

Pemetrexed Agents (Alimta, Pemfexy, Pemrydi)

Override(s)	Approval Duration
Prior Authorization	1 year

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

APPROVAL CRITERIA

Requests for Pemetrexed Agents (Alimta, 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 cisplatin or carboplatin **AND** bevacizumab (or bevacizumab biosimilar) (Label, NCCN 2A); **AND**
 1. Individual has an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2; **AND**
 2. Individual does not have a history of hemoptysis or thrombosis; **AND**
 3. Disease presentation is unresectable; **OR**
 - C. 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**
 - D. Individual is using as a single agent for first line systemic therapy;

OR

- II. Individual has a diagnosis of recurrent, locally advanced, or metastatic 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 as a first-line or induction therapy in combination with platinum-based chemotherapy with or without bevacizumab (or bevacizumab biosimilar) (NCCN 2A); **OR**
 - C. Individual is using as second-line therapy (first-line chemotherapy) in combination with platinum-based chemotherapy with or without bevacizumab (or bevacizumab biosimilar) if tyrosine-kinase inhibitor (TKI)/anaplastic lymphoma kinase (ALK) targeted agent was given as first-line therapy (NCCN 1); **OR**
 - D. Individual is using for maintenance therapy when disease has not progressed

- following four cycles of platinum-based, first-line therapy; **OR**
- E. 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**
 - F. 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**
 - G. Individual is using in combination with cemiplimab and platinum chemotherapy; **OR**
 - H. Individual is using in combination with tremelimumab, durvalumab, and platinum chemotherapy; **OR**
 - I. 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**
 - J. 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**
 - K. 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**
 - L. 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**
 - M. Individual is using as adjuvant or neoadjuvant therapy in combination with platinum-based chemotherapy;

OR

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

OR

- IV. Individual is using as a single-agent therapy; **AND**
- V. 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 and using as second-line therapy; **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.

***Note:** Actionable molecular markers include EGFR, ALK, ROS1, BRAF, NTRK, MET and RET mutations. The NCCN panel recommends testing prior to initiating therapy to help guide appropriate treatment. If there is insufficient tissue to allow testing for all of these markers, repeat biopsy and/or plasma testing should be done. If these are not feasible, treatment is guided by available results and, if unknown, these patients are treated as though they do not have driver oncogenes (NCCN 2A).

Pemetrexed Agents (Alimta, 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.: 2023. URL: <http://www.clinicalpharmacology.com>. Updated periodically.
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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
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10. NCCN Clinical Practice Guidelines in Oncology™. © 2022 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: <http://www.nccn.org/index.asp>.
11. Central Nervous System Cancers. V2.2022. Revised September 29, 2022.
 - a. Malignant Pleural Mesothelioma. V1.2023. Revised December 15, 2022.
 - b. Non-Small Cell Lung Cancer. V1.2023. Revised December 22, 2022.
 - c. Ovarian Cancer, including fallopian tube cancer and primary peritoneal cancer. V5.2022. Revised September 16, 2022.
 - d. Thymomas and Thymic Carcinomas. V1.2023. Revised December 15, 2022.
12. 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
13. 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.
14. 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.

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