Pemetrexed Agents
(Alimta, Axtle, Pemfexy, Pemrydi)

Override(s)	Approval Duration
Prior Authorization	1 year

Medications
Alimta (pemetrexed disodium) Axtle (pemetrexed dipotassium) Pemfexy (pemetrexed) Pemrydi (pemetrexed disodium hemipentahydrate)

APPROVAL CRITERIA

Requests for Pemetrexed Agents (Alimta, Axtle, Pemfexy, Pemrydi) may be approved if the following criteria are met:

I. Individual has a diagnosis of malignant mesothelioma; **AND**
   A. Individual is using in combination with cisplatin or carboplatin (Label, NCCN 2A); **OR**
   B. Individual is using as a first-line of therapy in combination with platinum-based chemotherapy AND bevacizumab (or bevacizumab biosimilar) (Label, NCCN 1A); **OR**
   C. Individual is using as a first-line therapy in combination with platinum-based chemotherapy and pembrolizumab (NCCN 1); **OR**
   D. Individual is using as single agent for subsequent therapy (NCCN 1); **AND**
      1. Pemetrexed was not administered as first-line; **OR**
      2. Pemetrexed was used as first-line with good sustained response; **OR**
   E. Individual is using as a single agent for first line systemic therapy (NCCN 2A);

OR

II. Individual has a diagnosis of non-squamous, non-small cell lung cancer (NSCLC); **AND**
   A. Individual is using as a single agent after prior chemotherapy; **OR**
   B. Individual is using in combination with platinum-based chemotherapy with or without bevacizumab (or bevacizumab biosimilar) (NCCN 2A); **OR**
   C. Individual is using as a single agent for maintenance therapy; **OR**
   D. Individual is using in combination with pembrolizumab (Keytruda) and platinum chemotherapy for initial treatment and without presence of actionable molecular markers (Label, NCCN 2A); **OR**
   E. Individual is using as continuous maintenance therapy until disease progression, if given first-line as part of Keytruda (pembrolizumab)/platinum chemotherapy/and pemetrexed regimen (NCCN 1); **OR**

F. Individual is using in combination with cemiplimab and platinum chemotherapy; **OR**
G. Individual is using in combination with tremelimumab, durvalumab, and platinum chemotherapy; **OR**
H. Individual is using in combination with bevacizumab as continuous maintenance therapy, if given first-line as part of bevacizumab/ platinum/and pemetrexed regimen (NCCN 2A); **OR**
I. Individual is using in combination with cemiplimab as continuous maintenance therapy, if given first-line as part of cemiplimab/ platinum/and pemetrexed regimen (NCCN 2A); **OR**
J. Individual is using in combination with durvalumab as continuous maintenance therapy if given first-line as part of tremelimumab/durvalumab/platinum/and pemetrexed regimen (NCCN 2A); **OR**
K. Individual is using as first-line therapy in combination with nivolumab, ipilimumab, *and* platinum-based chemotherapy and without presence of actionable molecular markers (NCCN 2A); **OR**
L. Individual is using as adjuvant or neoadjuvant therapy in combination with platinum-based chemotherapy; **OR**
M. Individual is using in combination with Rybrevant (amivantamab-vmjw) and carboplatin (NCCN 1); **OR**
N. Individual is using as first-line therapy for EGFR exon 19 deletion or exon 21 L858R recurrent, advanced, or metastatic disease in combination with osimertinib and platinum-based chemotherapy (NCCN 1, 2A);

OR

III. Individual has a diagnosis of for EGFR mutation positive non-small cell lung cancer with leptomeningeal metastases; **AND**
IV. Pemetrexed is being administered intrathecally;

OR

V. Individual has a diagnosis of non-nasopharyngeal head and neck cancer (NCCN 2A);

OR

VI. Individual is using as a single-agent therapy; **AND**
VII. Individual has one of the following (NCCN 2A):
A. Individual has a diagnosis for persistent or recurrent ovarian cancer; **OR**
B. Individual has a diagnosis for thymic cancer and thymomas; **OR**
C. Individual is using pemetrexed as second-line or subsequent therapy for cervical cancer; **OR**
D. Individual has a diagnosis for primary central nervous system lymphoma; **OR**
E. Individual is using pemetrexed as second-line or subsequent therapy for vaginal cancer.

Pemetrexed Agents (Alimta, Axtle, Pemfexy, Pemrydi) may not be approved for the:

I. Individual has a diagnosis of squamous cell non-small cell lung cancer; **OR**
II. When the above criteria are not met and for all other indications.

Key References:

1. Barlesi F, Scherpereel A, Rittmeyer A, et al. Randomized phase III trial of maintenance bevacizumab with or without pemetrexed after first-line induction with bevacizumab, cisplatin, and pemetrexed in advanced nonsquamous non-small-cell lung cancer: AVAPERL (MO22089). J Clin Oncol. 2013; 31(24):3004-3011
2. Carteni G, Manegold C, Garcia GM, et al. Malignant peritoneal mesothelioma-Results from the International Expanded Access Program using pemetrexed alone or in combination with a platinum agent. Lung Cancer. 2009; 64(2):211-218.
3. Clinical Pharmacology [database online]. Tampa, FL: Gold Standard, Inc.: 2025. URL: http://www.clinicalpharmacology.com. Updated periodically.
4. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically
5. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
6. Jänne PA, Wozniak AJ, Belani CP, et al. Open-label study of pemetrexed alone or in combination with cisplatin for the treatment of patients with peritoneal mesothelioma: outcomes of an expanded access program. Clin Lung Cancer. 2005; 7(1):40-46.
7. Kenmotsu H, Yamamoto N, Yamanaka T, et al. Randomized Phase III Study of Pemetrexed Plus Cisplatin Versus Vinorelbine Plus Cisplatin for Completely Resected Stage II to IIIA Nonsquamous Non-Small-Cell Lung Cancer. *J Clin Oncol*. 2020;38(19):2187-2196. doi:10.1200/JCO.19.02674
8. Kreuter M, Vansteenkiste J, Fischer JR, et al. Randomized phase 2 trial on refinement of early-stage NSCLC adjuvant chemotherapy with cisplatin and pemetrexed versus cisplatin and vinorelbine: the TREAT study. *Ann Oncol*. 2013;24(4):986-992. doi:10.1093/annonc/mds578
9. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc.; 2025; Updated periodically.
10. NCCN Clinical Practice Guidelines in Oncology™. © 2025 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed April 4, 2025.
    a. Central Nervous System Cancers. V4.2024. Revised February 10, 2025.
    b. Cervical Cancer. V3.2025. Revised January 21, 2025.
    c. Head and Neck Cancers. V2.2025. Revised January 17, 2025.
    d. Mesothelioma: Peritoneal. V2.2025. Revised January 14, 2025.
    e. Non-Small Cell Lung Cancer. V3.2025. Revised January 14, 2025.
    f. Ovarian Cancer, including fallopian tube cancer and primary peritoneal cancer. V1.2025. Revised March 5, 2025.
    g. Thymomas and Thymic Carcinomas. V1.2025. Revised October 30, 2024
    h. Vaginal Cancer. V5.2025. Revised February 28, 2025.
11. Patel JD, Socinski MA, Garon EB, et al. PointBreak: a randomized phase III study of pemetrexed plus carboplatin and bevacizumab followed by maintenance pemetrexed and bevacizumab versus paclitaxel plus carboplatin and bevacizumab followed by maintenance bevacizumab in patients with stage IIIB or IV nonsquamous non-small-cell lung cancer. J Clin Oncol. 2013; 31(34):4349-4357
12. Raizer JJ, Rademaker A, Evens AM, et al. Pemetrexed in the treatment of relapsed/refractory primary central nervous system lymphoma. Cancer. 2012; 118(15):3743-3748.
13. Zhang L, Ou W, Liu Q, Li N, Liu L, Wang S. Pemetrexed plus carboplatin as adjuvant chemotherapy in patients with curative resected non-squamous non-small cell lung cancer. *Thorac Cancer*. 2014;5(1):50-56. doi:10.1111/1759-7714.12058. Available at: https://onlinelibrary.wiley.com/doi/full/10.1111/1759-7714.12058. Accessed January 11, 2021.

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.