

Local Coverage Determination (LCD): MoIDX: MGMT Promoter Methylation Analysis (L36192)

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CONTRACTOR NAME	CONTRACT TYPE	CONTRACT NUMBER	JURISDICTION	STATE(S)
Noridian Healthcare Solutions, LLC	A and B MAC	02101 - MAC A	J - F	Alaska
Noridian Healthcare Solutions, LLC	A and B MAC	02102 - MAC B	J - F	Alaska
Noridian Healthcare Solutions, LLC	A and B MAC	02201 - MAC A	J - F	Idaho
Noridian Healthcare Solutions, LLC	A and B MAC	02202 - MAC B	J - F	Idaho
Noridian Healthcare Solutions, LLC	A and B MAC	02301 - MAC A	J - F	Oregon
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Noridian Healthcare Solutions, LLC	A and B MAC	02402 - MAC B	J - F	Washington
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Noridian Healthcare Solutions, LLC	A and B MAC	03401 - MAC A	J - F	South Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03402 - MAC B	J - F	South Dakota
Noridian Healthcare Solutions, LLC	A and B MAC	03501 - MAC A	J - F	Utah
Noridian Healthcare Solutions, LLC	A and B MAC	03502 - MAC B	J - F	Utah
Noridian Healthcare Solutions, LLC	A and B MAC	03601 - MAC A	J - F	Wyoming
Noridian Healthcare Solutions, LLC	A and B MAC	03602 - MAC B	J - F	Wyoming

LCD Information

Document Information

LCD ID

L36192

Original Effective Date

For services performed on or after 04/15/2016

LCD Title**Revision Effective Date**

MoIDX: MGMT Promoter Methylation Analysis

For services performed on or after 11/01/2019

Proposed LCD in Comment Period

N/A

Revision Ending Date

N/A

Source Proposed LCD

DL36192

Retirement Date

N/A

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Notice Period Start Date

02/25/2016

Notice Period End Date

04/14/2016

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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.”

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.

Coverage Guidance

Coverage Indications, Limitations, and/or Medical Necessity

As required by CR 10901, all billing and coding information has been moved to the companion article, this article is linked to the LCD.

Indications and Limitations of Coverage

This policy provides limited coverage for methylation analysis for hypermethylation of the O-6-methylguanine 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 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 performances 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 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 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

Strenght - 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.

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
11/01/2019	R4	<p>The LCD is revised to remove CPT/HCPCS codes in the Keyword Section of the LCD.</p> <p>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.</p>	<ul style="list-style-type: none"> Other (The LCD is revised to remove CPT/HCPCS codes in the Keyword Section of the LCD.)
11/01/2019	R3	<p>11/01/2019: This LCD is being revised in order to adhere to CMS requirements per chapter 13, section 13.5.1 of the Program Integrity Manual. There has been no change in coverage with this LCD revision. Regulations regarding billing and coding were removed from the CMS National Coverage Policy section of this LCD and placed in the related Billing and Coding: MGMT Promoter Methylation Article A57433.</p>	<ul style="list-style-type: none"> Provider Education/Guidance
11/01/2019	R2	<p>As required by CR 10901, all billing and coding information has been moved to the companion article, this article is linked to the LCD.</p>	<ul style="list-style-type: none"> Revisions Due To Code Removal
01/01/2018	R1	<p>This policy is revised to comply with the 21st Century Cures Act.</p>	<ul style="list-style-type: none"> Creation of Uniform LCDs With Other MAC Jurisdiction

Associated Documents

Attachments

N/A

Related Local Coverage Documents

Article(s)

A57433 - Billing and Coding: MoIDX: MGMT Promoter Methylation Analysis

A54896 - Response to Comments: MoIDX: MGMT Promoter Methylation Analysis

LCD(s)

DL36190

- (MCD Archive Site)DL36192

- (MCD Archive Site)

Related National Coverage Documents

N/A

Public Version(s)

Updated on 01/29/2020 with effective dates 11/01/2019 - N/A

Updated on 12/17/2019 with effective dates 11/01/2019 - N/A

Updated on 10/08/2019 with effective dates 11/01/2019 - N/A

Some older versions have been archived. Please visit the MCD Archive Site to retrieve them.

Keywords

N/A