Overview

Useful For
Supporting a morphological diagnosis of a diffuse glioma
Assisting in central nervous system tumor classification
Stratifying prognosis of diffuse gliomas
Supporting the differential diagnosis of chondroid bone tumors
Stratifying prognosis of acute myeloid leukemia

Additional Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLIRV</td>
<td>Slide Review in MG</td>
<td>No, (Bill Only)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Testing Algorithm
When this test is ordered, slide review will always be performed at an additional charge.

Special Instructions
- [Tissue Requirements for Solid Tumor Next-Generation Sequencing](#)

Method Name
Polymerase Chain Reaction (PCR)-Based Next-Generation Sequencing

NY State Available
Yes

Specimen

Specimen Type
Varies

Necessary Information
Pathology report (final or preliminary), at minimum containing the following information, must accompany specimen in order for testing to be performed:

1. Patient name
2. Block number—must be on all blocks, slides and paperwork (can be handwritten on the paperwork)
3. Tissue collection date
4. Source of the tissue
Specimen Required
This assay requires at least 20% tumor nuclei.

-Preferred amount of tumor area with sufficient percent tumor nuclei: tissue 144 mm(2)
-Minimum amount of tumor area: tissue 36 mm(2).
-These amounts are cumulative over up to 10 unstained slides and must have adequate percent tumor nuclei.
-Tissue fixation: 10% neutral buffered formalin, not decalcified

-For specimen preparation guidance, see Tissue Requirement for Solid Tumor Next-Generation Sequencing in Special Instructions. In this document, the sizes are given as 4mm x 4mm x 10 slides as preferred: approximate/equivalent to 144 mm(2) and the minimum as 3mm x 1mm x 10 slides: approximate/equivalent to 36mm(2).

Preferred:

Specimen Type: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block with acceptable amount of tumor tissue.

Acceptable:

Specimen Type: Tissue slide

Slides: 1 stained and 10 unstained

Collection Instructions: Submit 1 slide stained with hematoxylin and eosin and 10 unstained, nonbaked slides with 5-micron thick sections of the tumor tissue.

Note: The total amount of required tumor nuclei can be obtained by scraping up to 10 slides from the same block.

Specimen Type: Cytology slide (direct smears or ThinPrep)

Slides: 1 to 3 slides

Collection Instructions: Submit 1 to 3 slides stained and cover slipped with a preferred total minimum of 5000 total nucleated cells, minimum of 3000 nucleated cells.

Note: Glass coverslips are preferred; plastic coverslips are acceptable but will result in longer turnaround times.

Additional Information: Cytology slides will not be returned.

Forms
If not ordering electronically, complete, print, and send an Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume
IDH1/IDH2 Mutation Analysis, Tumor

See Specimen Required

**Reject Due To**

<table>
<thead>
<tr>
<th>Other</th>
<th>Specimens that have been decalcified (all methods)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Specimens that have not been formalin-fixed, paraffin-embedded</td>
</tr>
</tbody>
</table>

**Specimen Stability Information**

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
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<tbody>
<tr>
<td>Varies</td>
<td>Ambient (preferred)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Frozen</td>
<td></td>
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<tr>
<td></td>
<td>Refrigerated</td>
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**Clinical and Interpretive**

**Clinical Information**

*IDH1* and *IDH2 (IDH)* genes encode dehydrogenase enzymes that are involved in cellular glucose metabolism and oxidative damage control. *IDH* variants, primarily involving codons R132 in *IDH1* and R172 in *IDH2*, result in reduction of the enzyme physiological activity and gain of a neomorphic ability to generate oncometabolite R(-)-2-hydroxyglutarate, which contribute to tumorigenesis by altering numerous cellular responses, including genome-wide epigenetic changes that characterize the glioma CpG island methylator phenotype (G-CIMP). *IDH* variants seem to be an early event in gliomagenesis and have been identified in over 70% of lower-grade (grades II/III) diffuse gliomas and secondary glioblastoma. These variants are rarely seen in other central nervous system tumors and are not seen in reactive non-neoplastic processes, and define a group of lower and high-grade diffuse gliomas associated with a more favorable prognosis. Assessment of *IDH* variant status in central nervous system tumors may assist in tumor classification and provide prognostically relevant information for subgroups of patients with diffuse gliomas.

*IDH1* and *IDH2* gene variants are also observed in a variety of non-CNS tumor types. Assessment of *IDH* variant status may assist in the differential diagnosis of chondroid bone tumors and provide prognostically relevant information in other contexts, such as in the setting of acute myeloid leukemia (AML).

**Reference Values**

An interpretative report will be provided.

**Interpretation**

An interpretative report will be provided.

**Cautions**

This test cannot differentiate between somatic and germline alterations. Additional testing may be necessary to clarify the significance of results if there is a potential hereditary risk.

DNA variants of uncertain significance may be identified.

A negative (wild-type) result does not rule out the presence of a variant that may be present but below the limits of detection of this assay.
Point mutations and small insertion/deletion mutations will be detected within targeted regions of the \textit{IDH1}, and \textit{IDH2} genes only. This test does not detect structural variants, genomic copy number changes, or large single or multiexon deletions or duplications in the \textit{IDH1} and \textit{IDH2} genes.

Rare polymorphisms may be present that could lead to false-negative or false-positive results. Test results should be interpreted in the context of clinical findings, tumor sampling and other laboratory data. If results obtained do not match other clinical or laboratory findings, please contact the laboratory for updated interpretation. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

Reliable results are dependent on adequate specimen collection and processing. This test has been validated on cytology slides and formalin-fixed, paraffin-embedded tissues; other types of fixatives are discouraged. Improper treatment of tissues, such as decalcification, may cause PCR failure.

**Supportive Data**

We have developed a next-generation sequencing assay to detect somatic mutations that can be used to assist in tumor classification and prognostication of patients with central nervous system tumors.

This assay has been shown to be very reproducible, having a 100% concordance for intra- and interassay reproducibility experiments. All somatic mutations that had been previously identified by various other molecular methods were detected by this assay during accuracy studies. No pathogenic variants were detected in known mutation-negative samples.

**Clinical Reference**


**Performance**

**Method Description**

Next-generation sequencing is performed to test for the presence of a mutation in targeted regions of the \textit{IDH1} and \textit{IDH2} genes, including exon 4 (codons 113-138) of \textit{IDH1} and exon 4 (codons 137-174) of \textit{IDH2}. (Unpublished Mayo method)
<table>
<thead>
<tr>
<th>Gene</th>
<th>GenBank Accession Number</th>
<th>Nucleotide Start</th>
<th>Nucleotide End</th>
<th>Chromosome</th>
<th>Exon</th>
<th>Codons</th>
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<td>Chromosome 15</td>
<td>Exon 4</td>
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PDF Report
No

Day(s) and Time(s) Test Performed
Monday through Friday; Varies

Analytic Time
12 days

Maximum Laboratory Time
20 days

Specimen Retention Time
Unused portions of blocks will be returned to the client. Unused slides are stored indefinitely.

Performing Laboratory Location
Rochester

Fees and Codes

Fees
- Authorized users can sign in to Test Prices for detailed fee information.
- Clients without access to Test Prices can contact Customer Service 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact Customer Service.

Test Classification
This test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

CPT Code Information
IDH1:
81120
88381

IDH2:
81121

LOINC® Information
# Test Definition: IDH12

**IDH1/IDH2 Mutation Analysis, Tumor**

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