Alimta® (pemetrexed)
(Intravenous)

Document Number: IC-0007

Last Review Date: 12/04/2018
Date of Origin: 07/20/2010
Dates Reviewed: 09/2010, 12/2010, 03/2011, 06/2011,0 9/2011, 12/2011, 03/2012, 06/2012, 09/2012, 12/2012, 03/2013, 06/2013, 09/2013, 12/2013, 03/2014, 06/2014, 09/2014, 12/14, 03/2015, 05/2015, 08/2015, 11/2015, 02/2016, 05/2016, 08/2016, 11/2016, 02/2017, 05/2017, 08/2017, 11/2017, 02/2018, 05/2018, 09/2018, 12/2018

I. Length of Authorization

Coverage will be provided for six months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- Alimta 100 mg powder for injection: 4 vials every 21 days
- Alimta 500 mg powder for injection: 2 vials every 21 days

B. Max Units (per dose and over time) [Medical Benefit]:

- 130 billable units every 21 days

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient must be at least 18 years of age (unless otherwise specified); **AND**

Bladder Cancer/Urothelial Carcinoma ‡

- Must be used as a single agent; **AND**
- Must be used subsequently following prior treatment with a systemic therapy (i.e., platinum or checkpoint inhibitor); **AND**
- Patient has a diagnosis of one the following:
  - Locally advanced or metastatic disease; **OR**
  - Disease recurrence post-cystectomy; **OR**
  - Metastatic Upper GU tract tumors; **OR**
  - Metastatic carcinoma of the prostate; **OR**
  - Recurrent or metastatic primary carcinoma of the urethra; **AND**
    - Patient does not have recurrent stage T3-4 disease or palpable inguinal lymph nodes.

Primary central nervous system (CNS) lymphoma ‡

- Used as single agent therapy for relapsed or refractory disease; **AND**
  - Patient failed prior methotrexate-based regimen without prior radiation therapy; **OR**
  - Patient previously received whole brain radiation therapy; **OR**
  - Patient received prior high-dose therapy with stem cell rescue after a prolonged response of at least 12 months

Malignant pleural mesothelioma †

- Used in combination with a cisplatin- or carboplatin-based regimen; **OR**
- Used as a single agent therapy; **OR**
- Used in combination with bevacizumab and either cisplatin or carboplatin followed by single-agent bevacizumab maintenance therapy

Nonsquamous Non-small cell lung cancer (NSCLC) †

- Used in combination with carboplatin or cisplatin; **AND**
  - Used as induction, neoadjuvant or adjuvant therapy in patients; **OR**
  - Used as initial therapy for unresectable disease in patients; **OR**
  - Used with concurrent chemoradiation if radiation not previously given for locoregional recurrence or symptomatic local disease with mediastinal lymph nodes or for superior vena cava obstruction; **OR**
- Used for recurrent, advanced or metastatic disease in patients who do not have locoregional recurrence without evidence of disseminated disease; **AND**
  - Used in combination with pembrolizumab and either carboplatin or cisplatin; **AND**
    - Used as first-line therapy for PD-L1 expression positive (≥50%) tumors that are genomic tumor aberration EGFR and ALK negative or unknown; **OR**
  - Used in combination pembrolizumab; **AND**
    - Used as continuation maintenance therapy for PD-L1 expression positive (≥50%) tumors that are genomic tumor aberration EGFR and ALK negative or unknown; **OR**
  - Used as a single agent OR in combination with pembrolizumab and either carboplatin or cisplatin OR in combination with either carboplatin or cisplatin with or without bevacizumab; **AND**
    - Used as first-line therapy for genomic tumor aberration (e.g., EGFR, ALK, ROS1, BRAF) negative or unknown and PD-L1 <50% or unknown OR BRAF V600E-mutation positive; **OR**
    - Used as subsequent therapy for genomic tumor aberration (e.g., EGFR, ALK, ROS1) positive and prior targeted therapy OR BRAF V600E-mutation positive OR PD-L1 ≥ 50% and EGFR, ALK negative or unknown with no prior platinum doublets; **OR**
  - Used as continuation maintenance therapy with PS ≤ 2; **AND**
    - Patient's disease has not progressed (achieved tumor response or stable disease) after first-line chemotherapy; **AND**
    - Pemetrexed must have been included in patient's first-line chemotherapy regimen for recurrent, advanced, or metastatic disease; **AND**

- Used as single agent (or may be used for switch maintenance as well); **OR**
- Used in combination with bevacizumab if bevacizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; **OR**
- Used in combination with pembrolizumab if pembrolizumab was previously used first-line as part of pembrolizumab/pemetrexed/carboplatin or cisplatin regimen; **OR**

- Used as a single agent for subsequent therapy after progression on initial therapy, if not previously given, for recurrent, advanced or metastatic disease and a performance status score ≤ 2

Thymomas/Thymic carcinoma ‡

- For second-line treatment; **AND**
- Used as a single agent

Ovarian Cancer (epithelial ovarian/fallopian tube/primary peritoneal cancer) ‡

- For persistent or recurrent disease; **AND**
- Patient is not experiencing an immediate biochemical relapse; **AND**
- Used as a single agent

