Clinical Policy: Pemetrexed (Alimta, Pemfexy)

Reference Number: CP.PHAR.368
Effective Date: 10.31.17
Last Review Date: 02.22
Line of Business: HIM, Medicaid

Coding Implications
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.
  Limitations of Use: Alimta and Pemfexy are not indicated for the treatment of patients with squamous cell, non-small cell lung cancer.
- 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.

It is the policy of health plans affiliated with Centene Corporation® 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. Nonsquamous 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 per 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 the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication via Centene benefit or documentation supports that member has received 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 Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid.

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 policies – HIM.PA.154 for health insurance marketplace and CP.PMN.53 for Medicaid 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 vial 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.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9304	Injection, pemetrexed (pemfexy), 10 mg
J9305	Injection, pemetrexed, not otherwise specified, 10 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created.	10.31.17	02.18
1Q 2019 annual review; HIM-Medical Benefit line of business added; age added; new NSCLC labeled indication added to indication section; bladder cancer relabeled as UC, methotrexate trial removed from CNS lymphoma and FDA approved treatments removed from ovarian cancer to encompass NCCN uses; references reviewed and updated.	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: added HIM line of business, removed HIM-Medical Benefit, and removed HIM disclaimer for HIM NF drugs; no clinically significant changes; references reviewed and updated.	11.19.19	02.20
RT4: added new brand Pemfexy.	03.04.20	
1Q 2021 annual review: induction therapy offered for primary CNS lymphoma per NCCN; urothelial carcinoma off-label use removed per NCCN; references to HIM.PHAR.21 revised to HIM.PA.154; references reviewed and updated.	11.06.20	02.21
1Q 2022 annual review: 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; updated HCPCS codes.	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. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health

plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. 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. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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