COMPARATIVE GENOMIC HYBRIDIZATION (CGH)
Microarray Testing for Chromosomal Imbalances

Policy Number: 2016M0013C  Effective Date: February 1, 2016

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INSTRUCTIONS:

“Medical Policy assists in administering UCare benefits when making coverage determinations for members under our health benefit plans. When deciding coverage, all reviewers must first identify enrollee eligibility, federal and state legislation or regulatory guidance regarding benefit mandates, and the member specific Evidence of Coverage (EOC) document must be referenced prior to using the medical policies. In the event of a conflict, the enrollee’s specific benefit document and federal and state legislation and regulatory guidance supersede this Medical Policy. In the absence of benefit mandates or regulatory guidance that govern the service, procedure or treatment, or when the member’s EOC document is silent or not specific, medical policies help to clarify which healthcare services may or may not be covered. This Medical Policy is provided for informational purposes and does not constitute medical advice. In addition to medical policies, UCare also uses tools developed by third parties, such as the InterQual Guidelines®, to assist us in administering health benefits. The InterQual Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. Other Policies and Coverage Determination Guidelines may also apply. UCare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary and to provide benefits otherwise excluded by medical policies when necessitated by operational considerations.”
POLICY DESCRIPTION:
Comparative genomic hybridization (CGH), also referred to as chromosomal microarray analysis (CMA), and array CGH (aCGH), is a method of genetic testing in newborns or children promoted for the screening, diagnosis and treatment of congenital anomalies, autism spectrum disorder (ASD), developmental delays (DD), idiopathic mental retardation (MR); and screening for prenatal gene mutations.

COVERAGE RATIONALE / CLINICAL CONSIDERATIONS:
The use of array-based comparative genomic hybridization (aCGH) testing for neurodevelopmental chromosomal imbalances may be considered MEDICALLY NECESSARY for evaluating individuals, who are suspected of having an underlying genetic condition or syndrome, when no correlation can be well-delineated as to a specific genetic condition(s) after patient history, physical examination, family history, pedigree analysis, and the completion of conventional genetic evaluations.

The test must be ordered by a geneticist or care provider with expertise in the diagnosis and/or management of a condition associated with neurodevelopmental chromosomal imbalances. Testing should be accompanied by pre- and post-test genetic counseling from a qualified genetic counselor and should include a discussion about the limitations and possible outcomes of the analysis.

Array-based CGH may be used in the diagnostic evaluation of any of the following conditions, when the above criteria is met:

1. Prenatal diagnosis in patients with a fetus with abnormal structural findings on an ultrasonographic examination or magnetic resonance imaging, and a normal karyotype by conventional cytogenetics.

2. Cases of intrauterine fetal demise and stillbirths with a suspected genetic syndrome when the result of the test will directly impact the management or treatment being delivered to the member with a resulting improvement in health outcomes (e.g., results will have an impact on the member’s subsequent treatment plan, pregnancy planning, or family member genetic counseling).

3. Neonate in the neonatal intensive care unit (NICU) with clinically suspected congenital anomalies (the condition is life threatening and results will be used in urgent care management determinations).

4. Child or adult clinically suspected of having an underlying genetic condition or syndrome, and who presents developmental delay, dysmorphic features, or intellectual disabilities (e.g., mental retardation).

5. Multiple congenital anomalies or an isolated congenital anomaly with a family history of autosomal dominant or X-linked inheritance.

The use of array-based comparative genomic hybridization (aCGH) is considered EXPERIMENTAL AND/OR INVESTIGATIONAL for all other indications, including but not limited to:

- Detection of balanced rearrangements
- Evaluation of unexplained epilepsies
- Screening of autism spectrum disorder, developmental delays, attention deficit disorder, learning disabilities, speech articulation disorders, or idiopathic mental retardation (not acquired) in newborns or children
• Screening for gene mutations in pregnancies at low risk with fetuses without structural abnormalities, such as in advanced maternal age, positive maternal serum screen (alpha-fetoprotein, estriol, hCG, and inhibin-A), previous trisomy, or the presence of "soft markers" on fetal ultrasound
• Infertility and repeated first-trimester and second-trimester pregnancy losses
• Psychiatric disorders
• Growth retardation
• Neurodegenerative disorders
• Whole-genome arrays in prenatal diagnostic specimens

The use of Array-based CGH is considered EXPERIMENTAL AND/OR INVESTIGATIONAL when performed in the absence of symptoms or high risk factors for a genetic disease or when knowledge of genetic status will not affect treatment decisions or screening for the disease.

