Clinical Policy Bulletin: Pemetrexed (Alimta)

Number: 0687

Policy

Aetna considers pemetrexed disodium (Alimta) medically necessary for the treatment of the following:

- Non-small-cell lung cancer (NSCLC)
- As a second-line agent for thymic carcinoma and malignant thymoma
- Persistent or recurrent epithelial ovarian cancer/fallopian tube cancer/primary peritoneal cancer

Aetna considers pemetrexed experimental and investigational for any use that is not FDA approved or is not listed as an accepted off-label use in standard reference compendia.

Note: Physician administration of vitamin B-12 injections is considered medically necessary for individuals receiving pemetrexed (see CBP 536 - Vitamin B-12 Therapy).

Background

Mesothelioma refers to cancer of the mesothelium, a membrane that covers and protects most of the internal organs of the body. Mesothelioma is rare; approximately 2,000 new cases are diagnosed each year. Malignant mesothelioma is an aggressive malignancy that may be caused by environmental carcinogens (e.g., asbestos and erionite), viruses (SV40), and genetic predisposition. Malignant pleural mesothelioma is far more common than the peritoneal variants; it is a rapidly progressing malignancy with a median survival time of 6 to 9 months.

Most patients with mesothelioma are not candidates for radiation therapy or surgical treatment, and cytotoxic agents are the only options. Historically, no classes or combinations of cytotoxic agents consistently yielded response rates over 20%. Recently, pemetrexed, a new multi-targeted anti-folate that inhibits several enzymes involved in the folate pathway, has been reported to exhibit broad anti-tumor activity in clinical trials in various solid tumors, including mesothelioma, non-small cell lung, breast, cervical, colorectal, head and neck, and...
Pemetrexed (Alimta) was approved by the FDA on February 5, 2004. It is the first drug approved for mesothelioma. The recommended dose of Alimta is 500 mg/m2 administered as an intravenous infusion over 10 minutes on day 1 of each 21-day cycle. Patients must take daily doses of folic acid and vitamin B-12 to reduce the severity of side effects such as low white blood cell count, nausea, vomiting, fatigue, rash, and diarrhea.

Pemetrexed has also demonstrated clinical activity in non-small-cell lung cancer (NSCLC). In a randomized, controlled study (n = 571), Hanna et al (2004) compared the effectiveness and toxicity of pemetrexed versus docetaxel in patients with advanced NSCLC previously treated with chemotherapy. Eligible patients had a performance status 0 to 2, previous treatment with one prior chemotherapy regimen for advanced NSCLC, and adequate organ function. Patients received pemetrexed 500 mg/ m2 intravenously day 1 with vitamin B12, folic acid, and dexamethasone or docetaxel 75 mg/m2 intravenously day 1 with dexamethasone every 21 days. The primary end point was overall survival. Overall response rates were 9.1 % and 8.8 % for pemetrexed and docetaxel, respectively. Median progression-free survival was 2.9 months for each arm, and median survival time was 8.3 versus 7.9 months (p = not significant) for pemetrexed and docetaxel, respectively. The 1-year survival rate for each arm was 29.7 %. Patients receiving docetaxel were more likely to have grade 3 or 4 neutropenia (40.2 % versus 5.3 %; p < 0.001), febrile neutropenia (12.7 % versus 1.9 %; p < 0.001), neutropenia with infections (3.3 % versus 0.0 %; p = 0.004), hospitalizations for neutropenic fever (13.4 % versus 1.5 %; p < 0.001), hospitalizations due to other drug related adverse events (10.5 % versus 6.4 %; p = 0.092), use of granulocyte colony-stimulating factor support (19.2 % versus 2.6 %, p < .0001) and all grade alopecia (37.7 % versus 6.4 %; p < 0.001) compared with patients receiving pemetrexed. The authors concluded that treatment with pemetrexed resulted in clinically equivalent efficacy outcomes, but with
Pemetrexed (Alimta)

significantly fewer side effects compared with docetaxel in the second-line treatment of patients with advanced NSCLC and should be considered a standard treatment option for second-line NSCLC when available.

On August 20, 2004, the FDA approved Alimta (pemetrexed for injection) for the treatment of advanced NSCLC patients who have undergone chemotherapy. In October 2008, FDA-approved indications for Alimta were expanded to include use in combination with cisplatin, in the first-line treatment of locally-advanced and metastatic NSCLC, for patients with nonsquamous histology. According to available guidelines, pemetrexed is indicated for persons who have histological or cytological confirmation of NSCLC with stage III or IV disease not amenable to curative therapy, and who have had prior chemotherapy for advanced disease. According to these guidelines, candidates for pemetrexed should have an Eastern Cooperative Oncology Group (ECOG) performance status (PS) of 0 to 2, and have adequate bone marrow, renal and hepatic function.

The approval of Alimta in first-line advanced NSCLC for nonsquamous cell histology was based on a phase III, open-label randomized study (1,725 patients) that evaluated pemetrexed plus cisplatin (AC arm) versus gemcitabine plus cisplatin (GC arm) (Eli Lilly, 2008). The median survival was 10.3 months in the AC arm and 10.3 months in the GC arm [adjusted hazard ratio 0.94 (95% confidence interval [CI]: 0.84 to 1.05)] (Scagliotti et al, 2008). The median progression-free survival was 4.8 and 5.1 months for the AC and GC arms, respectively [adjusted hazard ratio [HR] 1.04 (95% CI: 0.94 to 1.15)]. The overall response rates were 27.1% and 24.7% for the AC and GC arms, respectively. The investigators reported that, in a pre-specified analysis, the impact of NSCLC histology on overall survival was examined. Clinically relevant differences in survival according to histology were observed. In the nonsquamous cell NSCLC subgroup, the median survival was 11.0 and 10.1 months in the AC and GC groups, respectively [unadjusted HR 0.84 (95% CI: 0.74 to 0.96)]. However, in the squamous cell histology subgroup, the median survival was 9.4 versus 10.8 months in the AC and GC groups, respectively [unadjusted HR 1.22 (95% CI: 0.99 to 1.50)]. The investigators reported that this unfavorable effect on overall survival associated with squamous cell histology observed with pemetrexed was also noted in a retrospective analysis of the single-agent trial of pemetrexed versus docetaxel in patients with stage III/IV NSCLC after prior chemotherapy (citing Peterson et al, 2007).

In a phase II study, Patel and colleagues (2009) evaluated the safety and effectiveness of pemetrexed, carboplatin, and bevacizumab followed by maintenance pemetrexed and bevacizumab in patients with chemotherapy-naive stage IIIB (effusion) or stage IV non-squamous NSCLC. Patients received pemetrexed 500 mg/m², carboplatin area under the concentration-time curve of 6, and bevacizumab 15 mg/kg every 3 weeks for 6 cycles. For patients with response or stable disease, pemetrexed and bevacizumab were continued until disease progression or unacceptable toxicity. A total of 50 patients were enrolled and received treatment. The median follow-up was 13.0 months, and the median number of treatment cycles was 7 (range of 1 to 51). Thirty patients (60%) completed greater than or equal to 6 treatment cycles, and 9 (18%) completed greater than or equal to 18 treatment cycles. Among the 49 patients assessable for response, the objective response rate was 55% (95% CI: 41% to 69%). Median progression-free and overall survival rates were 7.8 months (95% CI: 5.2 to 11.5 months) and 14.1 months (95% CI: 10.8 to 19.6 months),
respectively. The authors concluded that this regimen, involving a maintenance component, was associated with acceptable toxicity and relatively long survival in patients with advanced non-squamous NSCLC. These results justify a phase III comparison against the standard-of-care in this patient population.

Mok and Ramalingam (2009) noted that systemic chemotherapy with platinum-based regimens provides modest improvements in survival and quality of life for patients with advanced-stage NSCLC. Extended first-line chemotherapy with combination regimens for more than 4 to 6 cycles is not recommended because of cumulative toxicities and lack of proven advantage in survival with the increased duration of therapy. The early use of an anti-cancer agent as maintenance therapy after disease stabilization or maximal response with platinum-based regimens is, therefore, being recognized as a new treatment paradigm in NSCLC. Maintenance therapy can extend first-line treatment and provide an acceptable balance between efficacy and toxicity. The essential prerequisites for maintenance therapy include good tolerability, ability to administer extended cycles of therapy without cumulative toxicity, and an increase in the duration of progression-free survival (PFS). Pemetrexed has recently been shown to improve the median PFS in the maintenance setting.

On July 2, 2009, the FDA approved pemetrexed as maintenance therapy of patients with locally advanced or metastatic non-squamous NSCLC whose disease has not progressed after 4 cycles of platinum-based first-line chemotherapy. The FDA approval was based on a double-blind study of maintenance pemetrexed plus best supportive care versus placebo plus best supportive care. The study was designed to show superior PFS and overall survival (OS) of pemetrexed over placebo. The FDA-specified primary study objective was OS. Pemetrexed (500 mg/m2) was given as an intravenous infusion over 10 mins on day 1 of each 21-day cycle until disease progression. Folic acid, vitamin B12, and a corticosteroid were also given to all patients to reduce pemetrexed toxicity. There were 663 randomized patients (pemetrexed arm = 441 patients; placebo arm = 222 patients). Treatments were well-balanced with respect to the baseline disease characteristics and randomization factors. The majority of patients had ECOG Performance Status (PS) of 1 (60.2 %) and stage IV disease (80.8 %). Adenocarcinoma (49.6 %) was the predominant histologic subtype, followed by squamous cell histology (27.3 %).

The median OS for intent-to-treat (ITT) patients was 13.4 months for patients receiving pemetrexed and 10.6 months for those receiving placebo [HR of 0.79 (95 % CI: 0.65 to 0.95, p = 0.012)]. Median OS was 15.5 months versus 10.3 months for patients with non-squamous histologies receiving pemetrexed and placebo, respectively [HR of 0.70 (95 % CI: 0.56 to 0.88)]. The median OS in patients with squamous histology receiving pemetrexed was 9.9 months versus 10.8 months for those receiving placebo [HR of 1.07 (95 % CI: 0.77 to 1.50)]. A significant improvement in PFS for the ITT patient population receiving pemetrexed maintenance therapy compared to placebo was observed. The median PFS was 4.0 months for the pemetrexed-treated patients compared to 2.0 months for patients in the placebo arm [HR of 0.60 (95 % CI: 0.49 to 0.73, p < 0.00001)]. A treatment-by-histology interaction was also observed for PFS. The PFS for patients with non-squamous histologies receiving pemetrexed versus placebo was 4.4 months and 1.8 months, respectively [HR of 0.47 (95 % CI: 0.37 to 0.60)]. The PFS for pemetrexed therapy in patients with squamous cell histology was 2.4
The safety results for patients treated with pemetrexed are consistent with the known safety profile of single-agent pemetrexed previously described in product labeling. The most common (greater than 5 %) adverse reactions in patients receiving pemetrexed were hematologic toxicity, increase in hepatic enzymes, fatigue, gastrointestinal toxicity, sensory neuropathy and skin rash.

Guidelines from the National Comprehensive Cancer Network (NCCN, 2008) recommend pemetrexed or docetaxel as a second-line agent for thymoma or thymic carcinoma, in persons who have experienced disease progression either during or after first-line agents. The guidelines note that pemetrexed has been shown to be equivalent to docetaxel with less toxicity. NCCN guidelines list 6 combination chemotherapy regimens as first-line agents for thymic malignancies.

In a multi-center, phase II clinical trial, Miller and colleagues (2008) estimated the anti-tumor activity of pemetrexed in patients with advanced or recurrent carcinoma of the cervix that failed on higher priority treatment protocols and determined the nature and degree of toxicity. Pemetrexed at a dose of 900 mg/m(2) was administered as an intravenous infusion over a 10-min period every 21 days. A total of 29 patients were enrolled in this study. Two patients did not receive treatment and thus were inevaluable. A total of 128 cycles were administered with 37 % of patients receiving 6 or more cycles. The treatment was well-tolerated. More serious toxicities (grade 3 and 4) included anemia in 41 %, leukopenia in 30 %, neutropenia in 26 %, and infection in 26 %. No treatment related deaths were reported. Four patients (15 %) had partial responses with a median response duration of 4.4 months. The response rate for non-radiated or radiated disease sites was 25 % and 7 % respectively. A total of 16 patients (59 %) had stable disease and 7 (26 %) had increasing disease. Median PFS was 3.1 months and OS was 7.4 months. The authors concluded that pemetrexed at this dose and schedule showed moderate activity against advanced or recurrent cervical cancer that has failed prior chemotherapy. Data from other tumor sites has suggested synergy between pemetrexed and cisplatin and should be considered for further study.

Guidelines from the NCCN (2009) recommends the use of pemetrexed as a single agent for persons with recurrent ovarian cancer who are resistant to platinum-based chemotherapy. This recommendation was based upon clinical trial evidence that pemetrexed was active in ovarian cancer (Miller et al, 2009).

In a phase III clinical trial, Socinski et al (2009) compared pemetrexed-carboplatin with etoposide-carboplatin for the treatment of extensive-stage small-cell lung cancer (ES-SCLC). Chemotherapy-naive patients with ES-SCLC and an ECOG performance status of zero to 2 were randomly assigned to receive (i) pemetrexed-carboplatin (pemetrexed 500 mg/m(2) on day 1; carboplatin at area under the serum concentration-time curve [AUC] 5 on day 1) or (ii) etoposide-carboplatin (etoposide 100 mg/m(2) on days 1 through 3; carboplatin AUC 5 on day 1) every 3 weeks for up to 6 cycles. The primary objective of the study was non-inferiority of pemetrexed-carboplatin overall survival with a 15 % margin. Accrual was terminated with 908 of 1,820 patients enrolled after results of a planned interim analysis. In the final analysis, pemetrexed-carboplatin was inferior to etoposide-carboplatin for OS (median, 8.1 versus 10.6 months; HR,1.56; 95 % CI: 1.27 to

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and leukopenia than etoposide-carboplatin; grade 3 to 4 thrombocytopenia was comparable between arms and anemia was higher in the pemetrexed-carboplatin arm. The authors concluded that pemetrexed-carboplatin is inferior for the treatment of ES-SCLC. Planned translational research and pharmacogenomic analyses of tumor and blood samples may help explain the study results and provide insight into new treatment strategies.

In an open-label phase II study, Che et al (2010) attempted to confirm the efficacy and to assess the tolerability of a pemetrexed plus carboplatin combination in previously untreated patients with ES-SCLC. Subjects received pemetrexed 500 mg/m(2) and carboplatin (ACU of 5) every 21 days for a maximum 6 cycles. The primary endpoint for this trial was the confirmed response rate and the accrual goal was 70 patients. A total 46 eligible patients (29 aged less than 70 years, 17 aged greater than or equal to 70 years) were accrued to this study. The efficacy outcomes were similar between the 2 age groups. Overall, the confirmed response rate was 35% (16 of 46; 95% CI: 21% to 50%), where all 16 were partial responses. These results provided strong evidence that the study would not meet the preset efficacy criteria and thus this study closed before full accrual. The median duration of response was 4.4 months (95% CI: 2.9 to 5.2). Median OS for patients aged less than 70 years and aged greater than or equal to 70 years was 9.2 months (95% CI: 5.4 to 11.6) and 10.8 months (95% CI: 2.2 to 14.3), respectively. Grade 3 or higher toxicity rates were similar between the younger and older patients. Grade 3/4 and grade 4 hematological toxicities were observed in 46% and 26% of patients, respectively. The authors concluded that although well-tolerated, the combination of pemetrexed and carboplatin is not as effective as standard therapy in patients with untreated ES-SCLC.

Norris and Adamson (2010) noted that renewed interest in antifols for the treatment of childhood cancers has resulted from identification of novel antifols with broad spectrums of anti-cancer activity and from re-evaluation of the original clinical antifol, aminopterin. In this pre-clinical study, these researchers evaluated the in-vitro activity of both traditional antifols (e.g., methotrexate, aminopterin) and novel antifols (e.g., pemetrexed, talotrexin) in childhood acute leukemias and lymphomas. These researchers compared the in-vitro cytotoxicity of methotrexate, aminopterin, pemetrexed, and talotrexin in a panel of 6 pediatric leukemia and lymphoma cell lines using the sulforhodamine B assay. In addition to defining a 50% growth inhibitory concentration (IC50) for a 120-hr drug exposure, these researchers contrasted the activity of the drugs in the context of clinically achievable (tolerable) drug exposures using the area under the plasma concentration-time curve (AUC). They defined each agent's clinical potency index (CPI) as the AUC achieved with standard pediatric dosing regimens divided by the in-vitro IC50. Across all cell lines, talotrexin (median IC50 7 nM) and aminopterin (median IC50 17 nM) had lower IC50's than methotrexate (median IC50 78 nM) and pemetrexed (median IC50 155 nM). However, the CPI for methotrexate (median 0.9) was significantly greater than that for aminopterin (median 0.4). In contrast, pemetrexed had a significantly better CPI (median 13) than the traditional antifols. The authors concluded that aminopterin does not appear to offer any advantage over methotrexate for the treatment of childhood ALL. They stated that further study of pemetrexed in childhood leukemias is warranted.
In a phase I study, Abdel-Karim and colleagues (2011) examined the toxicity profile, activity, pharmacokinetics, and pharmacodynamics of pemetrexed in leukemia. Patients with refractory or relapsed acute leukemia were eligible. Pemetrexed was infused intravenously over 25 mins with vitamin B-12 supplementation. Courses were repeated every 3 to 4 weeks according to toxicity and efficacy. The starting dose of 900 mg/m² was escalated by approximately 33% until the dose-limiting toxicity (DLT) was determined. A total of 20 patients with acute myeloid (AML) or lymphocytic (ALL) leukemia received therapy. The main non-hematologic adverse event was liver dysfunction at several dose levels, including 2 DLTs at 3,600 mg/m². One patient with ALL (3,600 mg/m² dose level) achieved a partial response. Pemetrexed pharmacokinetics were linear with escalated dosing. Elevated plasma deoxyuridine was observed in a subset of patients following pemetrexed infusion, but was not correlated with dose levels. Changes in the nucleotide pools of circulating mononuclear cells were observed, but were variable. The authors concluded that recommended phase II dose of pemetrexed for future leukemia studies is intravenous 2,700 mg/m² over 25 mins every 3 to 4 weeks with vitamin B-12 supplementation. Deoxyuridine levels did not increase with increasing pemetrexed dose, suggesting pemetrexed inhibition of thymidylate synthase (TS) may be saturated by the 900 mg/m² dose level. However, no firm conclusion can be made regarding TS saturation in tumor cells. While tolerable, pemetrexed monotherapy had limited activity in this highly refractory population. These researchers noted that exploration of pemetrexed in combination with other active agents in leukemia is a reasonable future endeavor.

Guidelines from the National Comprehensive Cancer Network (2013) recommend the use of pemetrexed for the following indications:

**Bladder Cancer, Upper GU Tract Tumors, and Urothelial Carcinoma of the Prostate** - May be considered as second-line therapy as a single agent for metastatic disease

**Malignant Pleural Mesothelioma** - Induction therapy in combination with cisplatin for medically operable clinical stage I-III disease

**Malignant Pleural Mesothelioma** - Used as a single agent or in combination with cisplatin or carboplatin as

- treatment of unresectable or medically inoperable clinical stage I-III disease and tumors of epithelial or mixed histology
- treatment of resected clinical stage I-III disease in patients not treated with induction chemotherapy
- treatment of clinical stage IV disease or tumors of sarcomatoid histology.

**Malignant Pleural Mesothelioma** - Second-line treatment as a single agent

- if not administered first line
- if administered first line as rechallenge if good sustained response at the time initial chemotherapy was interrupted.

**Non-Small Cell Lung Cancer (NSCLC)** - Preoperative concurrent chemoradiation in combination with cisplatin or carboplatin for

- resectable or marginally resectable superior sulcus tumors (T3 invasion, T4 extension, N0-1)
- T3 invasion or T4 extension, N0-1 disease in the chest wall, proximal
Non-Small Cell Lung Cancer - Used in combination with cisplatin as

- neoadjuvant chemotherapy for T3 invasion or T4 extension, N0-1 disease in the chest wall, proximal airway, or mediastinum
- induction chemotherapy with or without radiation for T1-2 or T3 (7 cm or more), N2, M0.

Non-Small Cell Lung Cancer - Initial treatment as definitive concurrent chemoradiation in combination with carboplatin or cisplatin for

- medically inoperable stage I (peripheral T2a, N0), stage I (central T1ab-2a, N0), stage II (T1ab-2ab, N1 or T2b, N0), or stage IIB (T3, N0) with negative mediastinal nodes
- unresectable superior sulcus tumors (T4 extension, N0-1)
- unresectable stage IIIA (T4, N0-1)
- T1-2 or T3 (7 cm or more), N2, M0
- T3 invasion, N2, M0
- stage IIIB (T1-3, N3 positive, M0)
- contralateral or ipsilateral mediastinal node-positive stage IIIB (T4 extension, N2-3).

Non-Small Cell Lung Cancer - Adjuvant chemotherapy in combination with cisplatin

- for high-risk, margin-negative stage IB (T2a, N0) and IIA (T2b, N0)
- for margin-positive stage IB (T2a, N0) and IIA (T2b, N0)
- for margin-negative stage IIA (T2b, N0) following radiation
- for stage IIA (T1ab-2a, N1) and IIB (T3, N0; T2b, N1)
- following sequential chemoradiation for margin-positive, R1, stage IIA (T1ab-2a, N1) and IIB (T3, N0; T2b, N1)
- for margin-negative stage IIIA (T1-3, N2; T3, N1)
- following sequential chemoradiation for margin-positive, R1, stage IIIA (T1-3, N2; T3, N1)
- for resectable or marginally resectable superior sulcus tumors (T3 invasion, T4 extension, N0-1)
- for T3 invasion or T4 extension, N0-1 tumors in the chest wall, proximal airway, or mediastinum if not given as initial treatment
- following sequential chemoradiation for margin-positive, R1, T3 invasion or T4 extension, N0-1 tumors in the chest wall, proximal airway, or mediastinum if not given as initial treatment
- for T1-2, T3 7 or more cm, N2, M0 with no apparent progression or local progression
- for margin-negative separate pulmonary nodule(s) in the same lobe (T3, N0) or ipsilateral nonprimary lobe (T4, N0)
- following sequential chemoradiation for margin-positive, R1, separate pulmonary nodule(s) in the same lobe (T3, N0) or ipsilateral nonprimary lobe (T4, N0).

Non-Small Cell Lung Cancer - First-line therapy for recurrence or metastasis for tumors of nonsquamous cell histology
in combination with cisplatin or carboplatin in patients with performance status (PS) 0-2 or elderly patients
in cisplatin- or carboplatin-based regimens in combination with bevacizumab in patients with PS 0-1, tumors of nonsquamous cell histology, and no history of recent hemoptysis as a single agent in PS 2 or elderly patients.

**Non-Small Cell Lung Cancer** - Therapy for recurrence or metastasis in patients with performance status 0-2 with tumors of nonsquamous cell histology who achieve tumor response or stable disease following first-line chemotherapy as a single agent for continuation maintenance therapy if given first line with chemotherapy or in combination with bevacizumab if bevacizumab previously used with a first-line pemetrexed/platinum chemotherapy regimen a single agent for switch maintenance.

**Non-Small Cell Lung Cancer** - Therapy for recurrence or metastasis in patients with performance status 0-2 with tumors of nonsquamous cell histology who achieve tumor response or stable disease following first-line chemotherapy as a single agent for continuation maintenance therapy if given first line with chemotherapy or in combination with bevacizumab if bevacizumab previously used with a first-line pemetrexed/platinum chemotherapy regimen a single agent for switch maintenance.

**Epithelial Ovarian Cancer/Fallopian Tube Cancer/Primary Peritoneal Cancer** – Single agent therapy for persistent disease or recurrence.

**Thymomas and Thymic Carcinomas** - Second-line therapy as a single agent following radiation therapy for locally advanced unresectable disease.

**CPT Codes / HCPCS Codes / ICD-9 Codes**

**Other CPT codes related to the CPB:**

96365, 96366, 96367, 96368, 96379, 96409, 96411, 96413, 96415, 96416, 96417

**HCPCS codes covered if selection criteria are met:**

J9305 Injection, pemetrexed, 10 mg

**ICD-9 codes covered if selection criteria are met:**

For Mesothelioma (malignant) - see Neoplasm, by site, malignant

158.8 - 158.9 Malignant neoplasm of peritoneum [persistent or recurrent]
162.0 - 162.9  Malignant neoplasm of trachea, bronchus, and lung [non-cell lung cancer (NSCLC) only- not small cell lung cancer]

163.0 - 163.9  Malignant neoplasm of pleura

164.0  Malignant neoplasm of thymus [thymic carcinoma]

183.0  Malignant neoplasm of the ovary [persistent or recurrent]

183.2  Malignant neoplasm of fallopian tube [persistent or recurrent]

185  Malignant neoplasm of prostate

188.0 - 188.9  Malignant neoplasm of bladder

189.2 - 189.3  Malignant neoplasm of ureter or urethra

200.50 - 200.58  Primary central nervous system lymphoma [progressive or recurrent]

ICD-9 codes not covered for indications listed in the CPB (not all-inclusive):

140.0 - 158.0, 159.1 - 161.9, 164.1 - 179, 180 - 182.8, 183.3 - 187.9, 189.0 - 189.1, 189.3- 209.79

Lymphoid leukemia, acute

Myeloid leukemia, acute

Other ICD-9 codes related to the CPB:

501  Asbestosis

V84.09  Genetic susceptibility to other malignant neoplasm

The above policy is based on the following references:

Pemetrexed for Mesothelioma:


Pemetrexed for Non-Small-Cell Lung Cancer and Thymic Malignancies:


Pemetrexed for Other Types of Cancer:


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