APPLICATION STATEMENT

The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.
DISCLAIMER

The Clinical Coverage Guideline is intended to supplement certain standard WellCare benefit plans. The terms of a member's particular Benefit Plan, Evidence of Coverage, Certificate of Coverage, etc., may differ significantly from this Coverage Position. For example, a member's benefit plan may contain specific exclusions related to the topic addressed in this Clinical Coverage Guideline. When a conflict exists between the two documents, the Member's Benefit Plan always supersedes the information contained in the Clinical Coverage Guideline. Additionally, Clinical Coverage Guidelines relate exclusively to the administration of health benefit plans and are NOT recommendations for treatment, nor should they be used as treatment guidelines. The application of the Clinical Coverage Guideline is subject to the benefit determinations set forth by the Centers for Medicare and Medicaid Services (CMS) National and Local Coverage Determinations and state-specific Medicaid mandates, if any.

Note: The lines of business (LOB) are subject to change without notice; consult www.wellcare.com/Providers/CCGs for list of current LOBs.

BACKGROUND

NF1 is inherited in an autosomal dominant fashion. In approximately one half of patients, the condition is caused by a new mutation in that conception. In such instances, neither parent has any clinical features of NF1, and the risk for recurrence of NF1 is likely not to exceed 1%. Rare instances of recurrence from phenotypically unaffected parents are attributed to germ-line or somatic mosaicism. However, individuals with NF1 caused by a new mutation are at a 50% risk of transmitting the gene to each of their offspring. The NF1 gene has a high penetrance rate; therefore, an individual who carries the mutation can be expected to have clinical manifestations of the disorder. Some individuals are mosaic for an NF1 mutation and may have localized signs, referred to as “segmental neurofibromatosis.” These individuals may be at risk of transmitting the mutant gene to their offspring if the germ line includes cells with the mutation, which results in an increased risk of NF1 in their offspring.\(^1\ 2\ 3\)

The NF1 gene is located on the long arm of chromosome 17 at band q11.2. Neurofibromin, the protein product of the normal gene, acts as a tumor suppressor by down-regulating another cell protein, Ras that enhances cell growth and proliferation. A wide variety of mutations have been identified within the NF1 gene, which give rise to diminished function of neurofibromin in affected persons. Detection of mutations in the NF1 gene by DNA analysis has proven to be complex because of the gene’s large size, presence of pseudogenes, and great variety of possible abnormalities.\(^1\ 2\ 3\)

National Institutes of Health (NIH) Consensus Development Conference Criteria\(^7\)

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>709.09</td>
<td>Six or more cafe-au-lait spots (CLSs) equal to or greater than 5 mm in longest diameter in prepubertal patients and 15 mm in longest diameter in postpubertal patients;</td>
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<tr>
<td>237.71</td>
<td>Two or more neurofibromas of any type (or 215.9 - one plexiform neurofibroma);</td>
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<tr>
<td>709.09</td>
<td>Freckling in the axillary or inguinal regions;</td>
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<tr>
<td>192.0</td>
<td>One optic glioma (optic pathway glioma);</td>
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<td>759.6</td>
<td>Two or more Lisch nodules (iris hamartomas);</td>
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<tr>
<td>733.90</td>
<td>Distinctive osseous lesion, such as sphenoid wing dysplasia or cortical thinning of the cortex of long bones, with or without pseudoarthrosis; <strong>AND</strong></td>
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<tr>
<td>V18.9</td>
<td>First-degree relative (parent, sibling, or child) with NF1</td>
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POSITION STATEMENT

Applicable To:

- Medicaid – Hawaii, Kentucky*
- Medicare – Easy Choice Health Plan, Hawaii, Kentucky*

For markets noted below, please refer to Care Core National Lab Management criteria (program effective August 2014) available at www.wellcare.com/provider/CCGs.

- Medicaid – Florida, Georgia, Illinois, Missouri, New Jersey, New York, South Carolina
- Medicare – Arizona, Connecticut, Florida, Georgia, Illinois, Louisiana, Missouri, New Jersey, New York, Ohio, Texas, Windsor

* Kentucky (Medicaid and Medicare) pending state approval; CCG to be used until Care Core is effective in late 2014.
Genetic testing for the diagnosis of neurofibromatosis 1 (NF1) is considered medically necessary if the following criteria are met:

- Initial diagnosis using the National Institutes of Health (NIH) Consensus Development Conference criteria (see below) is inconclusive; AND,
- Results of the test will directly affect the treatment of the affected member; AND,
- The member will receive genetic counseling before testing occurs

NOTE: Molecular testing is typically not indicated because a diagnosis of NF1 in 95% of cases can be established on the basis of clinical findings alone by 11 years of age.

