Molina Clinical Policy
Genetic Testing: Policy No. 051

Last Approval: 2/9/2022
Next Review Due By: February 2023

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members.[1] References included were accurate at the time of policy approval and publication.

OVERVIEW

Genetic testing is defined by the National Human Genome Research Institute (NHGRI) as an array of techniques including analysis of human DNA, RNA, or protein. Genetic tests are used as a health care tool to detect gene variants associated with a specific disease or condition, as well as for non-clinical uses such as paternity testing and forensics. In the clinical setting, genetic tests can be performed to determine the genetic cause of a disease, confirm a suspected diagnosis, predict future illness, detect when an individual might pass a genetic mutation to his or her children, and predict response to therapy. They are also performed to screen newborns, fetuses, or embryos used in in vitro fertilization for genetic defects. (NHGRI, 2020; NHGRI, 2019).

Genetic testing is also useful to determine a person's genotype which can be determined for germline cells (those rising from the germ cells and relevant to the majority of the body's cells); somatic cells (e.g., tumor cells) can also be determined with genetic testing. A genotype is a DNA blueprint linked to the clinical appearances of a trait or disease (phenotype). Genotyping can refer to the determination of a genotype or to a certain type of microarray that identifies the genotype for a subset of selected nucleotide variants. Genetic testing also has ethical, legal, and psychosocial issues. These include psychosocial consequences of testing; disclosure to family members; testing children; undisclosed familial relationships; and genetic discrimination. Protections for discrimination are covered under the Americans with Disabilities Act (ADA), the Genetic Information Nondiscrimination Act (GINA), and Affordable Care Act (ACA). ([1] Raby et al., 2020).

Genetic Counseling

The National Society of Genetic Counselors defines genetic counseling as the process of aiding individuals to understand and acclimate to the medical, psychological, and familial implications of genetic contributions to disease. Genetic counseling includes the compilation of a detailed family history; interpretation of the family history with the medical history to assess the chance of disease occurrence or recurrence; patient and family education about the inheritance, testing, management, risk reduction, resources and research regarding the individual's specific condition; and counseling to help the individual make informed choices in order to provide appropriate interventions. ([2] Raby et al., 2020). Indications for referral can include, but are not limited to, personal or family history of a confirmed clinical diagnosis with a known genetic etiology (e.g., hemophilia, neurofibromatosis, Marfan syndrome). Genetic testing may also be warranted when an individual has an increased risk due to genetic or environmental factors; individual uncertainty about genetic basis; or patient anxiety / misunderstanding regarding risk. ([2] Raby et al., 2020).

Federal regulation of genetic tests is conducted by the Food and Drug Administration (FDA), the Centers for Medicare and Medicaid Services (CMS), and the Federal Trade Commission (FTC). (NHGRI, 2020). The FDA regulates medical products and devices while the CMS Clinical Laboratory Improvement Amendments of 1988 (CLIA) provides regulation of clinical laboratories and testing services. Additional regulation exists for laboratories that develop laboratory-developed tests (LDTs) – this includes tests developed for use only in that particular laboratory. While largely federally regulated, some States are regulated at the State-level (AACC, 2021; AACC, 2020; HHS, 2008).

Genetic Testing Access to Test Information

The Genetic Testing Registry (GTR) provides a central location for voluntary submission of genetic test information by providers. This includes the purpose of a given test, laboratory contact information and credentials, as well as the test's methodology, validity, and evidence of usefulness. Overall, the aim of the GTR is to advance the public health and research into the genetic basis of health and disease. (National Center for Biotechnology Information, n.d.).

GeneReviews are an international resource that provides clinically relevant and medically actionable information for inherited conditions. Diagnosis, management, and genetic counseling information are included. Experts on the specific condition write the individual chapters; GeneReviews contains over 800 chapters. Chapters are reviewed every four to five years (or as revisions are necessary). (Adam et al., 2022).

