 **Draft Revision Policy: Do Not Implement**

**Pemetrexed (Alimta®; Pemfexy™, Pemetrexed™, Pemrydi RTU, Axtle™)**

**IMPORTANT REMINDER**

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the medical policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

**The proposal is to add text/statements in red and to delete text/statements with strikethrough:**

**POLICY**

**INDICATIONS**

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Non-squamous non-small cell lung cancer (NSCLC)

- In combination with pembrolizumab and platinum chemotherapy, for the initial treatment of patients with metastatic non-squamous NSCLC, with no EFGR or ALK genomic tumor aberrations.
- In combination with cisplatin for the initial treatment of patients with locally advanced or metastatic, non-squamous 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**
Pemetrexed is not indicated for the treatment of patients with squamous cell, (NSCLC).

Mesothelioma
In combination with cisplatin, for the initial treatment of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery.

Compendial Uses

- Bladder cancer
- Pleural mesothelioma
- Peritoneal mesothelioma
- Pericardial mesothelioma
- Tunica vaginalis testis mesothelioma
- Nonsquamous non-small cell lung cancer (NSCLC)
- Ovarian cancer, fallopian tube cancer, and primary peritoneal cancer: epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, carcinosarcoma (malignant mixed Müllerian tumors), clear cell

carcinoma of the ovary, grade 1 endometrioid carcinoma, low-grade serous carcinoma/ovarian borderline epithelial tumor (low malignant potential), and mucinous carcinoma of the ovary
- Primary central nervous system (CNS) lymphoma
- Thyroid carcinoma
- Thymomas and thymic carcinomas
- Cervical cancer
- Vaginal cancer

All other indications are considered experimental/investigational and not medically necessary.

**EXCLUSIONS**

Coverage will not be provided for members with squamous cell NSCLC.

**COVERAGE CRITERIA**

**Bladder Cancer**

Authorization of 6 months may be granted for treatment of locally advanced, metastatic, or relapsed transitional cell urothelium cancer, as second-line treatment.

**Pleural or Peritoneal Mesothelioma**

Authorization of 6 months may be granted for treatment of pleural or peritoneal mesothelioma, including pericardial mesothelioma and tunica vaginalis testis mesothelioma, when any of the following criteria are met:
- The requested medication will be used as a single agent or in combination with cisplatin or carboplatin
- The requested medication will be used in combination with bevacizumab or durvalumab (Imfinzi) and either cisplatin or carboplatin
- The requested medication will be used as first-line therapy in combination with pembrolizumab and platinum chemotherapy.

**Non-Small Cell Lung Cancer (Non-Squamous Histology)**

Authorization of 6 months may be granted for treatment of non-squamous non-small cell lung cancer (including leptomeningeal metastases).

**Ovarian Cancer, Fallopian Tube Cancer, and Primary Peritoneal Cancer**

Authorization of 6 months may be granted for treatment of persistent or recurrent epithelial ovarian cancer, fallopian tube cancer, primary peritoneal cancer, carcinosarcoma (malignant mixed Müllerian tumors), clear cell carcinoma of the ovary, grade 1 endometrioid carcinoma, low-grade serous carcinoma/ovarian borderline epithelial tumor (low malignant potential), or mucinous carcinoma of the ovary, as single agent therapy.

**Primary Central Nervous System (CNS) Lymphoma**

Authorization of 6 months may be granted for treatment of primary CNS lymphoma, as a single agent.

**Thyroid Cancer**

Authorization of 6 months may be granted for treatment of progressive and/or symptomatic papillary or follicular thyroid carcinoma when all of the following criteria are met:

- Disease is unresectable or metastatic.
- Disease is not amenable to radioactive iodine (RAI) therapy.
- The requested medication will be used in combination with carboplatin.

Authorization of 6 months may be granted for treatment of progressive and/or symptomatic oncocytic/Hürthle cell thyroid carcinoma when all of the following criteria are met:

- Disease is unresectable or metastatic.
- The requested medication will be used in combination with carboplatin.

Authorization of 6 months may be granted for treatment of anaplastic carcinoma when all of the following criteria are met:

- Disease is metastatic.
- The requested medication will be used in combination with carboplatin after disease progression following prior treatment.

**Thymomas and Thymic Carcinomas**

Authorization of 6 months may be granted for treatment of thymoma or thymic carcinoma, as a single agent.

**Cervical Cancer**

Authorization of 6 months may be granted for treatment of persistent, recurrent or metastatic cervical cancer.

**Vaginal Cancer**

Authorization of 6 months may be granted for subsequent treatment of recurrent or metastatic vaginal cancer when used as a single agent.

## CONTINUATION OF THERAPY

Authorization of 6 months (up to 24 months total for use with pembrolizumab for pleural or peritoneal mesothelioma including pericardial mesothelioma and tunica vaginalis testis mesothelioma) may be granted for continued treatment in members requesting reauthorization for an indication in the coverage criteria section when there is no evidence of unacceptable toxicity or disease progression while on the current regimen.

## MEDICATION QUANTITY LIMITS

| Drug Name | Diagnosis | Maximum Dosing Regimen |
|---|---|---|
| Alimta (Pemetrexed) | Bladder Cancer | Route of Administration: Intravenous 500mg/m² every 21 days |
| Alimta (Pemetrexed) | Cervical Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| Alimta (Pemetrexed) | Malignant Pleural Mesothelioma, Malignant Peritoneal Mesothelioma, Pericardial Mesothelioma, or Tunica Vaginalis Testis Mesothelioma | Route of Administration: Intravenous 500mg/m² every 21 days |
| Alimta (Pemetrexed) | Non-Small Cell Lung Cancer (NSCLC) | Route of Administration: Intravenous 500mg/m² every 21 days |

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| Alimta (Pemetrexed) | Ovarian, Fallopian, Primary Peritoneal Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| ~~Alimta (Pemetrexed)~~ | ~~Primary CNS Lymphoma~~ | ~~Route of Administration: Intravenous 900mg/m² every 21 days~~ |
| Alimta (Pemetrexed) | Primary CNS Lymphoma | Route of Administration: Intravenous 900mg/m² every 14 days |
| Alimta (Pemetrexed) | Thymoma or Thymic Carcinoma | Route of Administration: Intravenous 500mg/m² every 21 days |
| Alimta (Pemetrexed) | Thyroid Carcinoma (including Papillary, Follicular, Oncocytic, and Anaplastic Carcinomas) | Route of Administration: Intravenous 500mg/m² every 21 days |
| Alimta (Pemetrexed) | Vaginal Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| Axtle (Pemetrexed Dipotassium) | Bladder Cancer | Route of Administration: Intravenous 500mg/m² every 21 days |
| Axtle (Pemetrexed Dipotassium) | Cervical Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| Axtle (Pemetrexed Dipotassium) | Malignant Pleural Mesothelioma, Malignant Peritoneal Mesothelioma, Pericardial Mesothelioma, or Tunica Vaginalis Testis Mesothelioma | Route of Administration: Intravenous 500mg/m² every 21 days |
| Axtle (Pemetrexed Dipotassium) | Non-Small Cell Lung Cancer (NSCLC) | Route of Administration: Intravenous 500mg/m² every 21 days |
| Axtle (Pemetrexed Dipotassium) | Ovarian, Fallopian, Primary Peritoneal Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| ~~Axtle (Pemetrexed Dipotassium)~~ | ~~Primary CNS Lymphoma~~ | ~~Route of Administration: Intravenous 900mg/m² every 21 days~~ |
| Axtle (Pemetrexed Dipotassium) | Primary CNS Lymphoma | Route of Administration: Intravenous 900mg/m² every 14 days |
| Axtle (Pemetrexed Dipotassium) | Thymoma or Thymic Carcinoma | Route of Administration: Intravenous 500mg/m² every 21 days |
| Axtle (Pemetrexed Dipotassium) | Thyroid Carcinoma (including Papillary, Follicular, Oncocytic, and Anaplastic Carcinomas) | Route of Administration: Intravenous 500mg/m² every 21 days |
| Axtle (Pemetrexed Dipotassium) | Vaginal Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| Pemetrexed (Pemetrexed) | Bladder Cancer | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemetrexed (Pemetrexed) | Cervical Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| Pemetrexed (Pemetrexed) | Malignant Pleural Mesothelioma, Malignant Peritoneal Mesothelioma, | Route of Administration: Intravenous 500mg/m² every 21 days |

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| | Pericardial Mesothelioma, or Tunica Vaginalis Testis Mesothelioma | |
| Pemetrexed (Pemetrexed) | Non-Small Cell Lung Cancer (NSCLC) | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemetrexed (Pemetrexed) | Ovarian, Fallopian, Primary Peritoneal Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| ~~Pemetrexed (Pemetrexed)~~ | ~~Primary CNS Lymphoma~~ | ~~Route of Administration: Intravenous 900mg/m² every 21 days~~ |
| Pemetrexed (Pemetrexed) | Primary CNS Lymphoma | Route of Administration: Intravenous 900mg/m² every 14 days |
| Pemetrexed (Pemetrexed) | Thymoma or Thymic Carcinoma | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemetrexed (Pemetrexed) | Thyroid Carcinoma (including Papillary, Follicular, Oncocytic, and Anaplastic Carcinomas) | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemetrexed (Pemetrexed) | Vaginal Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| Pemfexy (Pemetrexed) | Bladder Cancer | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemfexy (Pemetrexed) | Cervical Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| Pemfexy (Pemetrexed) | Malignant Pleural Mesothelioma, Malignant Peritoneal Mesothelioma, Pericardial Mesothelioma, or Tunica Vaginalis Testis Mesothelioma | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemfexy (Pemetrexed) | Non-Small Cell Lung Cancer (NSCLC) | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemfexy (Pemetrexed) | Ovarian, Fallopian, Primary Peritoneal Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| ~~Pemfexy (Pemetrexed)~~ | ~~Primary CNS Lymphoma~~ | ~~Route of Administration: Intravenous 900mg/m² every 21 days~~ |
| Pemfexy (Pemetrexed) | Primary CNS Lymphoma | Route of Administration: Intravenous 900mg/m² every 14 days |
| Pemfexy (Pemetrexed) | Thymoma or Thymic Carcinoma | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemfexy (Pemetrexed) | Thyroid Carcinoma (including Papillary, Follicular, Oncocytic, and Anaplastic Carcinomas) | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemfexy (Pemetrexed) | Vaginal Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| Pemrydi RTU (Pemetrexed Disodium) | Bladder Cancer | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemrydi RTU (Pemetrexed Disodium) | Cervical Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| Pemrydi RTU (Pemetrexed Disodium) | Malignant Pleural Mesothelioma, Malignant Peritoneal Mesothelioma, Pericardial Mesothelioma, or Tunica Vaginalis Testis Mesothelioma | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemrydi RTU (Pemetrexed Disodium) | Non-Small Cell Lung Cancer (NSCLC) | Route of Administration: Intravenous 500mg/m² every 21 days |

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| Pemrydi RTU (Pemetrexed Disodium) | Ovarian, Fallopian, Primary Peritoneal Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |
| ~~Pemrydi RTU (Pemetrexed Disodium)~~ | ~~Primary CNS Lymphoma~~ | ~~Route of Administration: Intravenous 900mg/m² every 21 days~~ |
| Pemrydi RTU (Pemetrexed Disodium) | Primary CNS Lymphoma | Route of Administration: Intravenous 900mg/m² every 14 days |
| Pemrydi RTU (Pemetrexed Disodium) | Thymoma or Thymic Carcinoma | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemrydi RTU (Pemetrexed Disodium) | Thyroid Carcinoma (including Papillary, Follicular, Oncocytic, and Anaplastic Carcinomas) | Route of Administration: Intravenous 500mg/m² every 21 days |
| Pemrydi RTU (Pemetrexed Disodium) | Vaginal Cancer | Route of Administration: Intravenous 900mg/m² every 21 days |

## APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

## ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

## REFERENCES

1. Alimta [package insert]. Indianapolis, IN: Lilly USA, LLC; May 2023.
2. Pemfexy [package insert]. Woodcliff Lake, NJ: Eagle Pharmaceuticals, Inc.; December 2022.
3. Pemetrexed disodium [package insert]. Princeton, NJ: Dr. Reddy's Laboratories Inc.; September 2022.
4. Pemrydi RTU [package insert]. Ahmedabad, India: Zydus Lifesciences Limited; November 2024.
5. Axtle [package insert]. Parsippany, NJ: Avyxa Pharma, LLC; June 2025.
6. The NCCN Drugs & Biologics Compendium® © 2025 National Comprehensive Cancer Network, Inc. Available at: https://www.nccn.org. Accessed July 16, 2025.
7. Pemetrexed. Lexi-Drugs. UpToDate Lexidrug. UpToDate Inc. https://online.lexi.com. Accessed July 21, 2025.
8. CVS Caremark Clinical Programs Review: State of CT review; March 2018.
9. Durvalumab. Merative Micromedex. Merative. Ann Arbor, MI. Available at https://www.micromedexsolutions.com Accessed July 16, 2025.

## EFFECTIVE DATE

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