosis, treatment, appropriate management, or ongoing monitoring of an enrollee's disease or condition when biomarker testing is supported by medical and scientific evidence, including:

(1) labeled indications for a test approved or cleared by the United States Food and Drug Administration;

(2) indicated tests for a drug approved by the United States Food and Drug Administration;

(3) a warning or precaution on the label of a drug approved by the United States Food and Drug Administration;

(4) a national coverage determination of the Centers for Medicare and Medicaid Services (CMS);

(5) a local coverage determination of a Medicare administrative contractor; or

(6) nationally recognized clinical practice guidelines or consensus statements.

(b) The coverage required by this section must be provided in a manner that limits disruptions in care, including the need for multiple biopsies or biospecimen samples.

(c) Nothing in this section shall be construed to require coverage of biomarker testing for screening purposes.

(d) If a prior authorization requirement applies to biomarker testing under a health plan, the health plan or a third party acting on behalf of the health plan must:

(1) approve or deny a request for prior authorization for biomarker testing; and

(2) notify the covered individual and any person requesting prior authorization of the biomarker testing on behalf of the covered individual; in not more than five (5) business days after the request in the case of a nonurgent request or in not more than forty-eight (48) hours after the request in the case of an urgent request.

(e) A health plan shall ensure that a covered individual and the practitioner who prescribes biomarker testing for the covered individual have access to a clear, readily accessible, and convenient process for requesting an exception to:

(1) a coverage policy; or

(2) a prior authorization determination;

of the health plan that is adverse to the coverage of biomarker testing for the covered individual. The process required by this subsection shall be made readily accessible on the health plan's website.

VI. 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: This is not all inclusive, please see attached spreadsheet

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.

VII. Procedures

None

VIII. References/Citations

1. American College of Medical Genetics and Genomics. Copyright 2024. Practice Guidelines.

Practice Guidelines (acmg.net)
2. 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)
3. Centers for Medicare and Medicaid Services (CMS). LCD Reference Article; Billing and Coding Article. Billing and Coding: MolDx Molecular Diagnostic Tests (MDT). A57772. Revision Effective Date 7/1/2024. Article - Billing and Coding: MolDX: Molecular Diagnostic Tests (MDT) (A57772) (cms.gov)
4. National Institute of Health Intramural Sequencing Center. (02/21/2024) Whole Genome Sequencing. FAQ whole genome_FINAL3 (nih.gov)
5. 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
6. State of Indiana. Indiana Code for 2024. Title 27; Article8; Chapter 14.3 Coverage for Biomarker Testing. IGA | 2024 Indiana Code
7. 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

IX. Forms/Appendices

Attachment A- CMA & Genetic CPT codes

X. Responsibility

Medical Director