CLINICAL MEDICATION POLICY	
Policy Name:	Alimta® (Pemetrexed)
Policy Number:	MP-022-MC-PA
Approved By:	Medical Management; Clinical Pharmacy
Provider Notice Date:	07/01/2017
Original Effective Date:	08/01/2017
Annual Approval Date:	06/01/2018
Revision Date:	N/A
Products:	Pennsylvania Medicare Assured
Application:	All participating hospitals and providers
Page Number(s):	1 of 6

DISCLAIMER

Gateway Health℠ (Gateway) clinical medication policy is intended to serve only as a general reference resource regarding payment and coverage for the services described. This policy does not constitute medical advice and is not intended to govern or otherwise influence medical decisions.

POLICY STATEMENT

Gateway Health℠ provides coverage and reimbursement under the medical benefits for the intravenous administration of Alimta® (pemetrexed) of the Company's Medicare products when medically necessary.

This policy is designed to address medical necessity guidelines that are appropriate for the majority of individuals with a particular disease, illness or condition. Each person's unique clinical circumstances warrant individual consideration, based upon review of applicable medical records.

DEFINITIONS

Medical necessity – A service or benefit is medically necessary if it is compensable under the Medical Assistance program and if it meets any one of the following standards:

- The service or benefit will, or is reasonably expected to, prevent the onset of an illness, condition, or disability.
- The service or benefit will, or is reasonably expected to, reduce or ameliorate the physical, mental, or developmental effects of an illness, condition, injury, or disability.
- The service or benefit will assist the patient to achieve or maintain maximum functional capacity in performing daily activities, taking into account both the functional capacity of the patient and those functional capacities that are appropriate for patients of the same age.

Adjuvant therapy – Treatment given after the primary treatment to increase the chances of a cure; may include chemotherapy, radiation, hormone, or biological therapy.

Line of therapy –

- First-line therapy: The first or primary treatment for the diagnosis. This may include surgery, chemotherapy, radiation therapy or a combination of these therapies.
- Second-line therapy: Treatment given when initial treatment (first-line therapy) is not effective or there is disease progression.
- Third-line therapy: Treatment given when both initial (first-line therapy) and subsequent treatment (second-line therapy) are not effective or there is disease progression.

Metastasis – The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.

Monoclonal antibody – A protein developed in the laboratory that can locate and bind to a specific substance in the body.

Off-label drug use – Utilization of a United States Food and Drug Administration (FDA) approved drug for uses other than those listed in the FDA approved labeling.

Partial response (PR) – A decrease in the size of a tumor or in the amount of cancer in the body, resulting from treatment; also called partial remission.

Progression free survival (PFS) – The length of time during and after treatment that an individual lives but does not get worse (usually measured by the size of a tumor or amount of cancer in the body).

Refractory disease – Illness or disease that does not respond to treatment.

PROCEDURES

The following medical necessity criteria must be met:

1. Coverage may be provided when the indication is Malignant Pleural Mesothelioma in patients whose disease is unresectable or who otherwise is not a candidate for curative surgery; AND
    A. The patient is age 18 years or older; AND
    B. The prescriber is a hematologist/oncologist; AND
    C. Treatment will be used in combination with cisplatin; AND
    D. The dosing is within the following prescribing-supported parameter(s):
        1) Alimta in combination with cisplatin: Does not exceed 500 mg/m2 on Day 1 of each 21-day cycle in combination with cisplatin 75 mg/m2 beginning 30 minutes after Alimta administration;
        2) Supplementation with oral folic acid and intramuscular vitamin B12 should be initiated prior to Alimta administration. The member should be receiving folic acid and vitamin B12 supplementation throughout treatment. Corticosteroids should be administered the day before, the day of, and the day after Alimta administration;

