Local Coverage Determination (LCD):
MolDX: MGMT Promoter Methylation Analysis (L35974)

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Contractor Information

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LCD Information

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<td>CPT only copyright 2002-2015 American Medical Association. All Rights Reserved. CPT is a registered trademark of the American Medical Association. Applicable FARS/DFARS Apply to Government Use. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein.</td>
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The Code on Dental Procedures and Nomenclature (Code) is published in Current Dental Terminology (CDT). Copyright © American Dental Association. All rights reserved. CDT and CDT-2010 are trademarks of the American Dental Association.
• 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.

Background

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.

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.

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.

N/A

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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

CPT/HCPCS Codes

Group 1 Paragraph: N/A

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 N/A

ICD-10 Additional Information

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 and Basis for Decision

References


