Local Coverage Determination (LCD):
MolDX: MGMT Promoter Methylation Analysis (L37001)

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Contractor Information

Contractor Name	Contract Type	Contract Number	Jurisdiction	State(s)
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05101 - MAC A	J - 05	Iowa
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05102 - MAC B	J - 05	Iowa
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05201 - MAC A	J - 05	Kansas
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05202 - MAC B	J - 05	Kansas
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05301 - MAC A	J - 05	Missouri - Entire State
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05302 - MAC B	J - 05	Missouri - Entire State
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05401 - MAC A	J - 05	Nebraska
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	05402 - MAC B	J - 05	Nebraska
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	05901 - MAC A	J - 05	Alaska Alabama Arkansas Arizona Connecticut Florida Georgia Iowa Idaho Illinois Indiana Kansas Kentucky Louisiana Massachusetts Maine Michigan Minnesota Missouri - Entire State Mississippi Montana North Carolina North Dakota Nebraska New Hampshire New Jersey Ohio Oregon Rhode Island South Carolina South Dakota Tennessee Utah

Contractor Name	Contract Type	Contract Number	Jurisdiction	State(s)
				Virginia Virgin Islands Vermont Washington Wisconsin West Virginia Wyoming
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	08101 - MAC A	J - 08	Indiana
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	08102 - MAC B	J - 08	Indiana
Wisconsin Physicians Service Insurance Corporation	MAC - Part A	08201 - MAC A	J - 08	Michigan
Wisconsin Physicians Service Insurance Corporation	MAC - Part B	08202 - MAC B	J - 08	Michigan

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LCD Information

Document Information

LCD ID
L37001

LCD Title
MolDX: MGMT Promoter Methylation Analysis

Proposed LCD in Comment Period
N/A

Source Proposed LCD
DL37001

Original Effective Date
For services performed on or after 07/17/2017

Revision Effective Date
For services performed on or after 12/01/2017

Revision Ending Date
N/A

Retirement Date
N/A

Notice Period Start Date
06/01/2017

Notice Period End Date
07/16/2017

CMS National Coverage Policy
Title XVIII of the Social Security Act (SSA), §1862(a)(1)(A), states that no Medicare payment shall be made for items or services that "are not reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member."

Title XVIII of the Social Security Act, §1833(e), prohibits Medicare payment for any claim lacking the necessary documentation to process the claim.

42 Code of Federal Regulations (CFR) §410.32 Diagnostic x-ray tests, diagnostic laboratory tests, and other diagnostic tests: Conditions.

CMS Internet Online Manual Pub. 100-02 (Medicare Benefit Policy Manual), Chapter 15, Section 80, "Requirements for Diagnostic X-Ray, Diagnostic Laboratory, and Other Diagnostic Tests"

CMS Internet-Only Manuals, Publication 100-04, Medicare Claims Processing Manual, Chapter 16, §50.5 Jurisdiction of Laboratory Claims, 60.12 Independent Laboratory Specimen Drawing, 60.2. Travel Allowance.

CMS Internet Online Manual Pub. 100-04 (Medicare Claims Processing Manual), Chapter 23 (Section 10) "Reporting ICD Diagnosis and Procedure Codes"

CMS Internet-Only Manual, Pub 100-04, Medicare Claims Processing Manual, Chapter 12, §30-Correct Coding Policy

Coverage Guidance
Coverage Indications, Limitations, and/or Medical Necessity

This policy provides limited coverage for methylation analysis for hypermethylation of the O-6methylguanine DNA methyltransferase (MGMT) gene promoter. MGMT methylation analysis testing is considered to be reasonable and necessary for adult patients when the following criteria are met:

- Tumor type is high-¬grade malignant glioma (e.g. glioblastoma multiforme (GBM), anaplastic astrocytoma) **and**
- Patients are able to tolerate temozolomide therapy or radiation therapy, **and**
- The physician will use the of MGMT testing results to decide between radiation therapy and chemotherapy alone as 1st line adjuvant treatment, or between temozolomide and other chemotherapy for 1st line adjuvant treatment

Note: This assessment is predicated on the assumption that therapy is considered beneficial for the specific patient.

Summary of Evidence

Cancer is the consequence of genetic alterations that result in a deregulation of important cellular pathways responsible for various essential functions, including cell growth, cell cycle progression, and apoptosis (programmed cell death). One result of these genetic alterations is gliomas. The treatment of high-grade gliomas,

especially GBM, remains difficult as no contemporary treatments are curative. For the past several years, the standard treatment for GBM consists of maximal surgical resection, radiotherapy (RT), and concomitant and adjuvant chemotherapy with temozolomide.

Although surgical resection, RT, and chemotherapy with temozolomide are considered standard of care for most patients with high-grade glioma (including GBM and anaplastic astrocytoma), not all patients tolerate these treatments. For patients older than 70 years with a low performance rating, radiation or temozolomide alone is sometimes employed. Temozolomide treatment is not considered inferior to radiation therapy and may be tolerated better than RT by "frail" patients with low performance scores.

In patients for whom temozolomide is not the current standard of care, it has been proposed that MGMT methylation analysis can be used to predict the efficacy of temozolomide treatment. Epigenetic silencing of the MGMT (O-6-methylguanine–DNA methyltransferase) DNA repair gene, by promoter methylation, leads to a lack of MGMT protein expression. Lack of MGMT protein expression immunohistochemically is related to drug responses in patients with malignant glioma treated with alkylating agents. In particular, MGMT hypermethylation is a known predictive biomarker of response to temozolomide treatment with favorable outcomes in terms of overall survival (OS) and progression free survival (PFS) in GBM patients.