See Genetic Testing medical policy, 2015M0038B.

**Clinical Considerations:**

**Role Of Genetic Counseling.**

For pediatric and adult patients, pretest counseling should include a description of the test methodology; the objective of the test; risks, benefits, and limitations; the sample required; and the possible outcomes of testing. Possible outcomes include a negative result, identification of an imbalance known to be pathogenic, identification of benign copy number variants (CNVs), and identification of an imbalance of unknown clinical significance. Counseling should also include the procedures for following up on an ambiguous result, such as parental testing. Post-test counseling for a positive test (a conclusive diagnosis) should include a review of the family history, and testing should be offered to at-risk family members. Post-test counseling for a negative result should include a review of the limitations of aCGH (the test does not rule out an imbalance in a region not covered by the array and it does not test for sequence variations in individual genes). Pretest counseling for prenatal diagnosis should include the same aspects described for pediatric/adult settings. Additional points to cover include discussing the spectrum of phenotypes of the conditions covered by the array, and explaining that conditions represented on the array may have multiple etiologies (not all of which are being tested). Finally, the potential to reveal nonpaternity should also be discussed.

Chromosomal microarray analysis should not be ordered without informed consent, which should be documented in the medical record. (ACOG, 2013).

**Clinical Alternatives.**

For prenatal diagnoses, alternatives include detailed ultrasonography, biochemical maternal serum screening, conventional karyotype analysis, and FISH studies for specific microdeletion and microduplication syndromes. Karyotyping and FISH studies require either amniocentesis or chorionic villus sampling (CVS) to obtain fetal specimens for analysis. Alternatives to aCGH in pediatric or adult patients and in miscarried fetuses and stillbirths include a clinical evaluation with a dysmorphology examination and detailed medical, developmental, and family histories; conventional karyotype analysis; and FISH studies for specific microdeletion and microduplication syndromes.
BACKGROUND:

Chromosome abnormalities are a significant cause of morbidity and mortality in fetuses, infants, and children. Using conventional cytogenetics, which refers to a standard chromosome analysis by light microscopy, a chromosome abnormality can be identified in approximately 0.5% to 0.6% of live births. This prevalence increases to 5% to 6% for stillbirths or neonatal deaths, and to 50% to 60% for first-trimester miscarriages. Among those with developmental delays or intellectual disability, approximately 3% to 5% will have cytogenetically visible chromosome abnormalities, and another 5% to 6% will have subtelomeric alterations identified by fluorescence in situ hybridization (FISH). For patients undergoing prenatal diagnosis, approximately 5% to 10% will have an abnormal karyotype following amniocentesis or chorionic villus sampling (CVS).

Conventional cytogenetics has several limitations. First, with a high-resolution karyotype (at a band level of 550 Giemsa bands [G-bands] or higher), only alterations larger than 3 to 5 megabases (Mb) can be reliably detected. Second, results take between one and two weeks because of the need for cell culture prior to analysis. These limitations were in part addressed by the introduction of FISH, which uses fluorescently labeled DNA probes to identify specific submicroscopic imbalances. However, this test is targeted and, therefore, it provides information only about the specific locus or loci being examined but not about the rest of the genome. Therefore, it requires the affected individual to exhibit specific clinical features consistent with a known microdeletion or microduplication syndrome. In addition, FISH may not be able to determine the exact amount of material gained or lost (e.g., the breakpoints), and it is more sensitive for detecting deletions than duplications. Finally, both conventional karyotype analysis and FISH are considered labor intensive and are not amenable to automation.

Comparative genomic hybridization (CGH) utilizing microarray technology has been used for several years in the clinical diagnosis of children and adults with a suspected genetic syndrome of unknown etiology. More than 70 disorders are known to be associated with birth defects or developmental problems that are caused by deletion or duplication of genomic material, which are called "copy number variants" or "CNVs". Comparative genomic hybridization is intended to increase the chromosomal resolution for detection of CNVs, and as a result, to increase the diagnostic yield and the genomic detail beyond that of conventional methods. It is intended to combine the speed of DNA analysis with a large capacity to scan for genomic abnormalities in a single assay. It has been estimated that approximately 10,000 array-based CGH tests (aCGH) are performed each year in the United States. Not only has this led to the diagnosis of more patients, it has led to the identification of new microdeletion and microduplication syndromes.

