

MedStar Health, Inc.

POLICY AND PROCEDURE MANUAL

Policy Number: PA.204.MH
Last Review Date: 11/14/2019
Effective Date: 01/01/2020

PA.204.MH – Genetic Testing- Whole Genome-Exome Sequencing

This policy applies to the following lines of business:

- ✓ MedStar Employee (Select)
- ✓ MedStar CareFirst PPO

MedStar Health 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 a validated specific test (genetic or other).
3. Informed consent must be obtained and kept on file prior to testing.

PA.204.MH – Genetic Testing- Whole Genome-Exome Sequencing

Policy Number: PA.204.MH
Last Review Date: 11/14/2019
Effective Date: 01/01/2020

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 MedStar Health.

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

PA.204.MH – Genetic Testing- Whole Genome-Exome Sequencing

Policy Number: PA.204.MH
Last Review Date: 11/14/2019
Effective Date: 01/01/2020

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

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.

References

1. American College of Medical Genetics and Genomics (ACMG). ACMG policy statement: updated recommendations regarding analysis and reporting of secondary findings in clinical genome-scale sequencing. *Genetics in Medicine*. 2014 Nov; 17(1): 68-69.
<http://www.nature.com/gim/journal/v17/n1/full/gim2014151a.html>
2. American College of Medical Genetics and Genomics. Position Statement. Points to consider in the clinical application of genomic sequencing. 2012. Approved May 15, 2012. <https://www.nature.com/articles/gim201274>

PA.204.MH – Genetic Testing- Whole Genome-Exome Sequencing

Policy Number: PA.204.MH

Last Review Date: 11/14/2019

Effective Date: 01/01/2020

3. Baylor College of Medicine. Whole Exome Sequencing. Accessed 10/30/2018. https://www.bcm.edu/research/medical-genetics-labs/test_detail.cfm?testcode=1500
4. Bick D, Dimmock D. Whole exome and whole genome sequencing. *Curr Opin Pediatr*. 2011 Dec;23(6):594-600. doi: 10.1097/MOP.0b013e32834b20ec. <https://www.ncbi.nlm.nih.gov/pubmed/21881504>
5. Brock JK, Allen VM, Kieser K, et al. Family history screening: use of the three generation pedigree in clinical practice. *J Obstet Gynaecol Can* 2010; 37(7):663-672. <https://www.ncbi.nlm.nih.gov/pubmed/20707955>
6. Blue Cross/Blue Shield Technology Evaluation Center: Special Report: Exome Sequencing for Clinical Diagnosis of Patients with Suspected Genetic Disorders. Vol 28 No. 3 – August 2013. <https://www.ncbi.nlm.nih.gov/pubmed/24066368>
7. Burke W, Matheny Antommara AH, Bennett R, et al. Recommendations for returning genomic incidental findings? We need to talk! *Genet Med*. 2013 Nov;15(11):854-859. doi: 10.1038/gim.2013.113. Epub 2013 Aug 1. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3832423/>.
8. Caulfield T, Evans J, McGuire A, et al. Reflections on the Cost of "Low-Cost" Whole Genome Sequencing: Framing the Health Policy Debate. *PLoS Biol* 2013 Nov; 11(11): e1001699. doi:10.1371/journal.pbio.1001699 <http://www.plosbiology.org/article/info%3Adoi%2F10.1371%2Fjournal.pbio.1001699>
9. Green RC, Berg JS, Grody WW, et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing. *Genet Med*. 2013 Jul;15(7):565-574. doi: 10.1038/gim.2013.73. Epub 2013 Jun 20. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3727274/>
10. Hayes GTE Overview. Whole Exome Sequencing for Cancer Indications. Archived October 26, 2017.
11. Hayes GTE Overview. Whole Exome Sequencing for Noncancer Indications. Archived October 26, 2017
12. Johansen Taber KA, Dickinson BD, Wilson M. The promise and challenges of next-generation genome sequencing for clinical care. *JAMA Intern Med*. 2014 Feb 1;174(2):275-280. doi: 10.1001/jamainternmed.2013.12048. <http://archinte.jamanetwork.com/article.aspx?articleid=1770525>
13. Ombrello MJ, Sikora KA, Kastner DL. Genetics, genomics, and their relevance to pathology and therapy. *Best Pract Res Clin Rheumatol*. 2014 Apr;28(2):175-189. doi: 10.1016/j.berh.2014.05.001. <http://www.sciencedirect.com/science/article/pii/S1521694214000503>
14. Rehm HL, Bale SJ, Bayrak-Toydemir P, et al. ACMG clinical laboratory standards for next-generation sequencing. *Genet Med*. 2013 Sep;15(9):733-747. doi: 10.1038/gim.2013.92. Epub 2013 Jul 25. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4098820/>

PA.204.MH – Genetic Testing- Whole Genome-Exome Sequencing

Policy Number: PA.204.MH

Last Review Date: 11/14/2019

Effective Date: 01/01/2020

15. U.S. National Library of Medicine. Genetics Home Reference. What Is a Genome?
Published: 10/15/2019. <http://ghr.nlm.nih.gov/handbook/hgp/genome>

Disclaimer:

MedStar Health medical payment and prior authorization policies do not constitute medical advice and are not intended to govern or otherwise influence the practice of medicine. The policies constitute only the reimbursement and coverage guidelines of MedStar Health and its affiliated managed care entities. Coverage for services varies for individual members in accordance with the terms and conditions of applicable Certificates of Coverage, Summary Plan Descriptions, or contracts with governing regulatory agencies.

MedStar Health reserves the right to review and update the medical payment and prior authorization guidelines in its sole discretion. Notice of such changes, if necessary, shall be provided in accordance with the terms and conditions of provider agreements and any applicable laws or regulations.

These policies are the proprietary information of Evolent Health. Any sale, copying, or dissemination of said policies is prohibited.