OR

2. Coverage may be provided when the indication is Locally Advanced or Metastatic Nonsquamous Cell Non-Small Cell Lung Cancer (NSCLC); AND
    A. The patient is age 18 years or older; AND
    B. The prescriber is a hematologist/oncologist; AND
    C. Initial treatment will be used in combination with cisplatin; OR
    D. Maintenance treatment will be used in patients whose disease has not progressed after four cycles of platinum-based first-line chemotherapy; OR
    E. Treatment will be used after prior chemotherapy as a single-agent; AND
    F. The dosing is within the following prescribing-supported parameter(s):

1) Alimta in combination with cisplatin: Does not exceed 500 mg/m2 on Day 1 of each 21-day cycle in combination with cisplatin 75 mg/m2 beginning 30 minutes after Alimta administration; OR
2) Monotherapy: Does not exceed 500 mg/m2 Day 1 of each 21-day cycle;
3) Supplementation with oral folic acid and intramuscular vitamin B12 should be initiated prior to Alimta administration. The member should be receiving folic acid and vitamin B12 supplementation throughout treatment. Corticosteroids should be administered the day before, the day of, and the day after Alimta administration.

Note: When the medical necessity criteria are met for Alimta, the following laboratory studies must be monitored routinely for ANC, platelets and creatinine clearance including at the beginning of each cycle; the drug should not be given when:

A. ANC $\leq$ 1500 cells/mm3
B. Platelets < 100,000
C. Creatinine clearance < 45ml/min

3. When Alimta is not covered

All other indications not otherwise listed are considered experimental/investigational. Scientific evidence does not support the use of pemetrexed for any other indication.

When criteria are not met, the request will be forwarded to a Medical Director for review. The physician reviewer must override criteria when, in their professional judgment, the requested medication is medically necessary.

4. Warnings

The FDA-approved ALIMTA® (pemetrexed) package insert has the following warnings and precautions:

A. Premedication: patients should receive folic acid, vitamin B12 and corticosteroids as premedication to reduce instances of treatment-related hematologic toxicity, GI toxicity, and cutaneous adverse events.
B. Bone Marrow Suppression: myelosuppression is usually the dose-limiting toxicity and may require dose reductions for subsequent cycles.
C. Renal Function: ALIMTA® is eliminated unchanged in the urine. Decreased renal function will result in increased AUC; administration in patients with a CrCl of less than 45ml/min has not been studied and administration to these patients is not recommended.
D. Hepatic Function Impairment: dose adjustments based on hepatic impairment during treatment are required.
E. Fertility Impairment: administration in mice at sub-therapeutic doses resulted in reduced fertility, hypospermia and testicular atrophy.
F. Children: safety and efficacy in children has not been established.

5. Post-payment Audit Statement

The medical record must include documentation that reflects the medical necessity criteria and is subject to audit by Gateway Health℠ at any time pursuant to the terms of your provider agreement.

6. Place of Service

The place of service for the intravenous administration of Alimta is outpatient.

7. Coverage Determination
   Gateway Health ℠ follows the coverage determinations made by CMS as outlined in either the national coverage determinations (NCD) or the state-specific local carrier determination (LCD).

   For Pennsylvania, please use the following link for Novitas Solutions List of LCDS:
   https://www.novitassolutions.com/webcenter/portal/MedicareJL/page/pagebyid?contentId=00024370&_afrLoop=578664761207593#!%40%40%3F_afrLoop%3D578664761207593%26contentId%3D00024370%26_adf.ctrl-state%3D49ww9vpbm_55

GOVERNING BODIES APPROVAL

Pemetrexed disodium (Alimta®) was approved by the FDA on February 4, 2004. It is the first drug approved in combination with cisplatin for the treatment of patients with malignant pleural mesothelioma. The recommended dose of ALIMTA® is 500 mg/m2 administered as an intravenous infusion over 10 minutes on day 1 of each 21-day cycle. Patients must take daily doses of folic acid and vitamin B-12 to reduce the severity of side effects such as low white blood cell count, nausea, vomiting, fatigue, rash, and diarrhea.