This technique involves comparing the genomes of two individuals: the patient and a normal control. Through hybridization to a microarray containing thousands of DNA segments (typically, bacterial artificial chromosome [BAC] clones or oligonucleotide probes), genomic imbalances such as deletions and duplications may be identified. Array-based CGH (aCGH) offers a cytogenetic evaluation at a significantly higher resolution than a standard karyotype analysis, as well as the ability to look for genomic imbalances throughout the genome in a single assay. The array may be targeted in nature, assaying certain regions of the genome known to be associated with a specific syndrome or phenotype, or may be genome wide. The arrays vary by the number, size, and distribution of the clones, or targets, used. The use of a large number of small clones (oligonucleotides) that are more closely spaced leads to an increased resolution. The main issue with aCGH, particularly with the genome-wide arrays, is the identification of variants of unknown clinical significance. In addition, aCGH will not detect balanced rearrangements (i.e., balanced
translocations or inversions), certain forms of polyploidy (addition of full haploid sets of chromosomes), or imbalances not covered by the clones on the array. The applications of aCGH in prenatal and pediatric populations include testing for aneuploidy and segmental imbalances, and evaluating unclear or apparently balanced rearrangements.

**Description of the Technology/Patient Population:** In aCGH, differentially fluorescently labeled DNA from patient and control specimens are simultaneously hybridized to an array containing probes for various segments of the genome. The relative quantity of patient DNA compared to the control is determined by analyzing the ratio of fluorescence at each locus to assess the probability of a deletion or duplication. Array-based CGH may be used in the diagnosis of patients with birth defects, dysmorphic features, developmental delays, intellectual disability, and/or other developmental disabilities. It may also be used for prenatal diagnosis in patients who have an abnormal ultrasonographic examination or maternal biochemical serum screen, have a family history suggestive of a chromosome abnormality, or are of advanced maternal age (35 years of age or older at the time of delivery). In addition, aCGH may be used in the evaluation of chromosomal imbalances in miscarried fetuses and stillbirths.

A variety of software programs are used in the processing of data gathered by the hybridization. These include GenePix® (Axon Instruments Inc.); CGH Analytics (Agilent Technologies); SpectralWare® CGH Analysis (Spectral Genomics); Imagene (Biodiscovery Inc.); and ScanArray Lite (GSI Lumonics). Verification of imbalances is usually performed by FISH analysis, although real-time quantitative polymerase chain reaction (PCR) or multiplex ligation-dependent probe amplification (MLPA) may also be used.

To address the issue of variants of unknown significance, several databases have been established to catalog CNVs known to be benign. These include the Database of Chromosomal Imbalance and Phenotype in Humans using Ensemble Resources (DECIPHER), Database of Genomic Variants, European Cytogeneticists Association Register of Unbalanced Chromosome Aberrations (ECARUCA), and Mendelian Cytogenetics Network Online Database.

Comparative genomic hybridization may be ordered when conventional results are negative. It is not known, however, whether the diagnostic benefit gained from being able to test for a large number of genomic disorders and other chromosomal defects with CGH outweighs the risks of detecting CNVs of uncertain clinical significance.
Ambry Genetics (Aliso Viejo, CA).
- Chromosomal Microarray (Test-specific CPT code: 81228; Technology-specific CPT codes: 83891x1, 83892x2, 83894x1, 83912x1, 83838x1, 83838x1, 83838x1): 105,000 oligonucleotide probes with an average resolution of 30 kb, with increased coverage at approximately 270 disease loci.55

ARUP Laboratories (Salt Lake City, UT).
- Genomic SNP Microarray, Products of Conception: Oligo-SNP Array.56
- Microarray Genomic, Fetal (2002366) (Test-specific CPT code: 81228; Technology-specific CPT codes: 88235x1, 88386x6, 83891x2): Details not specified.57

Baylor College of Medicine Medical Genetics Laboratories (Houston, TX).
- Chromosomal Microarray Analysis (Test #8655) (Test-specific CPT code: 81228): Approximately 180,000 oligonucleotide probes with an average resolution of 30 kb, covering 1714 genes, 700 microRNAs, and the entire mitochondrial genome.58
- Chromosomal Microarray Analysis - Prenatal Amniotic Fluid (Test #8656) (Test-specific CPT code: 81228; Technology-specific CPT codes: 88271x82, 88235x1, 83901x11, 83898x2, 83909x2, 83896x2, 83900x1, 88291x1, 83891x2, 83912x2) and CVS (Test #8657): 105,000 oligonucleotide probes with an average resolution of 30 kb.59,60

