Drug Policy:

Alimta™ or Pemfexy™ (pemetrexed)

POLICY NUMBER UM ONC_1130	**SUBJECT** Alimta™ or Pemfexy™ (pemetrexed)		**DEPT/PROGRAM** UM Dept	**PAGE 1 of 4**
DATES COMMITTEE REVIEWED 07/22/11, 01/02/13, 03/13/13, 02/12/14, 12/16/15, 06/22/16, 04/04/17, 04/12/17, 04/11/18, 04/10/19, 12/11/19, 12/19/20, 03/11/20, 06/10/20, 02/10/21, 03/10/21, 09/08/21, 11/15/21, 03/09/22, 05/11/22, 08/10/22, 11/09/22, 01/11/23, 02/14/24, 03/13/24, 10/09/24	**APPROVAL DATE** October 9, 2024	**EFFECTIVE DATE** October 25, 2024	**COMMITTEE APPROVAL DATES** 07/22/11, 01/02/13, 03/13/13, 02/12/14, 12/16/15, 06/22/16, 04/04/17, 04/12/17, 04/11/18, 04/10/19, 12/11/19, 03/11/20, 06/10/20, 02/10/21, 03/10/21, 09/08/21, 11/15/21, 03/09/22, 05/11/22, 08/10/22, 11/09/22, 01/11/23, 02/14/24, 03/13/24, 10/09/24	
PRIMARY BUSINESS OWNER: UM		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
NCQA STANDARDS UM 2		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Commercial, Exchange, Medicaid	

I. PURPOSE

To define and describe the accepted indications for Alimta or Pemfexy (pemetrexed) usage in the treatment of cancer, including FDA approved indications, and off-label indications.

Evolent is responsible for processing all medication requests from network ordering providers. Medications not authorized by Evolent may be deemed as not approvable and therefore not reimbursable.

The use of this drug must be supported by one of the following: FDA approved product labeling, CMS-approved compendia, National Comprehensive Cancer Network (NCCN), American Society of Clinical Oncology (ASCO) clinical guidelines, or peer-reviewed literature that meets the requirements of the CMS Medicare Benefit Policy Manual Chapter 15.

II. INDICATIONS FOR USE/INCLUSION CRITERIA

A. Continuation requests for a not-approvable medication shall be exempt from this Evolent policy provided:

1. The member has not experienced disease progression on the requested medication AND
2. The requested medication was used within the last year without a lapse of more than 30 days of having an active authorization AND
3. Additional medication(s) are not being added to the continuation request.

B. Malignant Pleural Mesothelioma

1. The member has malignant pleural mesothelioma and Alimta/generic pemetrexed may be used in ONE of the following:

a. In combination with cisplatin/carboplatin for stage I-IIIA clinically operable disease OR

b. In combination with Keytruda (pembrolizumab) and cisplatin/carboplatin as first-line treatment of unresectable advanced or metastatic disease OR

c. As first line therapy for unresectable or metastatic disease as a single agent or in combination with cisplatin or carboplatin with or without bevacizumab OR

d. As subsequent therapy as a single agent (if not previously used in the first line setting).

2. NOTE: Per Evolent Policy, J9304 Pemfexy (pemetrexed) is not supported for the treatment of malignant pleural Mesothelioma; This recommendation is based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) to show superior outcomes with one pemetrexed product over another.

C. Non-Small Cell Lung Cancer (NSCLC)

1. The member has recurrent or metastatic non-squamous NSCLC and Alimta or Pemfexy (pemetrexed) may be used for ANY of the following:

   a. First line therapy in combination with carboplatin/cisplatin OR

   b. First line in combination with carboplatin/cisplatin + Keytruda (pembrolizumab) for EGFR negative and ALK negative disease OR

   c. First line in combination with Rybrevant (amivantamab-vmjw) + carboplatin for EGFR exon 20 insertion mutations OR

   d. Subsequent therapy in combination with carboplatin/cisplatin OR

   e. Subsequent therapy in combination with Rybrevant (amivantamab-vmjw) + carboplatin for EGFR exon 19 deletions or exon 21 L858R substitution mutations OR

   f. Subsequent therapy as a single agent OR

   g. Maintenance therapy as a single agent after response or stable disease following first-line chemotherapy or maintenance therapy in combination with pembrolizumab following first-line therapy with [pembrolizumab + pemetrexed + cisplatin/carboplatin].

2. NOTE 1: Per Evolent Policy, the following regimens are not supported based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) demonstrating superior outcomes compared to Evolent recommended alternatives agents/regimens, including but not limited to regimens at http://pathways.newcenturyhealth.com:

   a. Bevacizumab + Carboplatin/Cisplatin + Pemetrexed followed by maintenance Bevacizumab + Pemetrexed

   b. Nivolumab + Ipilimumab + Carboplatin/Cisplatin + Pemetrexed followed by maintenance Nivolumab + Ipilimumab (for a PDL-1 expression 1% or higher)

3. NOTE 2: Per Evolent Policy, J9304 Pemfexy (pemetrexed) is not supported for the treatment of NSCLC; This recommendation is based on the lack of Level 1 Evidence (randomized clinical trial and/or meta-analyses) to show superior outcomes with one pemetrexed product over another.

III. EXCLUSION CRITERIA

A. Dosing exceeds single dose limit of Alimta or Pemfexy (pemetrexed) 500 mg/m^2.

B. Disease progression on Pemetrexed or Pemetrexed containing regimen.

C. Investigational use of Alimta or Pemfexy (pemetrexed) with an off-label indication that is not sufficient in evidence or is not generally accepted by the medical community. Sufficient evidence that is not supported by CMS recognized compendia or acceptable peer reviewed literature is defined as any of the following:

1. Whether the clinical characteristics of the patient and the cancer are adequately represented in the published evidence.
2. Whether the administered chemotherapy/biologic therapy/immune therapy/targeted therapy/other oncologic therapy regimen is adequately represented in the published evidence.
3. Whether the reported study outcomes represent clinically meaningful outcomes experienced by patients. Generally, the definition of Clinically Meaningful outcomes are those recommended by ASCO, e.g., Hazard Ratio of less than 0.80 and the recommended survival benefit for OS and PFS should be at least 3 months.
4. Whether the experimental design, in light of the drugs and conditions under investigation, is appropriate to address the investigative question. (For example, in some clinical studies, it may be unnecessary or not feasible to use randomization, double blind trials, placebos, or crossover).
5. That non-randomized clinical trials with a significant number of subjects may be a basis for supportive clinical evidence for determining accepted uses of drugs.
6. That case reports are generally considered uncontrolled and anecdotal information and do not provide adequate supportive clinical evidence for determining accepted uses of drugs.
7. That abstracts (including meeting abstracts) without the full article from the approved peer-reviewed journals lack supporting clinical evidence for determining accepted uses of drugs.

IV. MEDICATION MANAGEMENT

A. Please refer to the FDA label/package insert for details regarding these topics.

V. APPROVAL AUTHORITY

A. Review – Utilization Management Department

B. Final Approval – Utilization Management Committee

VI. ATTACHMENTS

A. None

VII. REFERENCES

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C. Passaro A, et al; MARIPOSA-2 Investigators. Amivantamab plus chemotherapy with and without lazertinib in EGFR-mutant advanced NSCLC after disease progression on osimertinib: primary results from the phase III MARIPOSA-2 study. Ann Oncol. 2024 Jan;35(1):77-90. doi: 10.1016/j.annonc.2023.10.117.

D. Zhou C, Tang KJ, et al; PAPILLON Investigators. Amivantamab plus Chemotherapy in NSCLC with *EGFR* Exon 20 Insertions. N Engl J Med. 2023 Nov 30;389(22):2039-2051. doi: 10.1056/NEJMoa2306441.

E. Alimta prescribing information. Eli Lilly and Company. Indianapolis IN 2024.

F. Pemfexy prescribing information. Eagle Pharrnaceuticals, Inc. Woodcliff Lake, NJ 2022.

G. Clinical Pharmacology Elsevier Gold Standard 2024.

H. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, CO 2024.

I. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium 2024.

J. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs . Bethesda, MD 2024.

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