On September 26, 2008, the FDA approved pemetrexed disodium for injection for use in combination with cisplatin therapy for the initial treatment of patients with locally advanced or metastatic nonsquamous non-small cell lung cancer (NSCLC).

On July 2, 2009, the FDA approved pemetrexed disodium injection for maintenance treatment of patients with locally advanced or metastatic nonsquamous non-small cell lung cancer (NSCLC) whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.

CODING REQUIREMENTS

Procedure Codes

HCPCS Codes	Description
J9305	Pemetrexed, Injection, 10 mg

Diagnosis Codes

ICD-10 Codes	Description
C33	Malignant neoplasm of trachea
C34.0	Malignant neoplasm of main bronchus
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.1	Malignant neoplasm of upper lobe, bronchus or lung
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.3	Malignant neoplasm of lower lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung

C34.0	Malignant neoplasm of overlapping sites of bronchus and lung
C34.00	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.01	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.02	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.9	Malignant neoplasm of unspecified part of bronchus or lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of the right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of the left bronchus or lung
C37	Malignant neoplasm of thymus (thymic carcinoma)
C38	Malignant neoplasm of heart, mediastinum and pleura
C38.4	Malignant neoplasm of pleura
C45.0	Mesothelioma of pleura
C78.0	Secondary malignant neoplasm of lung
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.2	Secondary malignant neoplasm of pleura
Z85.11	Personal history of malignant neoplasm of bronchus and lung
Z85.238	Personal history of other malignant neoplasm of thymus

REIMBURSEMENT

Participating facilities will be reimbursed per their Gateway Health℠ contract.

POLICY SOURCE(S)

ALIMTA® (Pemetrexed) [package insert]. Indianapolis, IN: Eli Lilly and Company; 09/2008.

ALIMTA® [product information]. Indianapolis, IN. Updated September, 2013. Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2013/021462s045lbl.pdf. Accessed on August 25, 2016.

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Scagliotti G, Brodowicz T, Shepherd FA, et al. Treatment-by-histology interaction analysis in three phase III trials show superiority of pemetrexed in nonsquamous non-small cell lung cancer. *J Thorac Oncol* 2011; 6:64-70. Available at: http://www.jto.org/article/S1556-0864(15)31897-9/pdf. Accessed on August 25, 2016.

Hanna N, Shepherd FA, Fossella FV, et al. Randomized phase III trial of pemetrexed versus docetaxel in patients with non-small-cell lung cancer previously treated with chemotherapy. *J Clin Oncol.* 2004; 22(9):1589-1597. Abstract available at: http://jco.ascopubs.org/content/22/9/1589.long. Accessed on August 25, 2016.

Peterson P, Park K, Fossella F, et al. Is Pemetrexed more effective in adenocarcinoma and large cell lung cancer than in squamous cell carcinoma? A retrospective analysis of a phase III trial of pemetrexed vs docetaxel in previously treated patients with advanced non-small cell lung cancer (NSCLC). *J Thorac Oncol.* 2012 World Conference on Lung Cancer. 2007; 2(8):S8510. Abstract available at: https://www.deepdyve.com/lp/elsevier/6521-poster-is-pemetrexed-more-effective-in-patients-with-non-squamous-rHiGWktMTU. Accessed on August 25, 2016.

Vogelzang NJ, Rusthoven JJ, Symanowski J, et al. Phase III study of pemetrexed in combination with cisplatin versus cisplatin alone in patients with malignant pleural mesothelioma. *J Clin Oncol.* 2003; 21(14):2636-2644. Available at: http://www3.med.unipmn.it/magnani/pdf/vogelzang.pdf. Accessed on August 25, 2016.

Policy History

Date	Activity
06/06/2017	Initial policy developed
06/21/2017	QI/UM Committee approval
08/01/2017	Provider effective date
07/19/2017	Revision: General formatting changes and reimbursement language removed from Position Statement