CombiMatrix Molecular Diagnostics (CMDX) (Irvine, CA).
- Oligo HD Scan™ Array CGH Test (Test-specific CPT code 81228; Technology-specific CPT codes: 83891x2): 105,000 oligonucleotide probes with a maximum spacing of 10 kb in clinically relevant regions and at least one probe every 35 kb throughout the rest of the genome.61
- BAC HD Scan™ v2 Array CGH Test: 3052 BAC clones with an average resolution of 0.8 Mb.62
- Prenatal Scan™ v2 Array CGH Test: More than 2100 BAC clones that test for 111 known disorders and have an increased resolution at the subtelomeric and pericentromeric regions.63
- POC Scan™ v2 Array CGH Test: BAC array containing 3052 clones, designed to evaluate products of conception (POC).64

GeneDx Inc. (Gaithersburg, MD).
- GenomeDX version 3.0 (Test-specific CPT code: 81228; Technology-specific CPT codes: 83891x1, 88271x81, 88291x1): 105,000 oligonucleotide probes with a spacing of 9 to 17 kb in clinically relevant regions (with the ability to detect imbalances as small as 50 kb) and an average spacing of 37 kb throughout the rest of the genome (with the ability to detect imbalances as small as 200 kb).65
- FISHonChipDX (Test-specific CPT code: 81228; Technology-specific CPT codes: 83891x1, 88271x65, 88291x1): 15,000 oligonucleotide probes covering 65 common microdeletion/duplication syndromes and all subtelomeric and pericentromeric regions, with additional probes every 400 to 500 kb throughout the genome.66

Genzyme Genetics (Cambridge, MA).
- Array CGH Postnatal 44K Oligonucleotide Array (Test-specific CPT code: 81228): Approximately 44,000 oligonucleotide probes with unspecified spacing.67

Laboratory Corporation of America (LabCorp) (Burlington, NC).
- Chromosome SNP Microarray (510002) (Test-specific CPT code: 81229): Probes for approximately
1.8 million single nucleotide polymorphisms (SNPs), with an average spacing of 700 base pairs.\(^6\)

**Quest Diagnostics Inc. (Madison, NJ).**
- Clarisure™ CGH (Test-specific CPT code: 81228): More than 3000 BAC clones with an average spacing of 1 Mb.\(^6\)

**Signature Genomic Laboratories LLC (Spokane, WA).**
- SignatureChip Oligo Solution™ (SignatureChipOS™) (Test-specific CPT code: 81228; Technology-specific CPT codes: 88386x6, 83891x1): 135,000 oligonucleotide probes with a maximum spacing of 35 kb and a probe spaced every 10 kb in clinically relevant regions.\(^7\)
- Signature PrenatalChip®OS (Test-specific CPT code: 81228; Technology-specific CPT codes: 88386x6, 83891x1, 88241x1): 135,000 oligonucleotide probes with a maximum spacing of 35 kb and a probe spaced every 10 kb in clinically relevant regions.\(^7\)
- Signature PrenatalChip®TE [Targeted Enhanced] (Test-specific CPT code 81228; Technology-specific CPT codes: 88386x4, 83891x1, 88241x1): More than 55,000 oligonucleotide probes spaced every 10 kb in targeted regions (loci associated with known syndromes, as well as subtelomeric and pericentromeric regions) and every 100 kb throughout the rest of the genome.\(^7\)

2. **CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS):**
There is no CMS National Coverage Determination (NCD) or Local Coverage Determination (LCD) for Comparative genomic hybridization (CGH), microarray testing for chromosomal imbalances.

3. **MINNESOTA DEPARTMENT OF HUMAN SERVICES (DHS):**
Minnesota DHS does not have a policy statement regarding Comparative genomic hybridization (CGH), microarray testing in its Provider Manual or other specific provider references.

**Cytogenetic Testing**
MHCP covers cytogenetic testing performed on an MHCP recipient. Documentation in the medical record must reflect the medical necessity for the testing. All claims submitted for payment of cytogenetic testing must contain the specific diagnosis related to the tests being performed. Use the most specific procedure code available with the genetic coding modifier and number of units. (Some cytogenetic tests require authorization.)

