Medical Policy:
ALIMTA® (pemetrexed)

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.68	August 10, 2023	

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The treating physician or primary care provider must submit to EmblemHealth, or ConnectiCare, as applicable (hereinafter jointly referred to as "EmblemHealth"), the clinical evidence that the member meets the criteria for the treatment or surgical procedure. Without this documentation and information, EmblemHealth will not be able to properly review the request preauthorization or post-payment review. The clinical review criteria expressed below reflects how EmblemHealth determines whether certain services or supplies are medically necessary. This clinical policy is not intended to pre-empt the judgment of the reviewing medical director or dictate to health care providers how to practice medicine. Health care providers are expected to exercise their medical judgment in rendering appropriate care. Health care providers are expected to exercise their medical judgment in rendering appropriate care.

EmblemHealth established the clinical review criteria based upon a review of currently available clinical information (including clinical outcome studies in the peer reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). EmblemHealth expressly reserves the right to revise these conclusions as clinical information changes and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered and/or paid for by EmblemHealth, as some programs exclude coverage for services or supplies that EmblemHealth considers medically necessary.

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Definitions

Alimta is a folate analog metabolic inhibitor that exerts its antineoplastic activity by disrupting folate-dependent metabolic processes essential for cell replication.

Length of Authorization

Coverage will be provided for six months and may be renewed

Thymomas/Thymic Carcinoma: Coverage will be provided for six 21-day cycles and may not be renewed.

MPeM and MPM: Coverage will be provided for six 21-day cycles and may not be renewed when used in combination with platinum therapy and bevacizumab

Dosing Limits [Medical Benefit]

Max Units (per dose and over time):

- CNS Lymphoma and Ovarian Cancer: 230 billable units every 21 days
- All other indications: 130 billable units every 21 days

Guideline

I. INITIAL APPROVAL CRITERIA

Coverage is provided in the following conditions:

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

2. <u>Primary central nervous system (CNS) lymphoma ‡</u>

A. Used as single agent; **AND**

i. Used as induction therapy in patients unsuitable for or intolerant to high-dose methotrexate (MTX); **OR**

ii. Used for relapsed or refractory disease

3. <u>Malignant pleural mesothelioma (MPM) †</u>

A. Used as induction therapy; **AND**

i. Used in combination with cisplatin or carboplatin (if cisplatin ineligible) in patients with epithelioid histology; **OR**

B. Used as first-line therapy; **AND**

i. Used in combination with bevacizumab and cisplatin followed by single-agent maintenance bevacizumab (preferred) as first-line systemic therapy ; **OR**

ii. Used as a single agent **OR** in combination with cisplatin or carboplatin (if cisplatin ineligible) for resected or recurrent disease; **OR**

C. Used as subsequent therapy; **AND**

i. Used in combination with cisplatin or carboplatin (if cisplatin ineligible), with or without bevacizumab, if immunotherapy was administered as first-line treatment; **OR**

ii. Used as a single agent; **AND**

a. Pemetrexed was not administered first-line; **OR**

b. Used as rechallenge if pemetrexed was administered first-line with a good sustained response at the time initial chemotherapy was interrupted

4. <u>Malignant Peritonial Mesothelioma (MPeM) ‡</u>

A. Used as first-line therapy; **AND**

ii. Used in combination with bevacizumab and cisplatin followed by single-agent maintenance bevacizumab (preferred) as first-line systemic therapy for unresectable disease; **OR**

iii. Used as a single agent **OR** in combination with cisplatin or carboplatin (if cisplatin ineligible) for diffuse or recurrent disease; **OR**

B. Used as subsequent therapy; **AND**

i. Used in combination with cisplatin or carboplatin (if cisplatin ineligible), with or without bevacizumab, if immunotherapy was administered as first-line treatment; **OR**

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ii. Used as a single agent; **AND**

a. Pemetrexed was not administered first-line; **OR**

b. Used as rechallenge if pemetrexed was administered first-line with a good sustained response at the time initial chemotherapy was interrupted

5. <u>Nonsquamous Non-small cell lung cancer (NSCLC) †</u>

A. Used in combination with carboplatin or cisplatin-containing regimen; **OR**

B. Used as single-agent therapy; **AND**

i. Patient has recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; **AND**

a. Used as first-line therapy for PD-L1 ≥1% tumors that have negative actionable molecular biomarkers*; **OR**

b. Used as first-line therapy for PD-L1 <1% and tumors that have negative actionable molecular markers * OR BRAF V600E-mutation, NTRK1/2/3 gene fusion, MET exon-14 skipping mutation, EGFR exon 20 mutation, KRAS G12C mutation, or RET rearrangement positive tumors; **OR**

c. Used as subsequent therapy for first progression after initial systemic therapy; **OR**

d. Used continuation or switch maintenance therapy in patients who have achieved tumor response or stable disease following initial therapy *(Note: Continuation maintenance therapy may also be given in combination with bevacizumab or pembrolizumab)*

