Clinical Policy: Pemetrexed (Alimta, Pemfexy)

Reference Number: ERX.SPA.307
Effective Date: 03.01.19
Last Review Date: 02.22
Line of Business: Commercial, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
Pemetrexed (Alimta®, Pemfexy™) is an antifolate antineoplastic agent.

FDA Approved Indication(s)
Alimta is indicated:

- In combination with pembrolizumab and platinum chemotherapy, for the initial treatment of patients with metastatic non-squamous NSCLC, with no EGFR or ALK genomic tumor aberrations.

Alimta and Pemfexy are indicated:

- In combination with cisplatin for the initial treatment of patients with locally advanced or metastatic, non-squamous, non-small cell lung cancer (NSCLC).
- As a single agent for the maintenance treatment of patients with locally advanced or metastatic, non-squamous NSCLC whose disease has not progressed after four cycles of platinum-based first-line chemotherapy.
- As a single agent for the treatment of patients with recurrent, metastatic non-squamous, NSCLC after prior chemotherapy.
  Limitation(s) of use: Alimta and Pemfexy are not indicated for the treatment of patients with squamous cell NSCLC.
- Initial treatment, in combination with cisplatin, of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Health plan approved formularies should be reviewed for all coverage determinations. Requirements to use preferred alternative agents apply only when such requirements align with the health plan approved formulary.

It is the policy of health plans affiliated with Envolve Pharmacy Solutions™ that Alimta and Pemfexy are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Non-Small Cell Lung Cancer or Mesothelioma (must meet all)**:**

1. Diagnosis of one of the following (a or b):
   a. Non-squamous NSCLC;
   b. One of the following malignant mesotheliomas (i, ii, iii, or iv):
      i. Pleural;
      ii. Peritoneal (off-label);
      iii. Pericardial (off-label);
      iv. Tunica vaginalis testis (off-label);
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. If Alimta or Pemfexy is requested, member must use generic pemetrexed, unless contraindicated or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed 500 mg/m^2 every 21 days;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 6 months

B. Thymoma or Thymic Carcinoma (off-label) (must meet all)**:**
1. Diagnosis of thymoma or thymic carcinoma;
2. Prescribed by or in consultation with an oncologist:
3. Age ≥ 18 years;
4. Prescribed as second-line therapy *(initial treatment may include surgery, radiation therapy, chemotherapy)*;
5. Prescribed as a single agent;
6. If Alimta or Pemfexy is requested, member must use generic pemetrexed, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 6 months

C. Ovarian/Fallopian Tube/Primary Peritoneal Cancer (off-label) (must meet all)**:**
1. Diagnosis of ovarian, fallopian tube, or primary peritoneal cancer;
2. Prescribed by or in consultation with an oncologist:
3. Age ≥ 18 years;
4. Disease is persistent or recurrent;
5. Prescribed as a single agent;
6. If Alimta or Pemfexy is requested, member must use generic pemetrexed, unless contraindicated or clinically significant adverse effects are experienced;
7. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 6 months

D. Primary Central Nervous System Lymphoma (off-label) (must meet all)**:**
1. Diagnosis of primary central nervous system lymphoma;
2. Prescribed by or in consultation with an oncologist or hematologist;
3. Age ≥ 18 years;
4. Prescribed as a single agent for one of the following (a or b):
   a. Relapsed or refractory disease;
   b. Induction therapy if member is unsuitable for or intolerant to high-dose methotrexate;
5. If Alimta or Pemfexy is requested, member must use generic pemetrexed, unless contraindicated or clinically significant adverse effects are experienced;
6. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 6 months

E. Other diagnoses/indications
1. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions, or documentation supports that member is currently receiving Alimta or Pemfexy for a covered indication and has had at least one dose in the last 90 days;

2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b):
   a. New dose does not exceed 500 mg/m^2 every 21 days;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via a health plan affiliated with Envolve Pharmacy Solutions and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to ERX.PA.01 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – ERX.PA.01 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ALK: anaplastic lymphoma kinase
EGFR: epidermal growth factor receptor
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network
NSCLC: non-small cell lung cancer

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): history of severe hypersensitivity reaction to pemetrexed
- Boxed warning(s): none reported

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
NSCLC	500 mg/m^2 IV on Day 1 of each 21-day cycle as a single agent or in combination with cisplatin, or platinum therapy and pembrolizumab	500 mg/m^2 IV infusion every 21 days
Malignant pleural mesothelioma	500 mg/m^2 IV on Day 1 of each 21-day cycle in combination with cisplatin	

VI. Product Availability

Single-dose vials for injection: 100 mg (Alimta), 500 mg (Alimta, Pemfexy)

VII. References

1. Alimta Prescribing Information. Indianapolis, IN: Eli Lilly Pharmaceuticals; January 2019. Available at: www.alimta.com. Accessed November 13, 2021.
2. Pemfexy Prescribing Information. Woodcliff Lake, NJ: Eagle Pharmaceuticals, Inc. February 2020. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/209472s000lbl.pdf. Accessed November 13, 2021.
3. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed November 13, 2021.
4. Non-Small Cell Lung Cancer Version 7.2021. National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed November 13, 2021.

5. Malignant Pleural Mesothelioma Version 2.2021. National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed November 13, 2021.
6. Thymomas and Thymic Carcinomas Version 1.2021. National Comprehensive Cancer Network Guidelines. Available at www.nccn.org. Accessed November 13, 2021.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	11.13.18	02.19
No significant changes: added updated FDA indication: NSCLC without EGFR or ALK gene mutation in combination with platinum chemotherapy and pembrolizumab; this is already a covered use, therefore no modification to criteria was required; references reviewed and updated.	03.14.19	
1Q 2020 annual review: no significant changes; references reviewed and updated.	11.19.19	02.20
1Q 2021 annual review: induction therapy offered for primary CNS lymphoma per NCCN; urothelial carcinoma off-label use removed per NCCN; references reviewed and updated.	11.06.20	02.21
1Q 2022 annual review: added Pemfexy brand to policy; added other sources of malignant mesotheliomas per NCCN; added criterion for use as single-agent therapy for thymomas/thymic carcinomas, ovarian/fallopian tube/primary peritoneal cancers, and primary central nervous system lymphomas per NCCN; references reviewed and updated.	11.13.21	02.22
Added redirection to generic pemetrexed.	05.31.22	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information.

This Clinical Policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members.