MHCP does not cover cytogenetic testing for:
- Legal, paternity, or informational purposes, unless it is medically necessary for the recipient to receive cytogenetic testing
- Family members who are not MHCP recipients
- Fetus testing

**State Mandates.** The National Newborn Screening and Genetics Resource Center (NNSGRC) provides information on state mandates for both genetic and nongenetic newborn screening.\(^1\) The state of Minnesota does not have a newborn screening or genetic program for early identification and treatment of infants who are affected by certain heritable disorders and genetic disease.
**CLINICAL EVIDENCE:**

This review is based on the ACCE model developed by the Centers for Disease Control and Prevention (CDC) and that continues to be used by the CDC-funded Evaluation of Genomic Applications in Practice and Prevention (EGAPP) project. The ACCE model takes its name from an abbreviation of its main components: Analytical validity; Clinical validity; Clinical utility; and Ethical, legal, and social implications. Analytical validity is the ability of a genetic test to measure accurately and reliably the genotype of interest, whereas clinical validity is the ability of a genetic test to detect or predict the associated disorder or phenotype. Clinical utility focuses on what needs to be considered when evaluating the risks and benefits of introducing a genetic test into routine practice, and includes studies that seek to determine improvements in health outcomes when using the genetic test in clinical practice.

**Summary:**

Array-based CGH is a relatively new technology that is being utilized in the diagnosis of genetic syndromes, both postnatally and prenatally. It may be performed using a targeted array that assesses loci known to be associated with a specific condition or phenotype, or it may be performed with a genome-wide array, with clones located throughout the genome at a specified density. Both BAC and oligonucleotide arrays are available, with a resolution as low as 50 kb. Array-based CGH has also been used to detect low-level mosaicism and to characterize unclear or apparently balanced karyotypes.

Array-based CGH has been validated in a number of studies utilizing samples with known chromosomal imbalances. Array-based CGH consistently demonstrates a high sensitivity and specificity with nearly all segmental and whole-chromosome imbalances being detected. Array-based CGH may also be able to characterize unclear abnormalities identified by conventional cytogenetics, such as identifying the origin of an SMC, or more clearly define the breakpoints of a given rearrangement. However, aCGH is not able to detect balanced rearrangements, such as balanced translocations or inversions, and cannot detect certain forms of polyploidy. Mosaic abnormalities are consistently detected down to a level of 20%, but lower levels of mosaicism may be missed.

Studies of the clinical validity of aCGH indicate that the diagnostic yield in pediatric patients varies depending on the population examined and the array used. Most studies involving patients with developmental concerns, dysmorphic features, and/or congenital anomalies, and with no known karyotypic abnormality, demonstrate a detection rate between 5.4% and 12.1%, when using a targeted array. When a whole-genome array is utilized, the diagnostic yield is typically increased, with most studies demonstrating a detection rate between 7.5% and 15.6%. For the same population, the frequency of benign copy number changes and of CNVs of unknown clinical significance are up to 15% and up to 4.2%, respectively. The majority of studies involving prenatal samples suggest that the detection rate for aCGH is likely between 1% and 6%, while the frequency of benign copy number changes and CNVs of unclear significance are 6% to 13.3% and 0% to 2%, respectively.

Studies of the clinical utility of aCGH suggest that the diagnosis of a chromosomal imbalance using this technique may lead to changes in the medical management of the patient, including referrals to new specialists, initiating screening protocols, avoiding additional diagnostic tests, and improving access to services. In addition, establishing a specific diagnosis typically allows for more accurate genetic counseling and recurrence risk estimation, and for more informed reproductive decision making.