COVERAGE POLICY

MHI utilizes eviCore and MCG criteria for evaluation of all genetic testing requests. MCP-051: *Genetic Testing* must be applied to ALL requests with the exception of any genetic testing MCPs (e.g., *MCP-157: Non-Invasive Prenatal Testing)*. All genetic test requests are referred to a Medical Director for review when the Member meets the criteria below.

- **EviCore Lab Management** https://policydelivery.carecorenational.com/dnapreauth/partner (login required)
- **MCG** https://careweb.careguidelines.com/ (login required)

Genetic testing **is considered medically necessary and may be authorized** when the following criteria are met:
(National Society of Genetic Counselors; Adam et al., 2022; Miller et al., 2021; AMR, 2018; [1-4] ACOG; Hampel et al., 2015; Robson et al., 2015; AAP, 2013; Green et al., 2013; Rehm et al., 2013; Ross et al., 2013; ACMG, 2012)

1. The genetic test must be ordered by a board-certified physician within the scope of their practice or a board-certified MD medical geneticist; **AND**

2. Pre-and post- test genetic counseling must be performed by a board-certified MD medical geneticist, certified genetic counselor or appropriate MD specialist; **AND**

3. Presence of documented key risk factors that suggest a genetic disorder:
   a. Clinical features indicative of a condition or disease; **OR**
   b. High risk of inheriting the disease based upon personal history, family history, documentation of a genetic mutation and/or ethnic background; **OR**
   c. Following history, physical examination, pedigree analysis and completion of conventional diagnostic testing, a definitive diagnosis remains uncertain and a hereditary diagnosis is suspected.

AND

4. Carrier or predictive testing requires documentation confirming that a causative genetic change has been identified in an affected family member;

   NOTE: Genetic testing of an asymptomatic person in a family with several relatives affected with disease is considered predictive genetic testing. Targeted predictive genetic testing of individual diseases is appropriate when the specific indications for each test are met.

AND

5. Documentation is provided that supports the clinical utility of test results that will be used to significantly alter the management or treatment of the disease (e.g. surgery, the extent of surgery, a change in surveillance, hormonal manipulation, or a change from standard therapeutic or adjuvant chemotherapy);

   OR

   Scientific literature providing evidence of **ALL** of the following:
   a. > 3 published studies from widely recognized peer reviewed scientific journals that clearly establish the phenotype/genotype relationship of the condition; **OR**

b. ≥1 from widely recognized peer reviewed scientific journals published study on clinical validity with high accuracy that a test predicts the presence or absence of a clinical predisposition or condition (e.g., prediction of overall survival or recurrence-free survival).

AND

There is a clinically significant impact from a positive or negative test result on patient care/an effective treatment option, or other measurable clinical benefit is available following the test results to significantly improve health-related outcomes. Conditions with no available treatment or prevention options such as Alzheimer disease must be evaluated by a Medical Director for authorization.

AND

6. The clinical testing laboratory must be accredited by CLIA, the State and/or other applicable accrediting agencies.

Continuation of Therapy

1. Testing is allowed once during the member's lifetime per disease for diagnostic purposes.
2. A second genetic test may be authorized in one of the following circumstances:
   a. The genetic test identifies other mutations not previously tested and is considered to be different from the original test; **OR**
   b. If the genetic test measures gene expressions or identifies somatic mutations which can vary over time, only when clinically appropriate.

Limitations and Exclusions

Genetic testing **is considered not medically necessary** under the following circumstances (Nambot et al, 2018; Sawyer et al., 2016):

1. Criteria other than those outlined under the "Coverage Criteria" section above.
2. Testing for conditions or purposes where the test results would not directly influence the management or treatment of the disease or condition (e.g., disease without known treatment). Refer to the Corporate / Health Plan experimental and investigational policy as appropriate.
3. Testing for informational purposes or management of a member's family member.
4. Predictive or carrier testing without documentation supporting that a causative genetic change has been identified in an affected family member.
5. Minors under the age of 18 for adult onset conditions that have no preventative or therapeutic options.
6. Population screening in individuals without a personal or family history (with the exception of State mandated or required newborn screening or prenatal screening for certain conditions).
7. More than one lifetime test for each disease or condition.
8. Whole Genome Sequencing (WGS).

