09-J1000-01

Original Effective Date: 05/15/09

Reviewed: 01/09/19

Revised: 02/15/19

Subject: Pemetrexed Disodium (Alimta®) IV

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Pemetrexed (Alimta) was initially approved by the U.S. Food and Drug Administration (FDA) in February 2004 for use in combination with cisplatin for the treatment of malignant pleural mesothelioma in adults whose disease is unresectable or who are not otherwise candidates for curative surgery. The FDA has since approved pemetrexed as single agent therapy in locally advanced or metastatic non-small cell lung cancer following prior chemotherapy, for use in combination with cisplatin for first-line therapy in locally advanced or metastatic non-squamous non-small cell lung cancer, and for maintenance treatment of advanced or metastatic nonsquamous non-small cell lung cancer after first-line treatment with platinum-based chemotherapy. The agent received orphan drug status from the FDA for the malignant pleural mesothelioma. Pemetrexed acts as a multi-targeted antifolate compound that disrupts folate-dependent metabolic processes that are essential for cell replication.

National Comprehensive Cancer Network (NCCN) Guidelines for Bladder Cancer (Version 1.2019), Malignant Pleural Mesothelioma (Version 2.2018), Non-Small Cell Lung Cancer (Version 2.2019), Ovarian Cancer (Version 2.2018), Thymomas and Thymic Carcinomas (Version 2.2018), and Central Nervous System Cancers (Version 2.2018) include recommendations for use of pemetrexed.

POSITION STATEMENT:

Initiation of pemetrexed **meets the definition of medical necessity** for members diagnosed with **ANY** of the following conditions when **ALL** associated criteria are met:

1. Bladder Cancer (including primary carcinoma of the urethra, upper genitourinary tract tumors, and urothelial carcinoma of the prostate)

a. Member is diagnosed with locally advanced, recurrent, or metastatic disease
b. Pemetrexed is used as second-line or subsequent systemic therapy
c. Pemetrexed is used alone
d. Pemetrexed dose does not exceed 500 mg/m^2 every 21 days

2. Malignant Pleural Mesothelioma
    a. Member meets one of the following:
        i. Pemetrexed is used alone
        ii. Pemetrexed is used in combination with cisplatin or carboplatin
        iii. Pemetrexed is used in combination with bevacizumab and cisplatin
        iv. Pemetrexed is used in combination with bevacizumab and carboplatin
        v. Pemetrexed is used in combination with bevacizumab for maintenance therapy
    b. Pemetrexed dose does not exceed 500 mg/m^2 every 21 days
3. Non-Small Cell Lung Cancer
    a. Member meets one of the following:
        i. Pemetrexed is used alone
        ii. Pemetrexed is used in combination with cisplatin or carboplatin
        iii. Pemetrexed is used in combination with bevacizumab
        iv. Pemetrexed is used in combination with pembrolizumab for maintenance therapy
        v. Pemetrexed is used in combination with bevacizumab and either cisplatin or carboplatin
        vi. Pemetrexed is used in combination with pembrolizumab and either cisplatin or carboplatin
    b. Pemetrexed dose does not exceed 500 mg/m^2 every 21 days
4. Ovarian Cancer
    a. Member is diagnosed with persistent or recurrent disease
    b. Pemetrexed is used alone
    c. Pemetrexed dose does not exceed 500 mg/m^2 every 21 days
5. Thymoma or Thymic Carcinoma
    a. Pemetrexed is used as second-line therapy
    b. Pemetrexed is used alone
    c. Pemetrexed dose does not exceed 500 mg/m^2 every 21 days
6. Primary Central Nervous System Lymphoma
    a. Member is diagnosed with relapsed or refractory disease
    b. Pemetrexed is used alone
    c. Pemetrexed dose does not exceed 500 mg/m^2 every 21 days
7. Other FDA-approved or NCCN supported diagnosis (not previously listed above)
    a. Member meets one of the following:

i. Member is diagnosed with a condition that is consistent with an indication listed in the product's FDA-approved prescribing information (or package insert) AND member meets any additional requirements listed in the "Indications and Usage" section of the FDA-approved prescribing information (or package insert)

ii. Indication **AND** usage is recognized in NCCN Drugs and Biologics Compendium as a Category 1 or 2A recommendation

b. Pemetrexed dose does not exceed 500 mg/m2 every 21 days

Duration of approval: 1 year

Continuation of pemetrexed (Alimta) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization for pemetrexed has been previously approved by Florida Blue or another health plan in the past two years for the treatment of bladder cancer, malignant pleural mesothelioma, non-small cell lung cancer, ovarian cancer, thymoma or thymic carcinoma, or primary central nervous system lymphoma or other FDA-approved or NCCN supported diagnosis; OR the member currently meets all indication-specific initiation criteria
2. Member's disease has not progressed during treatment with pemetrexed
3. Pemetrexed dose does not exceed 500 mg/m2 every 21 days

Approval duration: 1 year

DOSAGE/ADMINISTRATION:

THIS INFORMATION IS PROVIDED FOR INFORMATIONAL PURPOSES ONLY AND SHOULD NOT BE USED AS A SOURCE FOR MAKING PRESCRIBING OR OTHER MEDICAL DETERMINATIONS. PROVIDERS SHOULD REFER TO THE MANUFACTURER'S FULL PRESCRIBING INFORMATION FOR DOSAGE GUIDELINES AND OTHER INFORMATION RELATED TO THIS MEDICATION BEFORE MAKING ANY CLINICAL DECISIONS REGARDING ITS USAGE.

FDA-approved

- 500 mg/m2 IV on Day 1 of each 21-day cycle

Dose Adjustments

Renal impairment

- CrCl < 45 mL/min: Not recommended

Drug Availability

- 100 mg and 500 mg vial for injection

Usual Dosage: Pemetrexed disodium is administered 500mg/m2 every 21 days.

PRECAUTIONS:

Precautions/Warnings

- Premedication regimen: Prior to treatment with ALIMTA, initiate supplementation with oral folic acid and intramuscular vitamin B12 to reduce the severity of hematologic and gastrointestinal toxicity

- Bone marrow suppression: Reduce doses for subsequent cycles based on hematologic and nonhematologic toxicities
- Do not administer when CrCl <45 mL/min
- Do not initiate a cycle unless ANC ≥1500 cells/mm3, platelets ≥100,000 cells/mm3, and CrCl ≥45 mL/min
- Fetal harm can occur when administered to a pregnant woman

BILLING/CODING INFORMATION:

The following codes may be used to describe:

HCPCS Coding:

J9305	Injection, pemetrexed, 10mg

ICD-10 Diagnosis Codes That Support Medical Necessity:

C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of main bronchus, unspecified side
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, bronchus or lung, unspecified side
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, right bronchus or lung
C34.30	Malignant neoplasm of lower lobe, bronchus or lung, unspecified side
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of bronchus and lung, unspecified side
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of bronchus or lung, unspecified, unspecified side
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C37	Malignant neoplasm of thymus
C38.4	Malignant neoplasm of pleura
C45.0	Mesothelioma of pleura
C45.1	Mesothelioma of peritoneum
C48.1	Malignant neoplasm of specified parts of peritoneum
C48.2	Malignant neoplasm of peritoneum, unspecified
C48.8	Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum
C56.1	Malignant neoplasm of right ovary
C56.2	Malignant neoplasm of left ovary
C56.9	Malignant neoplasm of ovary, unspecified side
C57.00	Malignant neoplasm of fallopian tube, unspecified side
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C57.10	Malignant neoplasm of broad ligament, unspecified side

C57.11	Malignant neoplasm of right broad ligament
C57.12	Malignant neoplasm of left broad ligament
C57.20	Malignant neoplasm of round ligament, unspecified side
C57.21	Malignant neoplasm of right round ligament
C57.22	Malignant neoplasm of left round ligament
C57.3	Malignant neoplasm of parametrium
C57.4	Malignant neoplasm of uterine adnexa, unspecified
C61	Malignant neoplasm of prostate
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of renal pelvis, unspecified side
C66.1	Malignant neoplasm of right ureter
C66.2	Malignant neoplasm of left ureter
C66.9	Malignant neoplasm of ureter, unspecified side
C67.0	Malignant neoplasm of trigone of bladder
C67.1	Malignant neoplasm of dome of bladder
C67.2	Malignant neoplasm of lateral wall of bladder
C67.3	Malignant neoplasm of anterior wall of bladder
C67.4	Malignant neoplasm of posterior wall of bladder
C67.5	Malignant neoplasm of bladder neck
C67.6	Malignant neoplasm of ureteric orifice
C67.7	Malignant neoplasm of urachus
C67.8	Malignant neoplasm of overlapping sites of bladder
C67.9	Malignant neoplasm of bladder, unspecified
C68.0	Malignant neoplasm of urethra
C83.30	Diffuse large B-cell lymphoma, unspecified site
C83.31	Diffuse large B-cell lymphoma, lymph nodes of head, face, and neck
C83.39	Diffuse large B-cell lymphoma, extranodal and solid organ sites
C83.80	Other non-follicular lymphoma, unspecified site
C83.81	Other non-follicular lymphoma, lymph nodes of head, face, and neck
C83.89	Other non-follicular lymphoma, extranodal and solid organ sites
D09.0	Carcinoma in situ of bladder
D15.0	Benign neoplasm of thymus

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage: The following Local Coverage Determination (LCD) was reviewed on the last guideline revised date: PEMETREXED, (L33978) located at fcso.com. No National Coverage Determination (NCD) was found at the time of the last guideline revised date.

DEFINITIONS:

No guideline specific definitions apply.

RELATED GUIDELINES:

Carboplatin (Paraplatin®) IV, 09-J0000-93

Docetaxel (Taxotere®) IV, 09-J0000-95

Gemcitabine (Gemzar®), 09-J0000-96

Irinotecan HCl (Camptosar®) IV, 09-J0000-99

Vitamin B-12 Injections, 09-J0000-10

OTHER:

None applicable.

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13. Thymomas and thymic carcinomas treatment guidelines [Internet]. Version 2.2018. Fort Washington (PA): National Comprehensive Cancer Network; 2019 [cited 1/1/19]. Available from: http://www.nccn.org/professionals/physician_gls/f_guidelines.asp/.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 01/09/19.

GUIDELINE UPDATE INFORMATION:

05/15/09	New Medical Coverage Guideline.
10/15/09	Revision; consisting of clarifying dosage.
01/15/10	Revision; consisting of update to codes.
08/01/10	Revision; consisting of update to codes.
11/15/10	Review and revision; consisting of updating coding and references.
11/15/11	Review and revision to guideline; consisting of updating position statement and references.
10/15/12	Review and revision to guideline; consisting of removing cervical cancer indication, reformatting position statement, updating dosage and administration, exceptions, coding and references.
11/15/13	Review and revision to guideline; consisting of revision and reformatting description, position statement, dosage/administration, precautions, references.
11/15/14	Review and revision to guideline; consisting of description, position statement, coding, references.
09/15/15	Revision to guideline; consisting of updating coding.
11/01/15	Revision: ICD-9 Codes deleted.
11/15/15	Review and revision to guideline; consisting of updating position statement, references
11/15/16	Review and revision to guideline; consisting of updating position statement, coding, references.
12/15/17	Review and revision to guideline; consisting of updating position statement, references, and coding.
08/15/18	Revision to guideline; updated description and position statement.
2/15/19	Review and revision to guideline; consisting of updating description, position statement, references.