In reviewing the studies used in this assessment, several limitations are noted. First, a number of studies...
examining the clinical validity of aCGH were performed by the commercial laboratories that offer this testing on a clinical basis, suggesting there could be a conflict of interest. Second, several studies examining the diagnostic yield in pediatric or adult patients involves a relatively small number of patients (i.e., < 50), particularly considering this patient population is the most common. Third, while most studies clearly describe the inclusion and exclusion criteria used for patient selection, two studies fail to mention whether the test subjects had any prior or concurrent testing, such as a conventional karyotype analysis and characteristics of their patient population. Another deficiency noted for several reports was the lack of information regarding the categorization of copy number changes (i.e., pathogenic versus benign versus unclear), information necessary for assessing the validity of the data presented. Finally, at least one study presented very limited information regarding the design of the microarray utilized, making it difficult to assess the impact of array resolution on diagnostic yield. Studies regarding the validation and utility of aCGH in all of the above populations will continue to increase, and may lead to changes in the management recommendations in the very near future. The use of this technology in clinical settings is also expected to increase, which will likely decrease the cost of this analysis and make it more readily accessible. It is also likely to have a significant impact on the screening and treatment of a variety of disorders, to increase the discovery of genetic syndromes not yet described, and to identify the causative genes associated with syndromes for which the etiology is unknown.

**APPLICABLE CODES:**

The Current Procedural Terminology (CPT®) codes and HCPCS codes listed in this policy are for reference purposes only. Listing of a service or device code in this policy does not imply that the service described by this code is a covered or non-covered health service. The inclusion of a code does not imply any right to reimbursement or guarantee claims payment. Other medical policies and coverage determination guidelines may apply.

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<tr>
<th>ICD-9 Codes</th>
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<tr>
<td>299.00 – 299.01</td>
<td>Autistic disorder</td>
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<tr>
<td>317-319</td>
<td>Mental Retardation</td>
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<tr>
<td>740.0 - 759.9</td>
<td>Congenital anomalies [for evaluating fetuses with structural abnormalities detected on fetal ultrasound or fetal MRI]</td>
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<tr>
<td>V28.0 – V28.9</td>
<td>Encounter for antenatal screening of mother</td>
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<tr>
<td>V79.2</td>
<td>Special screening for mental retardation</td>
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<tr>
<td>V82.71 – V82.79</td>
<td>Genetic screening</td>
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<td>V82.89</td>
<td>Special screening for other specified conditions</td>
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<th>HCPCS Codes</th>
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<tr>
<td>S3870</td>
<td>Comparative genomic hybridization (CGH) microarray testing for developmental delay, autism spectrum disorder and/or mental retardation</td>
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<tr>
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<th>Description</th>
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<tr>
<td>81228</td>
<td>Cytogenetic 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)</td>
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<tr>
<td>81229</td>
<td>Cytogenetic constitutional (genome-wide) microarray analysis; interrogation of genomic regions for copy number and single nucleotide polymorphism (SNP) variants for chromosomal abnormalities.</td>
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<tr>
<td>83890</td>
<td>Molecular diagnostics; molecular isolation or extraction, each nucleic acid type (e.g., DNA)</td>
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or RNA)

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<tr>
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<th>Description</th>
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<tr>
<td>83891</td>
<td>Molecular diagnostics; isolation or extraction of highly purified nucleic acid, each nucleic acid type (ie, DNA or RNA)</td>
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<td>83892</td>
<td>Molecular diagnostics; enzymatic digestion, each enzyme treatment</td>
</tr>
<tr>
<td>83893</td>
<td>Molecular diagnostics; dot/slot blot production, each nucleic acid preparation</td>
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<tr>
<td>83894</td>
<td>Molecular diagnostics; separation by gel electrophoresis (e.g., agarose, polyacrylamide), each nucleic acid preparation</td>
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<td>83895</td>
<td>Nitrogen, Total; Urine, 24-hour Specimen</td>
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<td>83896</td>
<td>Molecular diagnostics; nucleic acid probe, each</td>
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<td>83897</td>
<td>Molecular diagnostics; nucleic acid transfer (e.g., Southern, Northern), each nucleic acid preparation</td>
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<td>83898</td>
<td>Molecular diagnostics; amplification, target, each nucleic acid sequence</td>
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<td>83900</td>
<td>Molecular diagnostics; amplification, target, multiplex, first 2 nucleic acid sequences</td>
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<td>Molecular diagnostics; amplification, target, multiplex, each additional nucleic acid sequence beyond 2 (List separately in addition to code for primary procedure)</td>
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<td>Molecular diagnostics; mutation identification by allele specific transcription, single segment, each segment</td>
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<td>83906</td>
<td>Molecular diagnostics; mutation identification by allele specific translation, single segment, each segment</td>
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<td>83907</td>
<td>Molecular diagnostics; lysis of cells prior to nucleic acid extraction (e.g., stool specimens, paraffin embedded tissue), each specimen</td>
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<td>83908</td>
<td>Molecular diagnostics; amplification, signal, each nucleic acid sequence</td>
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<tr>
<td>83909</td>
<td>Molecular diagnostics; separation and identification by high resolution technique (e.g., capillary electrophoresis), each nucleic acid preparation</td>
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<td>83910</td>
<td>Nonprotein Nitrogen (npn), Blood</td>
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<td>83912</td>
<td>Molecular diagnostics; interpretation and report</td>
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<td>83913</td>
<td>Molecular diagnostics; RNA stabilization</td>
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<td>83884</td>
<td>Array-based evaluation of multiple molecular probes; 11 through 50 probes</td>
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<td>83885</td>
<td>Array-based evaluation of multiple molecular probes; 51 through 250 probes</td>
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<td>83886</td>
<td>Array-based evaluation of multiple molecular probes; 251 through 500 probes</td>
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**ICD-10 Codes**