NOTE: Exceptions for more than one lifetime test are outlined above – see *Continuation of Therapy* above.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member.

NATIONAL AND PROFESSIONAL ORGANIZATIONS

Please find below a listing on policy statements and committee opinions from the following national and professional organizations (links are below in the Reference section):

American Association for Clinical Chemistry (AACC)
- *Modernization of CLIA: Laboratory Developed Tests (LDTs)*
- *Oversight of Laboratory Developed Tests*

American Academy of Pediatrics (AAP) & American College of Medical Genetics and Genomics (ACMG)
- *Ethical and Policy Issues in Genetic Testing and Screening of Children*
- *Technical Report: Ethical and Policy Issues in Genetic Testing and Screening of Children*

American College of Medical Genetics and Genomics (ACMG)
- *ACMG Clinical Laboratory Standards for Next-Generation Sequencing*
- *ACMG SF v3. List for Reporting of Secondary Findings in Clinical Exome and Genome Sequencing*
- *Points to Consider in the Clinical Application of Genomic Sequencing*
- *Policy Statement: Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing*
- *A Practice Guideline from the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors: Referral Indications for Cancer Predisposition Assessment*
- *Addendum: A Practice Guideline from the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors: Referral Indications for Cancer Predisposition Assessment*

American College of Obstetricians and Gynecologists (ACOG)
- *Carrier Screening in the Age of Genomic Medicine (No. 690)*
- *Consumer Testing for Disease Risk (No. 816)*
- *Ethical Issues in Genetic Testing (No. 410)*
- *Personalized Genomic Testing for Disease Risk (No. 527)*

American Society of Clinical Oncology (ASCO)
- *Genetic and Genomic Testing for Cancer Susceptibility*

National Society of Genetic Counselors
- *Various Practice Guidelines*

APPROVAL HISTORY

2/9/2022	Policy reviewed; no changes to criteria; updated Overview, Summary of Medical Evidence and Reference sections.
2/8/2021	Policy reviewed; no criteria changes; added that Molina utilizes MCG and eviCore for genetic testing criteria.
4/23/2020	Policy reviewed, no changes.
9/18/2019	Policy reviewed, no changes.
7/10/2018	Policy reviewed; clinical criteria updated to remove exclusions for: whole exome sequencing (WES) and carrier testing in children < age 18 years; criteria updated to allow a MD specialist to perform pre/post genetic counseling; updated Summary of Medical Evidence and Reference sections.
6/22/2017	New policy.

REFERENCES

Government Agencies
1. Centers for Disease Control and Prevention (CDC). Genomic and precision health: Evaluating genomic tests. Available from CDC. Updated September 20, 2019. Accessed January 27, 2022.
2. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database. Available at CMS. Accessed January 27, 2022.
3. National Center for Biotechnology Information (NCBI). Genetic testing registry. Available at NIH. Accessed January 27, 2022.
4. National Human Genome Research Institute. Regulation of genetic tests. Available at NIH. Updated September 25, 2020. Accessed January 27, 2022.
5. National Human Genome Research Institute. Coverage and reimbursement of genetic tests. Available at NIH. Published August 15, 2019. Accessed January 27, 2022.
6. United States Department of Health and Human Services. U.S. system of oversight of genetic testing: A response to the charge of the Secretary of Health and Human Services – report of the Secretary's Advisory Committee on Genetics, Health, and Society. Available from HHS. Published April 2008. Accessed January 27, 2022.

