BlueCross BlueShield of North Carolina

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Corporate Medical Policy

Pemetrexed (Alimta®)

File Name:	pemetrexed_alimta
Origination:	8/2016
Last CAP Review:	4/2020
Next CAP Review:	4/2021
Last Review:	4/2020

Description of Procedure or Service

Pemetrexed (Alimta®) is a folate analog metabolic inhibitor indicated for non-squamous non-small cell lung cancer, mesothelioma, urothelial carcinoma, epithelial ovarian cancer and thymic carcinoma.

Alimta is indicated in combination with cisplatin therapy for the initial treatment of patients with locally advanced or metastatic non-squamous non-small cell lung cancer, and in combination with pembrolizumab and platinum chemotherapy for the initial treatment of patients with metastatic non-squamous non-small cell lung cancer and with no EGFR or ALK genomic tumor aberrations. Alimta is indicated for the maintenance treatment of patients with locally advanced or metastatic non-squamous non-small cell lung cancer whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.

Alimta is indicated as a single agent for the treatment of patients with recurrent, metastatic non-squamous non-small cell lung cancer after prior chemotherapy.

Alimta in combination with cisplatin is indicated for the treatment of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery.

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for Pemetrexed (Alimta®) when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Pemetrexed (Alimta) is covered

Pemetrexed (Alimta®) is considered medically necessary for the treatment of patients with:

- Non-squamous Non-Small Cell Lung Cancer when one of the following applies:
  - As adjuvant therapy (NCCN 2A)
    - in combination with cisplatin
    - in combination with cisplatin or carboplatin with radiation

  - As chemoradiotherapy in combination with cisplatin or carboplatin (NCCN 2A)
    - as definitive treatment
    - for locoregional recurrence
  - In combination with cisplatin or carboplatin with or without bevacizumab as: (NCCN, FDA label)
    - first-line therapy for unresectable, recurrent or metastatic disease OR
    - second line therapy after targeted therapy for EGFR mutation-positive or ALK-positive tumors
  - In combination with pembrolizumab and platinum chemotherapy as first-line therapy for metastatic disease in patients with no EGFR or ALK genomic tumor aberrations
  - As maintenance therapy after response or stable disease to at least 4 cycles of platinum-based first-line therapy (NCCN FDA label)
  - As a single agent after prior chemotherapy, if not already received

- Mesothelioma:
  - In combination with cisplatin (FDA label)
  - As first line treatment of unresectable or metastatic disease
    - as a single agent, (NCCN 2A)
    - or in combination with cisplatin or carboplatin with or without bevacizumab
  - As a single agent or in combination with cisplatin or carboplatin as post-operative treatment for individuals not treated with induction chemotherapy. (NCCN 2A)
  - As single agent (NCCN 2A)
    - as second line therapy for unresectable disease

- Urothelial carcinoma, recurrent or metastatic, when used, as a single agent for progressive disease (NCCN 2A)

- Epithelial ovarian cancer, as single agent therapy for persistent or recurrent disease (NCCN 2A)

- Thymic carcinoma or thymoma, as single agent therapy for recurrent or progressive disease (NCCN 2A)

Use of Pemetrexed (Alimta®) may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either:

- In accordance with FDA label (when clinical benefit has been established, see Policy Guidelines); **OR**

- In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

When Pemetrexed (Alimta) is not covered

Pemetrexed (Alimta®) is considered not medically necessary and therefore not covered when above criteria are not met.

Pemetrexed (Alimta®) is considered investigational when used for:

1. Non-cancer indications; **OR**

2. When criteria are not met regarding FDA labeling **OR** strong endorsement/support by

nationally recognized compendia, as stated under "When Pemetrexed (Alimta®) is covered."

Policy Guidelines

Combination use in Non-Small Cell Lung Cancer and Mesothelioma: Recommended dose of Alimta is 500 mg/m^2 IV on Day 1 of each 21-day cycle in combination with cisplatin 75 mg/m^2 IV beginning 30 minutes after Alimta administration.

Single-Agent use in Non-Small Cell Lung Cancer: Recommended dose of Alimta is 500 mg/m^2 IV on Day 1 of each 21-day cycle.

Prior to initiating Alimta, initiate supplementation with oral folic acid and intramuscular vitamin B12. Continue folic acid and vitamin B12 supplementation throughout treatment. Administer corticosteroids the day before, the day of, and the day after Alimta administration.

Dose Reductions: Dose reductions or discontinuation may be needed based on toxicities from the preceding cycle of therapy.

Alimta is not indicated for the treatment of patients with squamous cell non-small cell lung cancer.

Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy (CMP), "Investigational (Experimental) Services."