† FDA Approved Indication(s); ‡ Compendia Recommended Indication(s)

Genomic Aberration Targeted Therapies (*not all inclusive*) §
Sensitizing EGFR mutation-positive tumors – Erlotinib – Afatinib – Gefitinib – Osimertinib – Dacomitinib
ALK rearrangement-positive tumors – Crizotinib – Ceritinib – Brigatinib – Alectinib
ROS1 rearrangement-positive tumors – Crizotinib – Ceritinib
BRAF V600E-mutation positive tumors – Dabrafenib/Trametinib
PD-L1 expression-positive tumors (≥50%) – Pembrolizumab – Atezolizumab

IV. Renewal Criteria

Coverage can be renewed based upon the following criteria:

- Patient continues to meet criteria identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**

- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: bone marrow suppression, renal impairment, bullous and exfoliative skin toxicity, interstitial pneumonitis, radiation recall, etc.; **AND**

Non-squamous non-small cell lung cancer (continuation maintenance therapy)

- Used as maintenance therapy of locally advanced, recurrent, or metastatic disease; **AND**
  - Used as a single agent, if used as part of a first-line chemotherapy regimen; **OR**
  - Used in combination with bevacizumab if bevacizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; **OR**
  - Used in combination with pembrolizumab, if pembrolizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; **OR**
  - Used as a single agent for switch maintenance

V. Dosage/Administration

Indication	Dose
All indications	500 mg/m^2 every 21 days

VI. Billing Code/Availability Information

Jcode:

J9305 – Injection, pemetrexed, 10 mg; 1 billable unit = 10mg

NDC:

- Alimta 100 mg powder for injection; single-use vial: 00002-7640-xx
- Alimta 500 mg powder for injection; single-use vial: 00002-7623-xx

VII. References

1. Alimta [package insert]. Indianapolis, IN; Eli Lilly; June 2018. Accessed November 2018.
2. Referenced with permission from the NCCN Drugs & Biologics Compendium (NCCN Compendium®) for pemetrexed. National Comprehensive Cancer Network, 2018. The NCCN Compendium® is a derivative work of the NCCN Guidelines®. NATIONAL COMPREHENSIVE CANCER NETWORK®, NCCN®, and NCCN GUIDELINES® are trademarks owned by the National Comprehensive Cancer Network, Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed November 2018.
3. Castagneto B, Botta M, Aitini E, et al, "Phase II Study of Pemetrexed in Combination With Carboplatin in Patients With Malignant Pleural Mesothelioma (MPM)," Ann Oncol, 2008, 19(2):370-3. [PubMed 18156144]

4. Ceresoli GL, Zucali PA, Favaretto AG, et al, "Phase II Study of Pemetrexed plus Carboplatin in Malignant Pleural Mesothelioma," J Clin Oncol, 2006, 24(9):1443-8. [PubMed 16549838]
5. Jassem J, Ramlau R, Santoro A, et al, "Phase III Trial of Pemetrexed Plus Best Supportive Care Compared With Best Supportive Care in Previously Treated Patients With Advanced Malignant Pleural Mesothelioma," J Clin Oncol, 2008, 26(10):1698-704. [PubMed 18375898]
6. First Coast Service Options, Inc. Local Coverage Determinations (LCD) for Pemetrexed (L33978). Centers for Medicare & Medicaid Services. Updated on 8/18/2016 with effective date 8/18/2016. Accessed November 2018.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C33	Malignant neoplasm of trachea
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	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
C34.30	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
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus or lung
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 unspecified part of unspecified bronchus or lung
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

ICD-10	ICD-10 Description
C56.2	Malignant neoplasm of left ovary
C56.9	Malignant neoplasm of unspecified ovary
C57.00	Malignant neoplasm of unspecified fallopian tube
C57.01	Malignant neoplasm of right fallopian tube
C57.02	Malignant neoplasm of left fallopian tube
C57.10	Malignant neoplasm of unspecified broad ligament
C57.11	Malignant neoplasm of right broad ligament
C57.12	Malignant neoplasm of left broad ligament
C57.20	Malignant neoplasm of unspecified round ligament
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
C57.7	Malignant neoplasm of other specified female genital organs
C57.8	Malignant neoplasm of overlapping sites of female genital organs
C57.9	Malignant neoplasm of female genital organ, 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 unspecified renal pelvis
C66.1	Malignant neoplasm of right ureter
C66.2	Malignant neoplasm of left ureter
C66.9	Malignant neoplasm of unspecified ureter
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

ICD-10	ICD-10 Description
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
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.43	Personal history of malignant neoplasm of ovary
Z85.51	Personal history of malignant neoplasm of bladder
Z85.59	Personal history of malignant neoplasm of other urinary tract organ

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD):

Jurisdiction(s): N	**NCD/LCD Document (s):** L33978
https://www.cms.gov/medicare-coverage-database/search/lcd-date-search.aspx?DocID=L33978&bc=gAAAAAAAAAAAAA==	

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT,	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC