Chromosomal Microarray Analysis
Medical Necessity Guideline

Medical Necessity Guideline (MNG) Title: Chromosomal Microarray Analysis		
MNG #: 108	**☒ CCA Senior Care Options (HMO D-SNP) (MA)** **☒ CCA One Care (Medicare-Medicaid) (MA)**	**Prior Authorization Needed?** **☒ Yes (always required)** **☐ Yes (only in certain situations. See this MNG for details)** **☐ No**
Benefit Type: **☐ Medicare** **☒ Medicaid**	**Approval Date:** 9/1/2022;	**Effective Date:** 12/24/2022; 1/1/2025
Last Revised Date: 9/14/2023; 11/14/2024; 3/25/2025	**Next Annual Review Date:** 9/1/2023; 9/14/2024; 11/14/2025	**Retire Date:**

OVERVIEW:

Chromosomal microarray analysis (CMA) is a high-resolution, whole-genome screening technique that measures gains and losses of DNA throughout the human genome. It is used to identify chromosomal aneuploidies, large changes in the structure of the chromosomes, and submicroscopic abnormalities for the screening, diagnosis, and treatment of congenital anomalies, autism spectrum disorder, developmental delays, and intellectual disabilities.

The two types of CMA genetic tests that can be used for prenatal diagnosis are comparative genomic hybridization (CGH) arrays and single nucleotide polymorphism (SNP) arrays. Both methods can use DNA samples from uncultured amniocytes (from amniotic fluid), chorionic villus cells, cord blood, and products of conception by amniocentesis or chorionic villus sampling. CGH arrays help to detect copy number variants (CNVs) by comparing the fetal DNA sample with a normal reference. They are labelled with two different colored fluorescent dyes, combined, and then hybridized to an array platform. Thereafter, the relative intensities of the different colors are compared using bioinformatics tools. Signals of higher hybridization reflect cases with duplications and signals of lower hybridization reflect cases with deletions. SNP arrays help to identify triploidy, uniparental disomy, consanguinity, maternal cell contamination, and *mosaicism* by analyzing one specific DNA test sample. That one DNA test sample is hybridized to the array platform and signal intensities are detected in a similar manner as in CGH arrays.

Compared with conventional karyotyping, CMA arrays have higher diagnostic yield, increased sensitivity for cytogenetic abnormalities, faster availability of results, and better ability to obtain results from uncultured cells. CMA arrays are the preferred type of testing for fetal structural abnormalities and early fetal loss to confirm the diagnosis and to determine the precise genomic coordinates and probability of inheritance. Despite the advantages, CMA arrays are limited by their inability to detect genetic events that do not affect the relative copy-number of DNA sequences, low-level mosaicism, tumor-specific changes, tetraploidies, duplications and deletions below the detection levels, and *balanced chromosomal arrangements*. As such, the American College of Obstetricians and Gynecologists recommend comprehensive patient pre-test and post-test genetic counselling prior to the initiation of CMA.

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DEFINITIONS:

Aneuploidy – The presence of an abnormal (i.e., higher or lower) number of chromosomes in a cell, instead of the usual 46.

Balanced Chromosome Rearrangement: A chromosome rearrangement that does not result in deletion or duplication of genetic material. Examples include inversions and translocations.

Chromosomal Microarray Analysis (CMA): A method of measuring gains and losses of DNA throughout the human genome. It can identify chromosomal aneuploidy and other large changes in the structure of chromosomes that would otherwise be identified by standard karyotype analysis, as well as submicroscopic abnormalities that are too small to be detected by traditional modalities. This is also known as comparative genomic hybridization.

Comparative Genomic Hybridization: Type of CMA that combines chromosome and fluorescence in-situ hybridization (FISH) to detect aneuploidies, microdeletion, and microduplication disorders.

Copy Number Variants (CNVs): Duplicated or deleted sections of DNA of at least 1,000 base pairs in size that differ from a representative reference genome. This causes birth defects or neurodevelopmental problems. CNVs can be qualified as pathogenic or benign to clarify clinical relevance. In the context of prenatal diagnosis, the probability of finding a pathogenic CNV is highly correlated with the presence of structural fetal abnormalities.

Cytogenetic Abnormalities: Genetic defects that involve large regions of chromosomes rather than small pieces of DNA. These could be numerical abnormalities, which include aneuploidies, hypodiploidies, hyperdiploidies, and polyploidies; or structural abnormalities, which refer to deletion, duplication, triplication, amplification, translocations, inversions, insertions, and marker chromosomes.

Mosaicism: The presence of two or more populations of cells with different characteristics within one tissue or organ. It is a DNA variation in which a single nucleotide in the genome sequence is altered. But it may or may not cause disease.

Single Nucleotide Polymorphism: DNA variation in which a single nucleotide in the genome sequence is altered and may/may not cause disease.

