

## Medical Policy:

### Alimta® (pemetrexed) Intravenous

POLICY NUMBER	LAST REVIEW	ORIGIN DATE
MG.MM.PH.68	February 13, 2025	

**Medical Guideline Disclaimer Property of EmblemHealth. All rights reserved.**

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.

If there is a discrepancy between this guideline and a member's benefits program, the benefits program will govern. Identification of selected brand names of devices, tests and procedures in a medical coverage policy is for reference only and is not an endorsement of any one device, test or procedure over another. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and web site links are accurate at time of publication.

EmblemHealth may also use tools developed by third parties, such as the MCG™ Care Guidelines, to assist us in administering health benefits. The MCG™ Care Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. EmblemHealth Services Company, LLC, has adopted this policy in providing management, administrative and other services to EmblemHealth Plan, Inc., EmblemHealth Insurance Company, EmblemHealth Services Company, LLC, and Health Insurance Plan of Greater New York (HIP) related to health benefit plans offered by these entities. ConnectiCare, an EmblemHealth company, has also adopted this policy. All of the aforementioned entities are affiliated companies under common control of EmblemHealth Inc.

## 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, unless otherwise specified

- **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:

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

#### 1. Primary central nervous system (CNS) lymphoma ‡

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

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

B. Patient has leptomeningeal metastases from EGFR mutation-positive non-small cell lung cancer (NSCLC); **AND**

- Used as primary treatment in patients with good risk status (i.e., KPS  $\geq$ 60, no major neurologic deficits, minimal systemic disease, and reasonable systemic treatment options if needed); **OR**
- Used as maintenance treatment in patients with negative cerebrospinal fluid (CSF) cytology or in clinically stable patients with persistently positive CSF cytology

#### 2. Malignant pleural mesothelioma (MPM) †

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

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

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

- Used in combination with bevacizumab and cisplatin or carboplatin (if cisplatin ineligible) for unresectable disease; **OR**
- 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**

- Used as a single agent **OR** in combination with cisplatin or carboplatin (if cisplatin ineligible), with or without bevacizumab; **AND**
  - Nivolumab and ipilimumab was administered as first-line treatment; **OR**
  - Used as rechallenge if pemetrexed was administered first-line with a good sustained response

#### 3. Malignant Peritoneal Mesothelioma (MPeM) ‡

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

- Patient has unicavitary disease with epithelioid histology; **AND**
- Patient has surgical/pathologic high-risk features\*\* and no neoadjuvant therapy was given; **AND**
- Used as a single agent **OR** in combination with cisplatin or carboplatin (if cisplatin ineligible); **OR**

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

- Used in combination with bevacizumab **AND** cisplatin or carboplatin (if cisplatin ineligible) for unresectable diffuse or recurrent disease; **OR**
- Used as a single agent **OR** in combination with cisplatin or carboplatin (if cisplatin ineligible) for diffuse or recurrent disease; **OR**

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

- i. Used as a single agent OR in combination with cisplatin or carboplatin (if cisplatin ineligible), with or without bevacizumab; **AND**
  - a. Nivolumab and ipilimumab were administered as first-line treatment; **OR**
  - b. Used as a rechallenge if a pemetrexed-based treatment was administered first-line with a good response

**\*\* High-risk features include Ki-67 >9%, nodal metastasis, high tumor burden (Peritoneal Cancer Index [PCI] >17), completeness of cytoreduction (CC) score >1, biphasic disease, or bicavitary disease**

#### **4. Nonsquamous Non-small cell lung cancer (NSCLC) †**

- A. Used in combination with carboplatin or cisplatin-containing regimen; **OR**
- B. Used in combination with bevacizumab, pembrolizumab, cemiplimab, or durvalumab for continuation maintenance therapy if previously used first-line and patient achieved a tumor response or stable disease following initial therapy; **OR**
- C. 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 tumors that have negative actionable molecular biomarkers\*; **OR**
    - b. Used as first-line therapy for Used as first-line therapy for EGFR exon 20 mutation, KRAS G12C mutation, BRAF V600E-mutation, NTRK1/2/3 gene fusion, MET exon 14 skipping mutation, RET rearrangement, or ERBB2 (HER2) mutation positive tumors; **OR**
    - c. Used as subsequent 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.*

#### **5. Thymomas/Thymic carcinoma ‡**

- 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 preoperative systemic therapy for surgically resectable disease if R0 resection is considered uncertain; OR
  - iii. Used as second-line therapy for unresectable or metastatic disease

#### **6. Ovarian Cancer (epithelial ovarian/fallopian tube/primary peritoneal cancer) ‡**

- 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

**7. Vaginal Cancer ‡**

- A. Used as a single agent; **AND**
- B. Used as subsequent therapy for recurrent or metastatic disease

**8. Cervical Cancer ‡**

- A. Used as subsequent therapy for recurrent or metastatic disease; **AND**
- B. Patient has squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma; **AND**
- C. Used as a single agent

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

<b>Genomic Aberration Targeted Therapies (not all inclusive) §</b>
Sensitizing EGFR mutation-positive tumors <ul style="list-style-type: none"><li>– Erlotinib</li><li>– Afatinib</li><li>– Gefitinib</li><li>– Osimertinib</li></ul>
ALK rearrangement-positive tumors <ul style="list-style-type: none"><li>– Crizotinib</li><li>– Ceritinib</li><li>– Brigatinib</li><li>– Alectinib</li></ul>
ROS1 rearrangement-positive tumors <ul style="list-style-type: none"><li>– Crizotinib</li><li>– Ceritinib</li></ul>
BRAF V600E-mutation positive tumors <ul style="list-style-type: none"><li>– Dabrafenib/Trametinib</li></ul>
PD-L1 expression-positive tumors (≥50%) <ul style="list-style-type: none"><li>– Pembrolizumab</li></ul>

**II. RENEWAL CRITERIA**

Coverage can be renewed based upon the following criteria:

- A. Patient continues to meet 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

**Dosage/Administration**

Indication	Dose
Non-Squamous NSCLC	500 mg/m <sup>2</sup> every 21 days
MPM, MPeM	Administer 500 mg/m <sup>2</sup> 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
Ovarian, Fallopian Tube, and Primary Peritoneal Cancer, Cervical Cancer, Vaginal Cancer	Administer 900 mg/m <sup>2</sup> intravenously every 21 days, until disease progression or unacceptable toxicity
Thymomas/Thymic Carcinoma	Administer 500 mg/m <sup>2</sup> intravenously every 21 days for a maximum of 6 cycles in absence of disease progression or unacceptable toxicity
CNS Cancers	<u>Leptomeningeal metastases from EGFR mutation-positive non-small cell lung cancer</u> Administer 50 mg intrathecally every 28 days, until disease progression or unacceptable toxicity <u>Primary CNS Lymphoma</u> Administer 900 mg/m <sup>2</sup> intravenously every 21 days, until disease progression or unacceptable toxicity

## Applicable Procedure Codes

Code	Description
J9305	Injection, pemetrexed, 10 mg; 1 billable unit = 10mg
J9322	Injection, pemetrexed (bluepoint) not therapeutically equivalent to j9305, 10 mg
J9323	Injection, pemetrexed ditromethamine, 10 mg
J9292	Injection, pemetrexed (avyxa), not therapeutically equivalent to j9305, 10mg
J9314	Injection, pemetrexed (teva) not therapeutically equivalent to J9305, 10 mg
J9294	Injection, pemetrexed (hospira) not therapeutically equivalent to j9305, 10 mg
J9296	Injection, pemetrexed (accord) not therapeutically equivalent to j9305, 10 mg
J9297	Injection, pemetrexed (sandoz), 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
83831-0111-01	Pemetrexed dipotassium 100mg powder for injection; single-use vial
83821-0112-01	Pemetrexed dipotassium 500mg powder for injection; single-use vial

## ICD-10 Diagnoses

Code	Description
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
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
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
C79.32	Secondary malignant neoplasm of cerebral meninges
C83.30	Diffuse large B-cell lymphoma unspecified site
C83.39	Diffuse large B-cell lymphoma extranodal and solid organ sites
C83.80	Other non-follicular lymphoma, unspecified site
C83.89	Other non-follicular lymphoma, extranodal and solid organ sites
C85.89	Other specified types of non-Hodgkin lymphoma, extranodal and solid organ sites
C85.99	Non-Hodgkin's lymphoma extranodal and solid organ sites
D15.0	Benign neoplasm of thymus
D38.4	Neoplasm of uncertain behavior of thymus
Z85.118	Personal history of other malignant neoplasm of bronchus and lung
Z85.238	Personal history of other malignant neoplasm of thymus
Z85.43	Personal history of malignant neoplasm of ovary

## Revision History

Company(ies)	DATE	REVISION
--------------	------	----------

EmblemHealth & ConnectiCare	2/13/2025	<p>Update ICD10 codes</p> <p>Addition of <b>Cervical Cancer ‡</b> Used as subsequent therapy for recurrent or metastatic disease; <b>AND</b> Patient has squamous cell carcinoma, adenocarcinoma, or adenosquamous carcinoma; <b>AND</b> Used as a single agent</p> <p>Addition of Vaginal Cancer ‡ - Used as a single agent; <b>AND</b> Used as subsequent therapy for recurrent or metastatic disease</p> <p>Addition to Thymomas/Thymic Carcinomas- Used as preoperative systemic therapy for surgically resectable disease if R0 resection is considered uncertain; <b>OR</b></p> <p>Addition to CNS Cancers: Patient has leptomeningeal metastases from EGFR mutation-positive non-small cell lung cancer (NSCLC); <b>AND</b></p> <p>i. Used as primary treatment in patients with good risk status (i.e., KPS ≥60, no major neurologic deficits, minimal systemic disease, and reasonable systemic treatment options if needed); <b>OR</b></p> <p>ii. Used as maintenance treatment in patients with negative cerebrospinal fluid (CSF) cytology or in clinically stable patients with persistently positive CSF cytology</p>
EmblemHealth & ConnectiCare	4/23/2024	<p>Annual Review: Updated length of authorization and dosing chart</p> <p>Initial Criteria: Malignant pleural mesothelioma (MPM) †</p> <p>Added: " cisplatin or carboplatin (if cisplatin ineligible) for unresectable disease" to the statement: " Used in combination with bevacizumab and cisplatin or carboplatin (if cisplatin ineligible) for unresectable disease;" Removed: "followed by single-agent maintenance bevacizumab (preferred) as first-line systemic therapy"</p> <p>Added: "Used as a single agent <b>OR</b>" in combination with cisplatin or carboplatin (if cisplatin ineligible), with or without bevacizumab Removed", if immunotherapy was administered as first-line treatment; <b>OR</b>"; <b>AND</b></p> <p>ii. " Used as a single agent; <b>AND</b>"</p> <p>c. "Pemetrexed was not administered first-line; <b>OR</b> " and added: "Nivolumab and ipilimumab was administered as first-line treatment; <b>OR</b>"</p> <p>Used as rechallenge if pemetrexed was administered first-line with a good sustained response removed: " at the time initial chemotherapy was interrupted"</p> <p>Malignant Peritoneal Mesothelioma (MPeM) ‡</p> <p>Removed to reword the following: "Used as first-line therapy; <b>AND</b></p> <p>Used in combination with bevacizumab and cisplatin followed by single-agent maintenance bevacizumab (preferred) as first-line systemic therapy for unresectable disease; <b>OR</b> Used as a single agent <b>OR</b> in combination with cisplatin or carboplatin (if cisplatin ineligible) for diffuse or recurrent disease; <b>OR</b> Used as subsequent therapy; <b>AND</b> Used in combination with cisplatin or carboplatin (if cisplatin ineligible), with or without bevacizumab, if immunotherapy was administered as first-line treatment; <b>OR</b> Used as a single agent; <b>AND</b> Pemetrexed was not administered first-line; <b>OR</b> Used as rechallenge if pemetrexed was administered first-line with a good sustained response at the time initial chemotherapy was interrupted"</p> <p>Updated as: "Used as adjuvant therapy; <b>AND</b> Patient has unicavitary disease with epithelioid histology; <b>AND</b> Patient has surgical/pathologic high-risk features** and no neoadjuvant therapy was given; <b>AND</b> Used as a single agent <b>OR</b> in combination with cisplatin or carboplatin (if cisplatin ineligible); <b>OR</b> Used as first-line therapy; <b>AND</b> Used in combination with bevacizumab <b>AND</b> cisplatin or carboplatin (if cisplatin ineligible) for unresectable diffuse or recurrent disease; <b>OR</b> Used as a single agent <b>OR</b> in combination with cisplatin or carboplatin (if cisplatin ineligible) for diffuse or recurrent disease; <b>OR</b> Used as subsequent therapy; <b>AND</b> Used as a single agent <b>OR</b> in combination with cisplatin or carboplatin (if cisplatin ineligible), with or without bevacizumab; <b>AND</b> Nivolumab and ipilimumab were administered as first-line treatment; <b>OR</b> Used as a</p>

		<p>rechallenge if a pemetrexed-based treatment was administered first-line with a good response”</p> <p>Nonsquamous Non-small cell lung cancer (NSCLC) †</p> <p>Added: “Used in combination with bevacizumab, pembrolizumab, cemiplimab, or durvalumab for continuation maintenance therapy if previously used first-line and patient achieved a tumor response or stable disease following initial therapy; OR”</p> <p>Removed: “PD-L1 ≥1% “ from the following: “Used as first-line therapy for PD-L1 ≥1% tumors that have negative actionable molecular biomarkers*; OR”</p> <p>Updated wording of the following from: “Used as first-line therapy for PD-L1 &lt;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;” to” Used as first-line therapy for EGFR exon 20 mutation, KRAS G12C mutation, BRAF V600E-mutation, NTRK1/2/3 gene fusion, MET exon 14 skipping mutation, RET rearrangement, or ERBB2 (HER2) mutation positive tumors; OR”</p> <p>Removed: “for first progression after initial systemic therapy; OR” from the following: “Used as subsequent therapy for first progression after initial systemic therapy;”</p>
EmblemHealth & ConnectiCare	8/10/2023	<p>Annual Review:</p> <p><u>Length of Authorization:</u> Added “<u>Thymomas/Thymic Carcinoma:</u> Coverage will be provided for six 21-day cycles and may not be renewed.</p> <p><u>MPeM and MPM:</u> Coverage will be provided for six 21-day cycles and may not be renewed when used in combination with platinum therapy and bevacizumab”</p> <p><u>Dosing Limits:</u> Removed “130 billable units every 21 days”</p> <p>Added “CNS Lymphoma and Ovarian Cancer: 230 billable units every 21 days</p> <p>All other indications: 130 billable units every 21 days”</p> <p>Removed <u>Bladder Cancer/Urothelial Carcinoma</u> Indication and Criteria and codes</p> <p><u>Primary central nervous system (CNS) lymphoma: Initial Criteria:</u> 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”</p> <p>Added “Used as induction therapy in patients unsuitable for or intolerant to high-dose methotrexate (MTX); OR Used for relapsed or refractory disease”</p> <p><u>Malignant pleural mesothelioma (MPM): Initial Criteria:</u> 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”</p> <p>Added “Used as induction therapy; AND</p> <ul style="list-style-type: none"> <li>i. Used in combination with cisplatin or carboplatin (if cisplatin ineligible) in patients with epithelioid histology; OR</li> <li>D. Used as first-line therapy; AND <ul style="list-style-type: none"> <li>i. Used in combination with bevacizumab and cisplatin followed by single-agent maintenance bevacizumab (preferred) as first-line systemic therapy ; OR</li> <li>ii. Used as a single agent OR in combination with cisplatin or carboplatin (if cisplatin ineligible) for resected or recurrent disease; OR</li> </ul> </li> <li>E. Used as subsequent therapy; AND <ul style="list-style-type: none"> <li>i. Used in combination with cisplatin or carboplatin (if cisplatin ineligible), with or without bevacizumab, if immunotherapy was administered as first-line treatment; OR</li> </ul> </li> </ul>



		<ul style="list-style-type: none"> <li>ii. Used as a single agent; AND</li> <li>d. Pemetrexed was not administered first-line; OR</li> <li>e. Used as rechallenge if pemetrexed was administered first-line with a good sustained response at the time initial chemotherapy was interrupted”</li> </ul> <p><u>Added Malignant Peritoneal Mesothelioma (MPeM) Indication and Criteria</u></p> <p><u>Nonsquamous Non-small cell lung cancer (NSCLC): Initial Criteria: removed:</u></p> <p>“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</p> <ul style="list-style-type: none"> <li>a. Used as a single agent, if used as part of a first-line chemotherapy regimen; OR</li> <li>b. Used in combination with bevacizumab if bevacizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; OR</li> <li>c. Used in combination with pembrolizumab, if pembrolizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; OR</li> <li>d. Used as a single agent for switch maintenance; OR</li> </ul> <p>2. Used as a single agent subsequent therapy, if not previously used, for metastatic disease in patients who progressed following initial chemotherapy; AND</p> <ul style="list-style-type: none"> <li>a. Patient has NOT had further progression on other subsequent systemic therapy; OR</li> </ul> <p>3. Used for recurrent or metastatic disease as a single agent <u>OR</u> in combination with cisplatin/carboplatin (with or without bevacizumab) <u>OR</u> in combination with pembrolizumab and carboplatin (if pembrolizumab was not previously used); AND</p> <ul style="list-style-type: none"> <li>a. Patient does not have locoregional recurrence without evidence of disseminated disease; AND <ul style="list-style-type: none"> <li>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</li> <li>ii. Used as subsequent therapy for genomic tumor aberration (e.g., EGFR, BRAF V600E, ALK, ROS1, PD-L1) positive and prior targeted therapy\$ “</li> </ul> </li> </ul> <p>Added “Used in combination with carboplatin or cisplatin-containing regimen; OR</p> <p>D. Used as single-agent therapy; AND</p> <ul style="list-style-type: none"> <li>iii. 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</li> </ul> <p>Used as first-line therapy for PD-L1 ≥1% tumors that have negative actionable molecular biomarkers*; OR</p> <p>Used as first-line therapy for PD-L1 &lt;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</p> <p>Used as subsequent therapy for first progression after initial systemic therapy; OR</p> <p>Used continuation or switch maintenance therapy in patients who have achieved tumor response or stable disease following initial therapy (<i>Note: Continuation</i></p>
--	--	--

		<p><i>maintenance therapy may also be given in combination with bevacizumab or pembrolizumab)</i>"</p> <p><u>Thymomas/Thymic carcinoma</u>: Initial Criteria: Removed: "For second-line treatment; AND Used as a single agent"</p> <p>Added " Used as a single agent; AND</p> <ul style="list-style-type: none"> <li>i. Used as first line therapy or postoperative treatment in patients who are unable to tolerate first-line combination regimens; OR</li> <li>ii. Used as second-line therapy for unresectable or metastatic disease"</li> </ul> <p><u>Ovarian Cancer (epithelial ovarian/fallopian tube/primary peritoneal cancer) :</u> Initial Criteria: Removed "For persistent or recurrent disease; AND Patient is not experiencing an immediate biochemical relapse; AND Used as a single agent"</p> <p>Added " Used as single-agent therapy; AND</p> <ul style="list-style-type: none"> <li>i. Patient has recurrent or persistent disease; AND <ul style="list-style-type: none"> <li>a. Patient is not experiencing an immediate biochemical relapse (i.e., rising CA-125 without radiographic evidence of disease); OR</li> </ul> </li> <li>ii. Patient has recurrent low-grade serous carcinoma"</li> </ul> <p><u>Renewal Criteria:</u></p> <p>Removed: "Non-squamous non-small cell lung cancer (continuation maintenance therapy)</p> <ul style="list-style-type: none"> <li>F. Used as maintenance therapy of locally advanced, recurrent, or metastatic disease; AND <ul style="list-style-type: none"> <li>e. Used as a single agent, if used as part of a first-line chemotherapy regimen; OR</li> <li>f. Used in combination with bevacizumab if bevacizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; OR</li> <li>g. Used in combination with pembrolizumab, if pembrolizumab was previously used with a first-line pemetrexed/platinum chemotherapy regimen; OR</li> <li>h. Used as a single agent for switch maintenance"</li> </ul> </li> </ul> <p>Added: "MPeM and MPM</p> <ul style="list-style-type: none"> <li>j. May not be renewed when used in combination with platinum therapy and bevacizumab</li> </ul> <p><u>E. Thymomas/Thymic Carcinoma</u></p> <ul style="list-style-type: none"> <li>j. May not be renewed"</li> </ul> <p>Updated Dosing Chart</p>
EmblemHealth & ConnectiCare	5/30/2023	<p>Added JCODES:</p> <p>J9321 - Injection, pemetrexed (sandoz) not therapeutically equivalent to j9305, 10 mg</p> <p>J9322 -Injection, pemetrexed (bluepoint) not therapeutically equivalent to j9305, 10 mg</p> <p>J9323 -Injection, pemetrexed (hospira) not therapeutically equivalent to j9305, 10 mg</p>
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<sup>®</sup>) for pemetrexed. National Comprehensive Cancer Network, 2018. The NCCN Compendium<sup>®</sup> is a derivative work of the NCCN Guidelines<sup>®</sup>. NATIONAL COMPREHENSIVE CANCER NETWORK<sup>®</sup>, NCCN<sup>®</sup>, and NCCN GUIDELINES<sup>®</sup> 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 July 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 July 2018.