Evidence Based Reviews and Publications

1. Adam MP, Ardinger HH, Pagon RA, et al. (eds.). GeneReviews. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from NCBI.
2. GeneReviews. 2004-2020 Bio-Reference Laboratories, Inc. Available from NCBI. Accessed January 27, 2022.
3. Advanced Medical Reviews (AMR) Peer Review. Policy reviewed on April 26, 2018 by an AMR practicing, board-certified physician in the areas of Clinical Genetics and Pediatrics.
4. eviCore Healthcare. Lab management. Available from eviCore. Updated 2021. Accessed January 27, 2022. Registration and login required.
5. MCG. Search "genetic testing". https://www.mcg.com/. Updated 2021. Accessed January 27, 2022. Registration and login required.
6. [1] Raby BA, Kohlmann W, Hartzfel D. Genetic testing. http://www.uptodate.com. Updated July 14, 2020. Accessed January 27, 2022. Registration and login required.
7. [2] Raby BA, Kohlmann W, Hartzfel D. Genetic counseling: Family history interpretation and risk assessment. http://www.uptodate.com. Updated May 21, 2020. Accessed January 27, 2022. Registration and login required.

Peer Reviewed Publications

1. Nambot S, Thevenon J, Kuentz P, Duffourd Y, Tisserant E, Bruel AL, et al. Clinical whole-exome sequencing for the diagnosis of rare disorders with congenital anomalies and/or intellectual disability: Substantial interest of prospective annual reanalysis. Genet Med. 2018 Jun;20(6):645-654. doi: 10.1038/gim.2017.162. Accessed January 27, 2022.
2. Sawyer SL, Hartley T, Dyment DA, Beaulieu CL, Schwartzentruber J, Smith A, et al. Utility of whole-exome sequencing for those near the end of the diagnostic odyssey: Time to address gaps in care. Clin Genet. 2016 Mar;89(3):275-84. doi: 10.1111/cge.12654. Accessed January 27, 2022.

National and Specialty Organizations

1. ACMG Board of Directors. Points to consider in the clinical application of genomic sequencing. Genet Med. 2012 Aug;14(8):759-61. doi: 10.1038/gim.2012.74. Accessed January 28, 2022.
2. American Association for Clinical Chemistry (AACC). Modernization of CLIA: Laboratory developed tests (LDTs). Available from AACC. Published December 17, 2021. Accessed January 27, 2022.
3. American Association for Clinical Chemistry (AACC). Oversight of laboratory developed tests. Available from AACC. Published October 1, 2020. Accessed January 27, 2022.
4. American Academy of Pediatrics Committee on Bioethics and Committee on Genetics; American College of Medical Genetics and Genomics Committee on Social, Ethical and Legal Issues. Ethical and policy issues in genetic testing and screening of children. Pediatrics. 2013 Mar;131(3):620-2. doi: 10.1542/peds.2012-3680. Accessed January 28, 2022.
5. American College of Obstetricians and Gynecologists (ACOG). Consumer testing for disease risk (committee opinion no. 816). Available from ACOG. Published January 2021. Accessed January 28, 2022.
6. American College of Obstetricians and Gynecologists (ACOG) Committee on Genetics. Carrier screening the age of genomic medicine (no. 690). Published March 2017. Reaffirmed 2020. Available from ACOG. Accessed January 28, 2022.
7. American College of Obstetricians and Gynecologists (ACOG). Ethical issues in genetic testing (committee opinion no. 410). Available from ACOG. Published June 2008. Reaffirmed 2020. Accessed January 28, 2022.
8. American College of Obstetricians and Gynecologists (ACOG). ACOG committee opinion no. 527: Personalized genomic testing for disease risk. Obstet Gynecol. 2012 Jun;119(6):1318-9. doi: 10.1097/AOG.0b013e31825af3c6. Accessed January 28, 2022.
9. Bashford MT, Kohlman W, Everett J, Parrott A, Pollin TI, Practice Guidelines Committee of the National Society of Genetic Counselors, Professional Practice and Guidelines Committee of the American College of Medical Genetics and Genomics. Addendum: A practice guideline from the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors: referral indications for cancer predisposition assessment. Genet Med. 2019 Dec;21(12):2844. doi: 10.1038/s41436-019-0586-y. Accessed January 28, 2022.
10. Green RC, Berg JS, Grody WW, Kalia SS, Korf BR, Martin CL, et al. ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing: A policy statement of the American College of Medical Genetics and Genomics (ACMG). Genet Med 15, 565–574 (2013). https://doi.org/10.1038/gim.2013.73. Accessed January 28, 2022.
11. Hampel H, Bennett RL, Buchanan A, Pearlman R, Wiesner GL, American College of Medical Genetics and Genomics Professional Practice and Guidelines Committee, National Society of Genetic Counselors Practice Guidelines Committee. A practice guideline from the American College of Medical Genetics and Genomics and the National Society of Genetic Counselors: Referral indications for cancer predisposition assessment. Genet Med. 2015 Jan;17(1):70-87. doi: 10.1038/gim.2014.147. Accessed January 28, 2022.
12. Miller DT, Lee K, Chung WK, Gordon AS, Herman GE, Klein TE, et al. ACMG SF v3.0 list for reporting of secondary findings in clinical exome and genome sequencing. Genet Med 23, 1381–1390 (2021). https://doi.org/10.1038/s41436-021-01172-3. Accessed January 28, 2022.
13. National Society of Genetic Counselors. Practice guidelines. https://www.nsgc.org/Policy-Research-and-Publications/Practice-Guidelines. Accessed January 28, 2022.
14. Rehm HL, Bale SJ, Bayrak-Toydemir P, Berg JS, Brown KK, Deignan JL, et al. ACMG clinical laboratory standards for next-generation sequencing. Genet Med. 2013 Sep;15(9):733-47. doi: 10.1038/gim.2013.92. Accessed January 28, 2022.
15. Robson ME, Bradbury AR, Arun B, Domchek SM, Ford JM, Hampel HL, et al. American Society of Clinical Oncology policy statement update: Genetic and genomic testing for cancer susceptibility. J Clin Oncol. 2015 Nov 1;33(31):3660-7. doi: 10.1200/JCO.2015.63.0996. Accessed January 28, 2022.
16. Ross LF, Saal HM, David KL, Anderson RR, American Academy of Pediatrics, American College of Medical Genetics and Genomics. Technical report: Ethical and policy issues in genetic testing and screening of children. Genet Med. 2013 Mar;15(3):234-45. doi: 10.1038/gim.2012.176. Accessed January 28, 2022.

APPENDIX

Reserved for State specific information *(to be provided by the individual States, not Corporate). Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*

Washington State:
The following criteria are specific for codes (81228, 81229) related to genomic microarray for diagnosing genetic abnormalities in children (Previously found in the MHW Merge Criteria: Genomic Microarray Testing, which is now a retired policy).
Genomic microarray for diagnosing genetic abnormalities in children with **any one** of the following [ONE]:

- Significant dysmorphic features or congenital anomalies,
- Global developmental delay or clinical diagnosis of intellectual disability,
- Clinical diagnosis of autism spectrum disorder.

AND [ALL of the following]

- The genetic test must be ordered by board certified physician within the scope of their practice or a board certified MD medical geneticist; **and**
- Pre-and post- test genetic counseling is performed by a board-certified MD medical geneticist or certified genetic counselor; **and**
- Targeted genetic testing, if indicated, is negative; and
- Clinical presentation is not specific to a well-delineated genetic syndrome, and
- The results of testing could impact the clinical management; and
- The clinical testing laboratory must be accredited by CLIA, the State and/or other applicable accrediting agencies

Note: HCA uses the following definitions:

- For clients younger than age 5, **Global developmental delay (GDD)** - A significant delay in two or more developmental domains, including gross or fine motor, speech/language, cognitive, social/personal, and activities of daily living and is thought to predict a future diagnosis of ID. Such delays require accurate documentation by using norm-referenced and age-appropriate standardized measures of development administered by experienced developmental specialists, or documentation of profound delays based on age-appropriate developmental milestones are present. GDD is used to categorize children who are younger than 5.
- For clients age 5 and older, **intellectual disability (ID)** - A life-long disability diagnosed at or after age 5 when intelligence quotient (IQ) testing is considered valid and reliable. The Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association (DSM-V), defines patients with ID as having an IQ less than 70, onset during childhood, and dysfunction or impairment in more than two areas of adaptive behavior or systems of support.