IEHP UM Subcommittee Approved Authorization Guidelines
Microarray testing for Developmental Delay

Policy:
IEHP does not cover comparative genomic hybridization (CGH) Microarray, Chromosomal Microarray or SNP Microarray for the screening and diagnosis of autism spectrum disorder (ASD), developmental delays (DD) and idiopathic mental retardation (MR) in newborns or children. It is considered by Medi-Cal to be a non-covered benefit.

CPT Codes / HCPCS Codes related to this guideline:

- HCPCS Code S3870 Comparative genomic hybridization (CGH) microarray testing for developmental delay, autism spectrum disorder and/or mental retardation.

The test is usually requested using the following CPT codes:

- 83891-83898 plus 88271 and 88291.
- One testing center uses the following CPT bundle 83891; 88271(x83); 83894; 88291.

Medi-Cal non-benefit statement:

<table>
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<th>S3870 CGH TEST DEVELOPMENTAL DE</th>
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<tr>
<td>Procedure Level : Level II HCPCS code</td>
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<tr>
<td>Effective Date : 09/01/2009</td>
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<td>Gender : Both</td>
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<td>Max Age : 99</td>
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<td>Medi-Cal Max Allowable Amount : $0.00</td>
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This procedure is not a covered benefit. No TAR or medi-reservation required.
Literature Review:
Subramonia-Iyer, et al. (2007) reviewed the literature on the ability of CGH to detect chromosomal abnormalities in individuals with learning disabilities. The authors included seven studies (462 patients) in their review and found an overall diagnostic yield of causal abnormalities of 13%. The false-positive yield of non-causal abnormalities ranged from 5% to 67%, although this range was only 5% to 10% in six of the studies. The authors concluded, "although promising, there is insufficient evidence to recommend the introduction of CGH testing into routine clinical practice."

Shevell, et al. (2008) utilized CGH testing to assess potential etiologic yield on children with previously un-diagnosed non-syndromal global DD. The authors reported that in children with non-syndromal GDD, CGH has an etiologic yield of 6.4%, suggesting that this emerging technology may be of diagnostic value when applied subsequent to detailed history, physical examination, and targeted laboratory testing and may merit consideration as a first-tier test in the context of a child with un-explained GDD.

ECRI Findings:

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<th>Reference</th>
<th>Purpose of Systematic Review / Technology Assessment</th>
<th>Resources Searched and Inclusion Criteria</th>
<th>Findings</th>
<th>Conclusions Reported in the Abstract</th>
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<td>Hillman et al. 2010 (4)</td>
<td>To determine whether comparative genomic hybridization (CGH) is better than conventional karyotyping for diagnosis in the prenatal population</td>
<td>MEDLINE, EMBASE, and CINAHL were searched through December 2009. Of the 135 articles identified, 10 were included.</td>
<td>The reported data was pooled in a random-effects meta-analysis. CGH was found to detect an additional 3.67% (95% confidence interval: 1.5 to 8.5%) additional genomic imbalances compared to karyotyping.</td>
<td>&quot;There appears to be an increased detection rate of chromosomal imbalances when array CGH techniques are employed in the prenatal population over conventional karyotyping. However, some are copy number imbalances that are not clinically significant.&quot;</td>
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<td>Sagoo et al. 2009 (5)</td>
<td>To update a previous meta-analysis evaluating the diagnostic accuracy and utility of CGH for patients with learning disabilities and congenital anomalies</td>
<td>Not reported in the abstract. A total of 19 studies of 13,926 patients were included.</td>
<td>The overall diagnostic yield of CGH was 10%, and the false-positive rate was 7%.</td>
<td>&quot;This updated meta-analysis provides new evidence to support the use of array-based [CGH] in investigating patients with learning disability and congenital anomalies....However, given that this technology also identifies false positives at a similar rate to causal variants, caution in clinical practice should be advised.&quot;</td>
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<td>Blue Cross Blue Shield TEC Assessment Program 2009</td>
<td>To summarize the current status of CGH for patients with clinically diagnosed developmental disability or autism spectrum disorder See section 2 of the Search Summary</td>
<td>MEDLINE searches restricted to the past 3 years. Included studies were on-topic case reports, case series, or cohort studies published in peer-reviewed journals.</td>
<td>CGH generally achieves close to 100% sensitivity for known chromosomal abnormalities. False-positive rates were inconsistently reported. CGH is able to detect many chromosomal abnormalities that are undetectable by conventional cytogenetics. However, of concern is the potential for CGH to detect abnormalities of uncertain clinical relevance.</td>
<td>&quot;CGH arrays have the advantage of greatly improved resolution, which allows detection of smaller, clinically significant genomic abnormalities not detectable by conventional assays (improved diagnostic yield)...The results of neither conventional cytogenetic evaluation nor of [array] CGH evaluation have been systematically studied for impact on patient outcomes other than diagnostic yield, which is an intermediate outcome&quot;</td>
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Cigna Coverage Policy number 0493:
CIGNA does not cover comparative genomic hybridization testing (chromosomal microarray analysis) for any indication because it is considered experimental, investigational or unproven.
Aetna Clinical Policy Bulletin Number 0787:

Aetna considers comparative genomic hybridization (CGH) experimental and investigational for the screening, diagnosis and treatment of congenital anomalies, autism spectrum disorder (ASD), developmental delays (DD), idiopathic mental retardation (MR) in newborns or children, and for screening for prenatal gene mutations, and for all other indications (e.g., detection of balanced rearrangements) because of insufficient evidence of its effectiveness.

Background:

The Array CGH is designed to detect cytogenetic imbalances that are smaller than what can be detected through routine chromosome analysis. Probes are used on glass slides as arrays to hybridize a differentially labeled patient and normal DNA. The result is an identification of changes throughout the genome. They are arranged to correspond to genes that are known to affect development. The test will detect loss or duplication of chromosomes on the array.

Effective Date: **August 10, 2011**          Reviewed Annually: **November 9, 2016**

Revised:

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Bibliography:

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