Genetic and molecular testing for NF1 is considered NOT medically necessary for all other circumstances, including prenatal testing.

CODING

CPT® Codes
Reference: [http://www.uab.edu/medicine/genetics/medical-genomics-laboratory/testing-service/131-neurofibromatosis-type-1](http://www.uab.edu/medicine/genetics/medical-genomics-laboratory/testing-service/131-neurofibromatosis-type-1)

- 81265 Comparative analysis using Short Tandem Repeat (STR) markers; patient and comparative specimen (eg, pre-transplant recipient and donor germline testing, post-transplant non-hematopoietic recipient germline [eg, buccal swab or other germline tissue sample] and donor testing, twin zygozy testing, or maternal cell contamination of fetal cells)
- 81402 Molecular pathology procedure, Level 3 (eg, >10 SNPs, 2-10 methylated variants, or 2-10 somatic variants [typically using non-sequencing target variant analysis], immunoglobulin and T-cell receptor gene rearrangements, duplication/deletion variants of 1 exon, loss of heterozygosity [LOH], uniparental disomy [UPD])
- 81403 Molecular pathology procedure, Level 4 (eg, analysis of single exon by DNA sequence analysis, analysis of >10 amplicons using multiplex PCR in 2 or more independent reactions, mutation scanning or duplication/deletion variants of 2-5 exons)
- 81404 Molecular pathology procedure, Level 5 (eg, analysis of 2-5 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 6-10 exons, or characterization of a dynamic mutation disorder/triplet repeat by Southern blot analysis)
- 81405 Molecular pathology procedure, Level 6 (eg, analysis of 6-10 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of 11-25 exons)
- 81407 Molecular pathology procedure, Level 8, (eg, analysis of 26-50 exons by DNA sequence analysis, mutation scanning or duplication/deletion variants of >50 exons, sequence analysis of multiple genes on one platform)
- 81408 Molecular pathology procedure, Level 9, (eg, analysis of >50 exons in a single gene by DNA sequence analysis); NF1 (neurofibrin1)(eg, neurofibromatosis, type 1), full gene sequence
- 88230 Tissue Culture for non-neoplastic disorders; lymphocyte
- 88233 Tissue Culture for non-neoplastic disorders; skin or other solid tissue biopsy

HCPCS Level II ©Codes - No applicable codes

ICD-9-CM Procedure Codes - No applicable codes

Draft 2014 ICD-10-PCS Codes - No applicable codes

Covered ICD-9-CM Diagnosis Codes

- 192.0 Malignant neoplasm of cranial nerve, i.e. optic pathway glioma
- 215.9 Other benign neoplasm of connective and other soft tissue, Site unspecified
- 237.70 Neurofibromatosis, unspecified
- 709.09 Unspecified disorder of skin and subcutaneous tissue
- 733.90 Disorder of bone and cartilage
- 759.6 Other hamartoses, not elsewhere classified
- V18.9 Family history of genetic disease carrier
- V26.33 Genetic counseling
Covered Draft 2014 ICD-10-CM Diagnosis Codes
C72.30 - C73.32  Malignant neoplasm of optic nerve
D21.9     Benign neoplasm of connective and other soft tissue, unspecified
L81.2 - L81.3  Other disorders of pigmentation
M89.9     Disorder of bone, unspecified
Q85.00  Neurofibromatosis, unspecified
Q85.09  Other neurofibromatosis
Z31.5  Encounter for genetic counseling
Z84.81  Family history of carrier of genetic disease

REFERENCES

MEDICAL POLICY COMMITTEE HISTORY AND REVISIONS

<table>
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<tr>
<th>Date</th>
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<tr>
<td>8/7/2014</td>
<td>• Approved by MPC. Clarified lines of business. No other changes.</td>
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<tr>
<td>10/3/2013</td>
<td>• Approved by MPC. No changes.</td>
</tr>
<tr>
<td>10/4/2012</td>
<td>• Approved by MPC. No changes.</td>
</tr>
<tr>
<td>12/1/2011</td>
<td>• New template design approved by MPC.</td>
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<tr>
<td>9/15/2011</td>
<td>• Approved by MPC.</td>
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