** Note: Actionable molecular genomic biomarkers include EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET exon 14 skipping mutation, RET rearrangement, and ERBB2 (HER2). If there is insufficient tissue to allow testing for all of EGFR, KRAS, ALK, ROS1, BRAF, NTRK1/2/3, MET, RET, and ERBB2 (HER2) repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes.*

6. <u>Thymomas/Thymic carcinoma ‡</u>

A. Used as a single agent; **AND**

i. Used as first line therapy or postoperative treatment in patients who are unable to tolerate first-line combination regimens; **OR**

ii. Used as second-line therapy for unresectable or metastatic disease

7. <u>Ovarian Cancer (epithelial ovarian/fallopian tube/primary peritoneal cancer) ‡</u>

A. Used as single-agent therapy; **AND**

i. Patient has recurrent or persistent disease; **AND**

a. Patient is not experiencing an immediate biochemical relapse (i.e., rising CA-125 without radiographic evidence of disease); **OR**

ii. Patient has recurrent low-grade serous carcinoma

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

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Genomic Aberration Targeted Therapies (*not all inclusive*) §
Sensitizing EGFR mutation-positive tumors – Erlotinib – Afatinib – Gefitinib – Osimertinib
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

II. RENEWAL CRITERIA

Coverage can be renewed based upon the following criteria:

A. Patient continues to meet criteria identified in Section I: Initial Approval Criteria; **AND**

B. Tumor response with stabilization of disease or decrease in size of tumor or tumor spread; **AND**

C. 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 and radiation recall; **AND**

D. MPeM and MPM

i. May not be renewed when used in combination with platinum therapy and bevacizumab

E. Thymomas/Thymic Carcinoma

i. May not be renewed

j.

Dosage/Administration

Indication	Dose
Non-Squamous NSCLC	500 mg/m^2 every 21 days
MPM, MPeM	Administer 500 mg/m2 intravenously every 21 days -For 6 cycles only when used in combination with platinum therapy and bevacizumab -All others until disease progression or unacceptable toxicity
Primary CNS Lymphoma, Ovarian Cancer	Administer 900 mg/m2 intravenously every 21 days, until disease progression or unacceptable toxicity
Thymomas/Thymic Carcinoma	Administer 500 mg/m2 intravenously every 21 days for a maximum of 6 cycles in absence of disease progression or unacceptable toxicity

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Applicable Procedure Codes

Code	Description
J9305	Injection, pemetrexed, 10 mg; 1 billable unit = 10mg
J9321	Injection, pemetrexed (5andoz) not therapeutically equivalent to j9305, 10 mg
J9322	Injection, pemetrexed (bluepoint) not therapeutically equivalent to j9305, 10 mg
J9323	Injection, pemetrexed (hospira) not therapeutically equivalent to j9305, 10 mg

Applicable NDCs

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

ICD-10 Diagnoses

Code	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
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

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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
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
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

Revision History

Company(ies)	DATE	REVISION
EmblemHealth & ConnectiCare	8/10/2023	Annual Review: Length of Authorization: Added "Thymomas/Thymic Carcinoma: Coverage will be provided for six 21-day cycles and may not be renewed. MPeM and MPM: Coverage will be provided for six 21-day cycles and may not be renewed when used in combination with platinum therapy and bevacizumab" Dosing Limits: Removed "130 billable units every 21 days" Added "CNS Lymphoma and Ovarian Cancer: 230 billable units every 21 days All other indications: 130 billable units every 21 days" Removed Bladder Cancer/Urothelial Carcinoma Indication and Criteria and codes Primary central nervous system (CNS) lymphoma: Initial Criteria: Removed: " 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" Added "Used as induction therapy in patients unsuitable for or intolerant to high-dose methotrexate (MTX); OR Used for relapsed or refractory disease"

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		Malignant pleural mesothelioma (MPM): Initial Criteria: Removed: "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" Added "Used as induction therapy; AND i. Used in combination with cisplatin or carboplatin (if cisplatin ineligible) in patients with epithelioid histology; OR D. Used as first-line therapy; AND i. Used in combination with bevacizumab and cisplatin followed by single-agent maintenance bevacizumab (preferred) as first-line systemic therapy ; OR ii. Used as a single agent OR in combination with cisplatin or carboplatin (if cisplatin ineligible) for resected or recurrent disease; OR E. Used as subsequent therapy; AND i. Used in combination with cisplatin or carboplatin (if cisplatin ineligible), with or without bevacizumab, if immunotherapy was administered as first-line treatment; OR ii. Used as a single agent; AND a. Pemetrexed was not administered first-line; OR b. Used as rechallenge if pemetrexed was administered first-line with a good sustained response at the time initial chemotherapy was interrupted" Added Malignant Peritonial Mesothelioma (MPeM) Indication and Criteria Nonsquamous Non-small cell lung cancer (NSCLC): Initial Criteria: removed: "Used as neo-adjuvant, adjuvant, or first line therapy, with or without radiation therapy, in combination with either carboplatin or cisplatin; OR Used as maintenance chemotherapy of locally advanced, recurrent, or metastatic disease who achieve tumor response or stable disease following chemotherapy; AND a. Used as a single agent, if used as part of a first-line chemotherapy regimen; OR b. Used in combination with bevacizumab if bevacizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; OR c. Used in combination with pembrolizumab, if pembrolizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; OR d. Used as a single agent for switch maintenance; OR 2. Used as a single agent subsequent therapy, if not previously used, for metastatic disease in patients who progressed following initial chemotherapy; AND