Tetraploidy – A chromosomal abnormality characterized by the presence of four sets of chromosomes, instead of the usual two sets.

DECISION GUIDELINES:

Clinical Coverage Criteria:

CCA may cover chromosomal microarray testing using comparative genomic hybridization microarray testing or single nucleotide polymorphism microarray analysis when the following criteria are met:

1. The member is undergoing invasive prenatal diagnostic testing (e.g., amniocentesis or chorionic villus sampling); or
2. A member with a fetus with one or more major structural abnormalities identified on ultrasonographic examination and the member is undergoing invasive prenatal diagnosis. This test typically can replace the need for fetal karyotype; or

3. There is intrauterine fetal demise or stillbirth ≥ 20 weeks of gestational age, and the member desires cytogenetic analysis of fetal tissue (i.e., amniotic fluid, placenta, or products of conception) because of the test's increased likelihood of obtaining results and improved detection of causative abnormalities;

AND

4. Comprehensive genetic counselling has been performed pretest, and plans to be performed posttest, by an obstetrician–gynecologist or other health care provider with genetics expertise regarding the benefits, limitations, and results of chromosomal microarray analysis; and
5. Informed consent has been obtained, which includes a discussion of the potential to identify findings of uncertain significance, nonpaternity, consanguinity, and adult-onset disease.

LIMITATIONS/EXCLUSIONS:

CCA will not cover and does not consider chromosomal microarray analysis testing to be medically necessary in any of the following circumstances (but not limited to):

1. In cases of a single miscarriage or recurrent miscarriages with pregnancy loss < 20 weeks of gestation where the fetus is structurally normal, or pregnancy losses where structural condition of the pregnancy(ies) is unknown.
2. An obvious diagnosis, genetic disorder, or metabolic derangement is responsible for the obstetric ultrasound findings or pregnancy loss (including stillbirth).
3. For preimplantation genetic testing and diagnosis.
4. The routine use of whole-genome or whole-exome sequencing for prenatal diagnosis is not recommended outside of the context of clinical trials until sufficient peer-reviewed data and validation studies are published.
5. Chromosomal microarray analysis should not be ordered without informed consent, which should include discussion of the potential to identify findings of uncertain significance, nonpaternity, consanguinity, and adult-onset disease.

CODING:

When applicable, a list(s) of codes requiring prior authorization is provided. This list is for reference purposes only and may not be all inclusive. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment.

CPT Code	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

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Disclaimer:
Commonwealth Care Alliance (CCA) follows applicable Medicare and Medicaid regulations and uses evidence based InterQual© criteria, when available, to review prior authorization requests for medical necessity. This Medical Necessity Guideline (MNG) applies to all CCA Products unless a more expansive and applicable CMS National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), or state-specific medical necessity guideline exists. Medical Necessity Guidelines are published to provide a better understanding of the basis upon which coverage decisions are made. CCA makes coverage decisions on a case-by-case basis by considering the individual member's health care needs. If at any time an applicable CMS LCD or NCD or state-specific MNG is more expansive than the criteria set forth herein, the NCD, LCD, or state-specific MNG criteria shall supersede these criteria.

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. This Medical Necessity Guideline is subject to all applicable Plan Policies and Guidelines, including requirements for prior authorization and other requirements in Provider's agreement with the Plan (including complying with Plan's Provider Manual specifications).

This Medical Necessity Guideline is not a rigid rule. As with all CCA's criteria, the fact that a member does not meet these criteria does not, in and of itself, indicate that no coverage can be issued for these services. Providers are advised, however, that if they request services for any member who they know does not meet our criteria, the request should be accompanied by clear and convincing documentation of medical necessity. The preferred type of documentation is the letter of medical necessity, indicating that a request should be covered either because there is supporting science indicating medical necessity [supporting literature (full text preferred) should be attached to the request], or describing the member's unique clinical circumstances, and describing why this service or supply will be more effective and/or less costly than another service which would otherwise be covered. Note that both supporting scientific evidence and a description of the member's unique clinical circumstances will generally be required.

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REVISION LOG:

REVISION DATE	DESCRIPTION
3/25/2025	Template Update
12/17/2024	Utilization Management Committee approval
11/14/2024	Added 2 definitions; Added 2 Clinical Coverage Criteria, and expounded on 2 Clinical Coverage Criteria; Removed requirement for comprehensive history and exams in Limitation 2; Added 2 Limitations; Removed Authorization section; Formatted template to current.
9/14/2023	No changes

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APPROVALS:

Stefan Topolski	Medical Director
CCA Senior Clinical Lead [Print]	**Title [Print]**
	3/18/2025
Signature	**Date**

Nazlim Hagmann, MD	Chief Medical Officer
CCA CMO or Designee [Print]	**Title [Print]**
	3/18/2025
Signature	**Date**