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<td>F70-F79</td>
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<td>Q00.0-Q09</td>
<td>Congenital malformations, deformations and chromosomal abnormalities</td>
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<td>Z13.4</td>
<td>Encounter for screening for certain developmental disorders in childhood</td>
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<tr>
<td>Z13.71-Z13.79</td>
<td>Encounter for screening for genetic and chromosomal anomalies</td>
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<tr>
<td>Z36</td>
<td>Encounter for antenatal screening of mother</td>
</tr>
</tbody>
</table>

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**REFERENCES:**


61. Combimatrix Molecular Diagnostics (CMDX). Oligo HD Scan™ Array CGH Test.

62. Combimatrix Molecular Diagnostics (CMDX). BAC HD Scan™ v2 Array CGH Test.

63. Combimatrix Molecular Diagnostics (CMDX). Prenatal Scan™ v2 Array CGH Test.

64. Combimatrix Molecular Diagnostics (CMDX). POC Scan™ v2 Array CGH Test.


70. Signature Genomics Laboratories LLC. Signature Chip OS™.
71. Signature Genomic Laboratories LLC. Signature PrenatalChip® OS.
72. Signature Genomic Laboratories LLC. Signature PrenatalChip® TE.


111. Genzyme Genetics. CLIA Certification.


114. Signature Genomic Laboratories LLC. CLIA Certification.


116. Coalition of State Genetics Coordinators (CSGC) [website]. State Genetics websites. Available at:


126. Baylor College of Medicine Medical Genetics Laboratories. Chromosomal Microarray Analysis - Mitochondrial/Metabolic (MitoMet® tests available.


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POLICY HISTORY:

<table>
<thead>
<tr>
<th>DATE</th>
<th>ACTION/DESCRIPTION</th>
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<tbody>
<tr>
<td>01/27/2013</td>
<td>New policy 2012D0003A. Approved by the Interim Medical Policy Committee.</td>
</tr>
<tr>
<td>03/28/2013</td>
<td>Quality Improvement Advisory and Credentialing Council (QIACC).</td>
</tr>
<tr>
<td>11/01/2013</td>
<td>Published to UCare.org</td>
</tr>
<tr>
<td>03/02/2014</td>
<td>Annual Review:</td>
</tr>
<tr>
<td></td>
<td>• Policy Number has changed to 2014M0013B.</td>
</tr>
<tr>
<td></td>
<td>• Revised Coverage Rationale: New indications have been added.</td>
</tr>
<tr>
<td></td>
<td>• Updated Background, Clinical Evidence, and References sections.</td>
</tr>
<tr>
<td></td>
<td>• Updated Coding section to include ICD-10 codes.</td>
</tr>
<tr>
<td>03/12/2014</td>
<td>New Policy. Reviewed by the Medical Policy Committee.</td>
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<tr>
<td>03/27/2014</td>
<td>Reviewed and approved by the Quality Improvement Advisory and Credentialing Committee (QIACC).</td>
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<tr>
<td>12/7/2015</td>
<td>Updated policy reviewed by Medical Policy Committee.</td>
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<td>• Revised to Policy Number 2016M0013C.</td>
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<tr>
<td>12/17/2015</td>
<td>Reviewed and approved by the Quality Improvement Advisory and Credentialing Committee (QIACC).</td>
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<td>01/01/2016</td>
<td>Published to UCare.org</td>
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QUESTIONS AND ANSWERS:

Q1:                                                                 
A1:                                                               

ATTACHMENTS: