Clinical Policy Title:	pemetrexed
Policy Number:	RxA.350
Drug(s) Applied:	Alimta®, Pemfexy™
Original Policy Date:	03/06/2020
Last Review Date:	4/18/2022
Line of Business Policy Applies to:	All lines of business

Background

Pemetrexed (Alimta®) is indicated:

In combination with pembrolizumab and platinum chemotherapy, for the initial treatment of patients with metastatic non-squamous NSCLC, with no EGFR (Epidermal growth factor receptor) or ALK (Anaplastic lymphoma kinase) 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.
- 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.

Limitation(s) of use: Alimta®and Pemfexy™ are not indicated for the treatment of patients with squamous cell non-small cell lung cancer.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
pemetrexed (Alimta®, Pemfexy™)	NSCLC	500 mg/m^2 intravenously over 10 minute 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 intravenous infusion every 21 days
	Malignant pleural mesothelioma	500 mg/m^2 intravenously on Day 1 of each 21-day cycle in combination with cisplatin	

Dosage Forms

- Alimta®: 100 mg or 500 mg lyophilized powder in single-dose vial
- Pemfexy™ Injection: 500 mg/20 mL (25 mg/mL) in a multi-dose vial

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

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. Malignant pleural mesothelioma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. 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
Commercial: 6 months
Medicaid: 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 a single agent for second line therapy (initial treatment may include surgery, radiation therapy, chemotherapy);
5. 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
Commercial: 6 months
Medicaid: 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. 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
Commercial: 6 months
Medicaid: 6 months

D. Primary Central Nervous System Lymphoma (off-label) (must meet all)**:**

1. Diagnosis of relapsed or refractory 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. 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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy

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

1. Member is currently receiving medication that has been authorized by RxAdvance or member has met the initial approval criteria 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
Commercial: 12 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key
ALK: Anaplastic lymphoma kinase
EGFR: Epidermal growth factor receptor
NSCLC: Non-small cell lung cancer
FDA: Food and Drug Administration
NCCN: National Comprehensive Cancer Network

APPENDIX B: Therapeutic Alternatives

- Not applicable.

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - History of severe hypersensitivity reaction to pemetrexed.*

*Contraindications listed reflect direct statements made in the manufacturer's package insert; for additional uses, warnings, and precautions, please refer to clinical guidelines.

- Boxed warning(s):

- None reported.

APPENDIX D: General Information

- Myelosuppression: Can cause severe bone marrow suppression resulting in cytopenia and an increased risk of infection. Do not administer Alimta® when the absolute neutrophil count is less than 1500 cells/mm³ and platelets are less than 100,000 cells/mm³. Initiate supplementation with oral folic acid and intramuscular vitamin B12 to reduce the severity of hematologic and gastrointestinal toxicity of Alimta®.
- Renal Failure: Can cause severe, and sometimes fatal, renal failure. Do not administer when creatinine clearance is less than 45 mL/min.
- Bullous and Exfoliative Skin Toxicity: Permanently discontinue for severe and life-threatening bullous, blistering or exfoliating skin toxicity.
- Interstitial Pneumonitis: Withhold for acute onset of new or progressive unexplained pulmonary symptoms. Permanently discontinue if pneumonitis is confirmed.
- Radiation Recall: Can occur in patients who received radiation weeks to years previously; permanently discontinue for signs of radiation recall.
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception.
- CrCL less than 45 mL/min**:** Dosage recommendations are not available; do not administer pemetrexed.

References

1. Alimta® Prescribing Information. Indianapolis, IN: Eli Lilly Pharmaceuticals; February 2021. Available at: https://dailymed.nlm.nih.gov/dailymed/fda/fdaDrugXsl.cfm?setid=f5a860f3-37ec-429c-ae04-9c88d7c55c08&type=display. Accessed March 11, 2022.
2. Pemfexy™ Prescribing Information. Woodcliff Lake, NJ: Eagle Pharmaceuticals, Inc. June 2020. Available at: https://www.pemfexy.com/wp-content/uploads/2022/02/PEMFEXY-pemetrexed_injection-prescribing_information.pdf. Accessed March 11, 2022.
3. Non-small cell lung cancer (Version 2.2022). National Comprehensive Cancer Network Guidelines. Available at https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed March 11, 2022.
4. Thymoma or Thymic Carcinoma. Version 1.2022. National Comprehensive Cancer Network Guidelines. Available at: https://www.nccn.org/professionals/physician_gls/pdf/thymic.pdf. Accessed March 14, 2022.
5. Malignant pleural mesothelioma. Version 1.2022. National Comprehensive Cancer Network Guidelines. Available at https://www.nccn.org/professionals/physician_gls/pdf/mpm.pdf. Accessed March 11, 2022.
6. Ovarian/Fallopian Tube/Primary Peritoneal Cancer. Version 1.2022. National Comprehensive Cancer Network Guidelines. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed March 14, 2022.
7. Primary Central Nervous System Lymphoma. Version 2.2021. National Comprehensive Cancer Network Guidelines. Available at: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed March 14, 2022.
8. National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed March 11, 2022.
9. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.; 2018. Available at: http://www.clinicalpharmacology-ip.com/. Accessed March 11, 2022.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1) Policy title was updated.	07/28/2020	09/14/2020

2) Indications were updated. 3) Initial Approval criteria updated. 4) Continued Therapy Approval criteria II.A.1 was rephrased. 5) Appendices updated. 6) References were updated.		
Policy was reviewed: 1) Statement about provider sample ‘‘The provision of provider samples does not guarantee coverage…” was added to Clinical Policy. 2) Initial Approval Criteria and Continued Therapy Criteria approval duration was updated to remove HIM approval duration. 3) Appendix A was updated to include NCCN. 4) Appendix D was updated to include warnings and precautions “Myelosuppression: Can cause severe bone marrow suppression resulting in cytopenia…” 5) References were reviewed and updated.	06/01/2021	09/14/2021
Policy was reviewed: 1. Clinical Policy Title, Drug(s) Applied: Updated to include new drug Pemfexy™. 2. Background: Updated to include new drug Pemfexy™. 3. Dosage Forms: Updated to include new brand dosage form, Pemfexy™ Injection -500 mg/20 mL (25 mg/mL) in a multi-dose vial. 4. Initial Approval Criteria, 1.D.4.a and 1.D.4.b: Updated to include new diagnostic criteria Pemetrexed is prescribed for one of the following (a or b): Relapsed or refractory disease; Induction therapy as a single agent if member is unsuitable for or intolerant to high-dose methotrexate. 5. Initial Approval Criteria (I.D): Updated to be removed. 6. Disclaimer about contraindications "Contraindications listed reflect statements made in the manufacturer's package insert..." was added to Appendix C. 7. Appendix D, General Information: Updated to include new information regarding CrCL less than 45 mL/min: Dosage recommendations are not available; do not administer pemetrexed. 8. References were reviewed and updated.	03/11/2022	4/18/2022