Genetic Testing for TP53 Mutations (Li-Fraumeni Syndrome)

Last Review Date: November 11, 2016  Number: MG.MM.LA.35C

Definitions
Li-Fraumeni syndrome (LFS) is a rare, autosomal dominant, cancer predisposition syndrome caused by germline mutations in the TP53 gene and associated with a high risk cancer occurrence. Commonly occurring cancers in LFS include osteosarcoma, premenopausal breast cancer, brain tumor, adrenocortical carcinomas and soft tissue sarcoma. TP53 genetic mutations are highly penetrant and individuals with LFS are predisposed to multiple primary tumors.

Related Medical Guideline
Genetic Counseling and Testing

Guideline
TP53 gene mutation testing is considered medically necessary when any of the following criteria are met:

1. Individual has a suspected or known clinical diagnosis of LFS or Li-Fraumeni-Like syndrome
2. Individual has a known family history of a TP53 mutation
3. Individual has a personal or family history for ALL of the following:
   a. Sarcoma diagnosed at < age 45 years
   b. First-degree relative diagnosed with cancer at < 45 years
   c. An additional first- or second degree relative, same lineage, diagnosed with cancer at < age 45 years, or sarcoma at any age
4. Individual diagnosed with breast cancer at ≤ age 35 years with negative BRCA1/BRCA2 test.
5. Individual diagnosed with a tumor from the LFS tumor spectrum (including osteosarcoma, leukemia, soft tissue sarcoma, adrenocortical carcinoma, brain tumor, breast cancer, lung bronchoalveolar cancer) at < age 46 years; and:
   a. Has at least one first- or second-degree relative with any of the above LFS spectrum tumors (other than breast cancer, if the proband has breast cancer) diagnosed at < age 56 years or with multiple primaries at any age
6. Individual diagnosed with multiple tumors (except multiple breast tumors), with the initial tumor diagnosed at < age 46 years and two tumors are from the LFS tumor spectrum, with the initial cancer occurring prior to age 46
7. Individual diagnosed with adrenocortical carcinoma, choroid plexus carcinoma, or embryonal rhabdomyosarcoma anaplastic subtype, at any age.
Limitations/Exclusions

1. TP53 gene mutation testing is considered investigational and not medically necessary for all indications that do not meet the above criteria.

2. TP53 gene mutation testing for LFS using panels of genes (with or without next generation sequencing) is considered investigational and not medically necessary when all components of a panel do not meet the above criteria.

References


Applicable Procedure Codes

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<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>81404</td>
<td>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)</td>
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<td>81405</td>
<td>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, regionally targeted cytogenomic array analysis)</td>
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<td>81479</td>
<td>Unlisted molecular pathology procedure</td>
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Applicable ICD-10 Diagnosis Codes

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<th>Code</th>
<th>Description</th>
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<tr>
<td>C00.0–C96.9</td>
<td>Malignant neoplasms</td>
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<tr>
<td>Z15.01–Z15.09</td>
<td>Genetic susceptibility to malignant neoplasm</td>
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<tr>
<td>Z80.0–Z80.9</td>
<td>Family history of primary malignant neoplasm</td>
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<tr>
<td>Z85.00–Z85.9</td>
<td>Personal history of malignant neoplasm</td>
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