MGMT promoter methylation status is a strong and independent prognostic factor in patients with newly diagnosed GBM and a clinically relevant predictive marker in the subpopulation of elderly GBM patients. MGMT promoter methylation analysis can aid in treatment decisions for patients over 70. For patients older than 70 with a good performance rating, there is evidence of the benefit of temozolomide in addition to RT. In patients with lower performance, temozolomide can be used alone as it was found to be equally as effective as RT alone and it has lower toxicity for the frail population. In the temozolomide arm of both the Nordic and German trials, patients with MGMT promoter methylation had longer survival than those without. (9.7 vs 6.8 months; HR, 0.56; 95% CI, 0.34¬0.93)

MGMT promoter methylation analysis also has prognostic utility. However, performing MGMT analysis is only recommended by NCCN guidelines for temozolomide guidance and not for overall prognosis prediction. Lattanzio et al confirmed that patients carrying methylation of the MGMT promoter reported a longer OS and PFS than patients with an unmethylated promoter. Wang et al also evaluated the prognostic value of MGMT promoter methylation and TP53 mutation status and found similar results.

There is still a lack of consensus on the optimal assay for reliable MGMT promoter methylation testing and a variety of tests are being used in different laboratories. According to Berghoff et al, pyrosequencing is the only method for which an adequately high analytical performance (high intra¬ and inter-laboratory repeatability and reproducibility) has been demonstrated in a fully published trial. MGMT promoter methylation testing should be performed by an experienced laboratory in which this testing has been validated.

MGMT may also be useful for determining the prognosis of colorectal cancer patients and to identify those requiring more aggressive adjuvant therapies. Future studies will be necessary to determine its clinical utility in this area. Likewise, MGMT methylation may be an important biomarker in subsets of esophageal cancers where temozolomide may be utilized to successfully treat these patients, but where additional research on clinical utility is also needed. MGMT methylation analysis is also mentioned in the literature as a predictive marker for ovarian cancer and melanoma. However, evidence on the use of MGMT testing is unclear in these diagnoses and additional studies are needed on the clinical utility in these cancers.

Analysis of Evidence
(Rationale for Determination)

Level of Evidence:
Quality – Strong
Strength – Strong
Weight – Moderate

In summary, the current literature and NCCN guidelines support the use of MGMT methylation analysis to predict the usefulness of temozolomide treatment in adult patients with high-grade gliomas.

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Coding Information

Bill Type Codes:

Contractors may specify Bill Types to help providers identify those Bill Types typically used to report this service. Absence of a Bill Type does not guarantee that the policy does not apply to that Bill Type. Complete absence of all Bill Types indicates that coverage is not influenced by Bill Type and the policy should be assumed to apply equally to all claims.

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Revenue Codes:

Contractors may specify Revenue Codes to help providers identify those Revenue Codes typically used to report this service. In most instances Revenue Codes are purely advisory. Unless specified in the policy, services reported under other Revenue Codes are equally subject to this coverage determination. Complete absence of all Revenue Codes indicates that coverage is not influenced by Revenue Code and the policy should be assumed to apply equally to all Revenue Codes.

N/A
N/A
CPT/HCPCS Codes
Group 1 Paragraph: NA

Group 1 Codes:

81287	MGMT (O-6-METHYLGUANINE-DNA METHYLTRANSFERASE) (EG, GLIOBLASTOMA MULTIFORME), METHYLATION ANALYSIS

ICD-10 Codes that Support Medical Necessity
Group 1 Paragraph: N/A

Group 1 Codes:

ICD-10 Codes	Description
C71.0	Malignant neoplasm of cerebrum, except lobes and ventricles
C71.1	Malignant neoplasm of frontal lobe
C71.2	Malignant neoplasm of temporal lobe
C71.3	Malignant neoplasm of parietal lobe
C71.4	Malignant neoplasm of occipital lobe
C71.5	Malignant neoplasm of cerebral ventricle
C71.6	Malignant neoplasm of cerebellum
C71.7	Malignant neoplasm of brain stem
C71.8	Malignant neoplasm of overlapping sites of brain
C71.9	Malignant neoplasm of brain, unspecified

ICD-10 Codes that DO NOT Support Medical Necessity
Group 1 Paragraph: N/A

Group 1 Codes: N/A

ICD-10 Additional Information N/A Back to Top

General Information

Associated Information
Documentation Requirements
The patient's medical record must contain documentation that fully supports the medical necessity for services

included within this LCD. (See "Coverage Indications, Limitations, and/or Medical Necessity") This documentation includes, but is not limited to, relevant medical history, physical examination, and results of pertinent diagnostic tests or procedures.

Documentation supporting the medical necessity should be legible, maintained in the patient's medical record, and must be made available to the MAC upon request.

Sources of Information
N/A
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Revision History Information

Revision History Date	Revision History Number	Revision History Explanation	Reason(s) for Change
12/01/2017	R1	12/01/2017- At this time 21st Century Cures Act will apply to new and revised LCDs that restrict coverage which requires comment and notice. This revision is not a restriction to the coverage determination; and, therefore not all the fields included on the LCD are applicable as noted in this policy. Annual Review completed 11/06/2017	• Other (Annual Review)

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Associated Documents

Attachments N/A

Related Local Coverage Documents Article(s) A55535 - Response to Comments: MolDX: MGMT Promoter Methylation Analysis (DL37001). LCD(s) DL37001 - MolDX: MGMT Promoter Methylation Analysis

Related National Coverage Documents N/A

Public Version(s) Updated on 11/21/2017 with effective dates 12/01/2017 - N/A Updated on 05/15/2017 with effective dates 07/17/2017 - N/A Back to Top

Keywords

N/A Read the **LCD Disclaimer** Back to Top