		a. Patient has NOT had further progression on other subsequent systemic therapy; OR 3. Used for recurrent or metastatic disease as a single agent OR in combination with cisplatin/carboplatin (with or without bevacizumab) OR in combination with pembrolizumab and carboplatin (if pembrolizumab was not previously used); AND a. Patient does not have locoregional recurrence without evidence of disseminated disease; AND i. Used as first-line therapy for genomic tumor aberration (e.g., EGFR, ALK, ROS1, BRAF and PD-L1) negative or unknown OR BRAF V600E-mutation positive; OR ii. Used as subsequent therapy for genomic tumor aberration (e.g., EGFR, BRAF V600E, ALK, ROS1, PD-L1) positive and prior targeted therapy§ " Added "Used in combination with carboplatin or cisplatin-containing regimen; OR C. Used as single-agent therapy; AND ii. Patient has recurrent, advanced, or metastatic disease (excluding locoregional recurrence or symptomatic local disease without evidence of disseminated disease) or mediastinal lymph node recurrence with prior radiation therapy; AND a. Used as first-line therapy for PD-L1 ≥1% tumors that have negative actionable molecular biomarkers*; OR b. Used as first-line therapy for PD-L1 <1% and tumors that have negative actionable molecular markers * OR BRAF V600E-mutation, NTRK1/2/3 gene fusion, MET exon-14 skipping mutation, EGFR exon 20 mutation, KRAS G12C mutation, or RET rearrangement positive tumors; OR c. Used as subsequent therapy for first progression after initial systemic therapy; OR *d.* Used continuation or switch maintenance therapy in patients who have achieved tumor response or stable disease following initial therapy *(Note: Continuation maintenance therapy may also be given in combination with bevacizumab or pembrolizumab)"* Thymomas/Thymic carcinoma: Initial Criteria: Removed: "For second-line treatment; AND Used as a single agent" Added " Used as a single agent; AND i. Used as first line therapy or postoperative treatment in patients who are unable to tolerate first-line combination regimens; OR ii. Used as second-line therapy for unresectable or metastatic disease" Ovarian Cancer (epithelial ovarian/fallopian tube/primary peritoneal cancer) : Initial Criteria: Removed "For persistent or recurrent disease; AND Patient is not experiencing an immediate biochemical relapse; AND Used as a single agent"

		Added " Used as single-agent therapy; AND i. Patient has recurrent or persistent disease; AND a. Patient is not experiencing an immediate biochemical relapse (i.e., rising CA-125 without radiographic evidence of disease); OR ii. Patient has recurrent low-grade serous carcinoma" <u>Renewal Criteria:</u> Removed: "Non-squamous non-small cell lung cancer (continuation maintenance therapy) 8. Used as maintenance therapy of locally advanced, recurrent, or metastatic disease; AND a. Used as a single agent, if used as part of a first-line chemotherapy regimen; OR b. Used in combination with bevacizumab if bevacizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; OR c. Used in combination with pembrolizumab, if pembrolizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; OR d. Used as a single agent for switch maintenance" Added: "<u>MPeM and MPM</u> j. May not be renewed when used in combination with platinum therapy and bevacizumab <u>E. Thymomas/Thymic Carcinoma</u> k. May not be renewed" Updated Dosing Chart
EmblemHealth & ConnectiCare	5/30/2023	Added JCODES: J9321 - Injection, pemetrexed (sandoz) not therapeutically equivalent to j9305, 10 mg J9322 -Injection, pemetrexed (bluepoint) not therapeutically equivalent to j9305, 10 mg J9323 -Injection, pemetrexed (hospira) not therapeutically equivalent to j9305, 10 mg
EmblemHealth & ConnectiCare	3/18/2022	Transferred policy to new template
EmblemHealth & ConnectiCare	12/30/2020	Annual Review – no policy changes
EmblemHealth & ConnectiCare	9/30/2019	Annual Review – no policy changes

References

1. Alimta [package insert]. Indianapolis, IN; Eli Lilly; January 2019. Accessed December 2020.
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

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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 July 2018.

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