Please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: *J9305, S0353, S0354*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

U.S. Food and Drug Administration (FDA). Available at: http://www.accessdata.fda.gov/drugsatfda_docs/label/2008/021462s015lbl.pdf

Bambury RM, Benjamin DJ, Chaim JL, et al. The safety and efficacy of single-agent pemetrexed in platinum-resistant advanced urothelial carcinoma: a large single-institution experience. Oncologist. 2015 May;20(5):508-15. PMID: 25845990

Sweeney CJ, Roth BJ, Kabbinavar FF, et al. Phase II study of pemetrexed for second-line treatment of transitional cell cancer of the urothelium. J Clin Oncol. 2006;24(21):3451-3457. PMID: 16849761

Miller DS, Blessing JA, Krasner CN, et al. Phase II evaluation of pemetrexed in the treatment of recurrent or persistent platinum-resistant ovarian or primary peritoneal carcinoma: a study of the Gynecologic Oncology Group. J Clin Oncol. 2009 Jun 1;27(16):2686-91. PMID: 19332726

Liang Y, Padda SK, Riess JW et al. Pemetrexed in patients with thymic malignancies previously treated with chemotherapy. Lung Cancer. 2015 Jan;87(1):34-8. PMID: 25443273

Govindan, R., Bogart, J., Stinchcombe, T., et al. (2011). Randomized phase II study of pemetrexed, carboplatin, and thoracic radiation with or without cetuximab in patients with locally advanced unresectable non-small-cell lung cancer: Cancer and Leukemia Group B trial 30407. J Clin Oncol, 29(23), 3120-3125.

Choy, H., Gerber, D. E., Bradley, J. D., et al. (2015). Concurrent pemetrexed and radiation therapy in the treatment of patients with inoperable stage III non-small cell lung cancer: a systematic review of completed and ongoing studies. Lung Cancer, 87(3), 232-240.

Belani, C. P., Choy, H., Bonomi, P., et al. (2005). Combined chemoradiotherapy regimens of paclitaxel and carboplatin for locally advanced non-small-cell lung cancer: a randomized phase II locally advanced multi-modality protocol. J Clin Oncol, 23(25), 5883-5891.

Patel JD, Socinski MA, Garon EB, et al. PointBreak: a randomized phase III study of pemetrexed plus carboplatin and bevacizumab followed by maintenance pemetrexed and bevacizumab versus paclitaxel plus carboplatin and bevacizumab followed by maintenance bevacizumab in patients with stage IIIB or IV nonsquamous non-small-cell lung cancer. J Clin Oncol. 2013 Dec 1;31(34):4349-4357. PMID: 24145346

Medical Director review 3/2017

Specialty Matched Consultant Advisory Panel review 4/2017

Specialty Matched Consultant Advisory Panel review 4/2018

Lilly USA, LLC. Alimta (pemetrexed) injection for intravenous use. Highlights of prescribing information. January 2019. Available at: http://pi.lilly.com/us/alimta-pi.pdf. Accessed April 2019.

Specialty Matched Consultant Advisory Panel review 4/2019

Specialty Matched Consultant Advisory Panel review 4/2020

Policy Implementation/Update Information

12/30/16 New policy developed. Pemetrexed (Alimta®) is considered medically necessary for the treatment of patients with nonsquamous non-small cell lung cancer, mesothelioma, urothelial

carcinoma, epithelial ovarian cancer and thymic carcinoma. References added. Added HCPCS codes S0353, S0354 to Billing/Coding section. Notification given 12/30/16 for effective date 4/1/17. Medical Director review 8/2016. (lpr)

5/26/17 Added the following statement to "When Covered" section: "Use of Pemetrexed Alimta may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of cancer either: In accordance with FDA label (when clinical benefit has been established, see Policy Guidelines); OR In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached". Under "When Not Covered" section, added the statement "Pemetrexed Alimta is considered investigational when used for: 1)Non-cancer indications; **OR** 2) When criteria are not met regarding FDA labeling **OR** strong endorsement/ support by nationally recognized compendia, as stated under "When Pemetrexed Alimta is covered." Added the following statements under "Policy Guidelines" section: 1)Drugs prescribed for treatment of cancer in accordance with FDA label may be considered medically necessary when clinical benefit has been established, and should not be determined to be investigational as defined in Corporate Medical Policy, Investigational (Experimental) Services." 2) Please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia. Medical director review 3/2017. Specialty Matched Consultant Advisory Panel review 4/26/2017. No change to policy statement. (lpr)

6/8/18 Minor typographical edits made for clarity. Specialty Matched Consultant Advisory Panel review 4/25/2018. No change to policy intent. (krc)

4/30/19 Updated "When Covered" and "Description" sections with the following indication: "in combination with pembrolizumab and platinum chemotherapy as first-line therapy for metastatic disease in patients with no EGFR or ALK genomic tumor aberrations." References added. Specialty Matched Consultant Advisory Panel review 4/17/2019. (krc)

6/9/20 Specialty Matched Consultant Advisory Panel review 4/15/2020. No change to policy statement. (krc)