Policy Number: PA-098.MPC
Last Review Date: 02/25/2021
Effective Date: 04/01/2021

PA.098.MPC - Chromosomal Microarray Testing

Maryland Physicians Care considers **Chromosomal Microarray Testing** medically necessary for the following indications:

A. Prenatally, when the fetus has one or more major structural abnormalities identified on fetal ultrasound or magnetic resonance imaging (MRI)
B. Stillborn fetuses with congenital anomalies present
C. Members with multiple congenital anomalies not specific to a well-defined genetic syndrome
D. Members with apparently non-syndromic developmental delay/intellectual disability
E. Members with a clinical diagnosis of autism spectrum disorder (ASD) of sufficient severity that symptoms cause clinically significant impairment in social, occupational, or other important areas of current functioning
F. Members with clinical diagnoses or suspected early infantile epileptic encephalopathy.

And

Chromosome Microarray (CMA)/Chromosome Genomic Hybridization (CGH) testing is only considered medically necessary when all of the following criteria are met:

1. The test must be ordered after completion of a three generation pedigree, or documentation that there is insufficient familial information available to complete the pedigree.
2. The signs and symptoms of the member do not suggest a classic condition for which there is a validated specific test.
3. Consultation with a BC/BE genetics counselor or a medical geneticist is to be completed before and after testing with documentation of the benefits/limitations of genetic testing and the potential to identify:
    - findings of uncertain significance,
    - misattributed paternity,
    - consanguinity, and
    - adult-onset disease;
4. Informed consent must be obtained prior to testing and kept on file;
5. Financial consult or counseling as appropriate

6. The results of the molecular/genetic test will specifically determine medication, treatment, and/or clinical management of the patient, or family member covered by Maryland Physicians Care

A. Limitations

CMA/CGH testing is considered not medically necessary and therefore not covered for any of the following:

A. Evaluation of first and second trimester pregnancy losses without congenital anomalies
B. Members with multiple miscarriages, infertility, or who are suspected to have sex chromosome abnormalities, such as Turner or Klinefelter syndromes;
C. Members with any symptoms, conditions, or diagnoses not included in the indications section of this policy;
D. Members with suspected balanced chromosome rearrangements, such as balanced translocations and inversions;
E. Members without documentation of informed consent completed prior to testing;
F. Members who have not participated in counseling with a BC/BE genetics counselor or a medical geneticist before and after testing;
G. Members for whom there is not a high index of suspicion of conditions due to a copy number variant;
H. Members who present with signs and/or symptoms classic for a specific condition (a specific test should be ordered in lieu of a CMA).

Background
The American College of Obstetricians and Gynecologists (ACOG) define chromosomal microarray analysis as a technique that identifies chromosomal abnormalities, including submicroscopic abnormalities that are too small to be detected by conventional karyotyping. More specifically, it is a high-resolution whole-genome screening that can identify major chromosomal aneuploidy as well as the location and type of specific genetic changes that are too small to be detected by conventional karyotyping. ACOG recommends CMA as a first-line genetic test in pregnancies to detect fetal abnormalities on an ultrasound screen.

Two types of chromosomal microarrays are used in clinical prenatal testing:
1. Comparative genomic hybridization (CGH)
2. Single-Nucleotide Polymorphism (SNP) arrays

Codes:

PA.098.MPC - Genetic Testing – Chromosomal Microarray (CMA)

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CPT HCPCS Codes	
Code	Description
81228	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number variants (e.g. bacterial artificial chromosome (BAC) or oligo-based comparative genomic hybridization (CGH) microarray analysis)
81229	Cytogenomic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities
S3870	Comparative genomic hybridization (CGH) microarray testing for developmental delay, autism spectrum disorder (ASD), and/or intellectual disability

References

1. American College of Obstetricians and Gynecologists (ACOG) Committee on Genetics and Society for Maternal-Fetal Medicine. Microarrays and Next-Generation Sequencing Technology: The Use of Advanced Genetic Diagnostic Tools in Obstretrics and Gynecology. Committee Opinion No. 682. December 2016. Reaffirmed 2020. https://www.acog.org/clinical/clinical-guidance/committee-opinion/articles/2016/12/microarrays-and-next-generation-sequencing-technology-the-use-of-advanced-genetic-diagnostic-tools-in-obstetrics-and-gynecology
2. American College of Obstetricians and Gynecologists (ACOG). Ob-Gyns Release Revised Recommendations on Screening and Testing for Genetic Disorders. Committee Opinion No. 691 Released: March 01, 2017. Reaffirmed 2020. American College of Obstetricians and Gynecologists (ACOG). Ob-Gyns Release Revised Recommendations on Screening and Testing for Genetic Disorders
3. Capobianco S, Lava SA, Bianchetti MG, et al. Chromosomal microarray among children with intellectual disability: a useful diagnostic tool for the clinical geneticist. Dev Med Child Neurol. 2014 Mar;56(3):290. doi: 10.1111/dmcn.12341. Epub 2013 Nov 23. http://onlinelibrary.wiley.com/doi/10.1111/dmcn.12341/pdf
4. Carter MT, Scherer SW. Autism spectrum disorder in the genetics clinic: a review. Clin Genet. 2013 May;83(5):399-407. doi: 10.1111/cge.12101. Epub 2013 Feb 21. http://onlinelibrary.wiley.com/doi/10.1111/cge.12101/pdf
5. Centers for Disease Control and Prevention (CDC). Intellectual Disability Fact Sheet. Last Reviewed: October 25, 2019.

https://www.cdc.gov/ncbddd/developmentaldisabilities/facts-about-intellectual-disability.html
6. Centers for Disease Control and Prevention (CDC). Facts About Autism Spectrum Disorder. Page Reviewed: March 25, 2020 http://www.cdc.gov/ncbddd/autism/facts.html
7. Dale RC, Grattan-Smith P, Nicholson M, et al. Microdeletions detected using chromosome microarray in children with suspected genetic movement disorders: a single-centre study. Dev Med Child Neurol. 2012 Jul;54(7):618-623. doi: 10.1111/j.1469-8749.2012.04287.x. Epub 2012 Apr 19. http://onlinelibrary.wiley.com/doi/10.1111/j.1469-8749.2012.04287.x/pdf
8. Devlin B, Scherer SW. Genetic architecture in autism spectrum disorder. Curr Opin Genet Dev. 2012 Jun; 22(3):229-237. doi: 10.1016/j.gde.2012.03.002. Epub 2012 Mar 29 https://pubmed.ncbi.nlm.nih.gov/22463983/
9. Flore LA, Milunsky JM. Updates in the genetic evaluation of the child with global developmental delay or intellectual disability. Semin Pediatr Neurol. 2012 Dec; 19(4): 173-180. https://europepmc.org/article/med/23245550Hayes Genetic Test Evaluation Overview. Genomic Microarray Analysis for Intellectual Disability and/or Developmental delay and Multiple Congenital Abnormalities, or Autism Spectrum Disorders (various manufacturers). Reviewed May 6, 2015. Archived: May 04, 2017.
10. Heil KM, Schaaf CP. The genetics of autism spectrum disorders – A guide for clinicians. Curr Psychiatry Rep. 2013 Jan;15(1):334. doi: 10.1007/s11920-012-0334-3. https://www.ncbi.nlm.nih.gov/pubmed/23250815
11. Kurian MA. The clinical utility of chromosomal microarray in childhood neurological disorders. Dev Med Child Neurol. 2012 Jul;54(7):582-583. doi: 10.1111/j.1469-8749.2012.04304.x. Epub 2012 Apr 19 http://onlinelibrary.wiley.com/doi/10.1111/j.1469-8749.2012.04304.x/pdf
12. Manning M, Hudgins L. Array-based technology and recommendations for utilization in medical genetics practice for detection of chromosomal abnormalities (ACMG Guidelines). Genet Med. 2010 Nov; 12(11): 742-745. https://pubmed.ncbi.nlm.nih.gov/20962661/
13. Miller DT, Adam MP, Aradhya S, et al. Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies. Am J Hum Genet. 2010 May; 86(5): 749-764. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2869000/pdf/main.pdf
14. Michelson DJ, Shevell MI, Sherr EH, et al. Evidence report: Genetic and metabolic testing on children with global developmental delay: report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology. 2011 Oct; 77(17): 1629-1635, http://www.neurology.org/content/77/17/1629.full.pdf+html

15. National Library of Medicine. Genetics Home Reference: Glossary. Published: July 28, 2020 http://ghr.nlm.nih.gov/glossary
16. Park SJ, Jung EH, Ryu RS, et al. Clinical implementation of whole-genome array CGH as a first-tier test in 5080 pre and postnatal cases. Mol Cytogenet. 2011 May 9;4:12. doi: 10.1186/1755-8166-4-12. http://www.molecularcytogenetics.org/content/pdf/1755-8166-4-12.pdf
17. Rare Chromosome Disorder Support Group. Microarray-based comparative genomic hybridisation (array CGH). 2013. Available at: http://www.rarechromo.org/files/Array%20CGH%20QFN.pdf
18. Reiff M, Bernhardt BA, Mulchandani S. Genomic variation: what does it mean? Leonard Davis Institute of Health Economics Issue Brief. 2013 Feb/March; 18(4). https://ldi.upenn.edu/policy/issue-briefs/2013/03/19/genomic-variation-what-does-it-mean
19. Resta N, Memo L. Chromosomal microarray (CMA) analysis in infants with congenital anomalies: when is it really helpful? J Matern Fetal Neonatal Med. 2012 Oct; 25 Suppl 4:124-126. doi: 10.3109/14767058.2012.715004. https://www.ncbi.nlm.nih.gov/pubmed/22958042
20. Rosti RO, Sadek AA, Vaux KK, et al. The genetic landscape of autism spectrum disorders. Dev Med Child Neurol. 2014 Jan;56(1):12-8. doi: 10.1111/dmcn.12278. Epub 2013 Oct 1. http://onlinelibrary.wiley.com/doi/10.1111/dmcn.12278/pdf
21. Sagoo GS, Butterworth AD, Sanderson S, et al. Array CGH in patients with learning disability (mental retardation) and congenital anomalies: updated systematic review and meta-analysis of 19 studies and 13,926 subjects. Genet Med. 2009 Mar; 11(3): 139-146. https://pubmed.ncbi.nlm.nih.gov/19367186/
22. South ST, Lee C, Lamb AN, et al. ACMG Standards and Guidelines for constitutional cytogenomic microarray analysis, including postnatal and prenatal applications: revision 2013. Genet Med. 2013 Nov;15(11):901-9. doi: 10.1038/gim.2013.129. Epub 2013 Sep 26. https://pubmed.ncbi.nlm.nih.gov/24071793/
23. Trevathan E. So what? Does the test lead to improved health outcomes? Neurology. Feb 2012, 78 (6) 440-442; DOI:10.1212/WNL.0b013e318248042c http://www.neurology.org/content/78/6/440.full.pdf+html
24. Wain KE, Thorland EC. Clinical Utility of Chromosomal Microarray Testing. Pediatrics. 2012 Nov;130(5):e1085-95. doi: 10.1542/peds.2012-0568. Epub 2012 Oct 15. https://www.ncbi.nlm.nih.gov/pubmed/23071206

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