AXTLE®
(pemetrexed) for Injection

Ordering Information

To order AXTLE (pemetrexed) for Injection, please contact one of these authorized specialty distributors and use the appropriate order number:

100 mg/vial
NDC: 83831-0131-01

500 mg/vial
NDC: 83831-0132-01

Institutions/Hospitals	100 mg/vial	500 mg/vial
Cardinal Health Specialty	5962121	5962139
CENCORA - ASD Healthcare	10295451	10295442
McKesson Plasma & Biologics	3005485	3005410
Physician Office	**100 mg/vial**	**500 mg/vial**
Cardinal Health Specialty	5962121	5962139
Oncology Supply	10295426	10295460
McKesson Specialty Health	5019191	5019190

Highlights[1]

- Available as pemetrexed dipotassium
- Free from preservative
- Reconstitute with 5% Dextrose Injection, USP (preservative-free) or 0.9% Sodium Chloride Injection, USP (preservative-free)
- Not made with natural rubber latex
- Unique J-Code: J9292

UNIQUE
J-CODE
J9292

INDICATIONS AND IMPORTANT SAFETY INFORMATION

INDICATIONS

Non-Squamous Non-Small Cell Lung Cancer (NSCLC)

AXTLE® (pemetrexed) for injection is indicated:

- in combination with pembrolizumab and platinum chemotherapy, for the initial treatment of patients with metastatic non-squamous non-small cell lung cancer (NSCLC), with no EGFR 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: AXTLE is not indicated for the treatment of patients with squamous cell, non-small cell lung cancer.

Mesothelioma

AXTLE is indicated, 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.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATION

AXTLE is contraindicated in patients with a history of severe hypersensitivity reaction to pemetrexed.

WARNINGS AND PRECAUTIONS

Myelosuppression and Increased Risk of Myelosuppression without Vitamin Supplementation

AXTLE can cause severe myelosuppression resulting in a requirement for transfusions and which may lead to neutropenic infection. The risk of myelosuppression is increased in patients who do not receive vitamin supplementation. In Study JMCH, incidences of Grade 3-4 neutropenia (38% versus 23%), thrombocytopenia (9% versus 5%), febrile neutropenia (9% versus 0.6%), and neutropenic infection (6% versus 0) were higher in patients who received pemetrexed plus cisplatin without vitamin supplementation as compared to patients who were fully supplemented with folic acid and vitamin B_{12} prior to and throughout pemetrexed plus cisplatin treatment.

Initiate supplementation with oral folic acid and intramuscular vitamin B_{12} prior to the first dose of AXTLE; continue vitamin supplementation during treatment and for 21 days after the last dose of AXTLE to reduce the severity of hematologic and gastrointestinal toxicity of AXTLE. Obtain a complete blood count at the beginning of each cycle. Do not administer AXTLE until the ANC is at least 1500 cells/mm^3 and platelet count is at least 100,000 cells/mm^3. Permanently reduce AXTLE in patients with an ANC of less than 500 cells/mm^3 or platelet count of less than 50,000 cells/mm^3 in previous cycles.

In Studies JMDB and JMCH, among patients who received vitamin supplementation, incidence of Grade 3-4 neutropenia was 15% and 23%, the incidence of Grade 3-4 anemia was 6% and 4%, and incidence of Grade 3-4 thrombocytopenia was 4% and 5%, respectively. In Study JMCH, 18% of patients in the pemetrexed arm required red blood cell transfusions compared to 7% of patients in the cisplatin arm. In Studies JMEN, PARAMOUNT, and JMEI, where all patients received vitamin supplementation, incidence of Grade 3-4 neutropenia ranged from 3% to 5%, and incidence of Grade 3-4 anemia ranged from 3% to 5%.

Please see full Prescribing Information for AXTLE.

IMPORTANT SAFETY INFORMATION (CONTINUED)

Renal Failure

AXTLE can cause severe, and sometimes fatal, renal toxicity. The incidences of renal failure in clinical studies in which patients received pemetrexed with cisplatin were: 2.1% in Study JMDB and 2.2% in Study JMCH. The incidence of renal failure in clinical studies in which patients received pemetrexed as a single agent ranged from 0.4% to 0.6% (Studies JMEN, PARAMOUNT, and JMEI). Determine creatinine clearance before each dose and periodically monitor renal function during treatment with AXTLE. Withhold AXTLE in patients with a creatinine clearance of less than 45 mL/minute.

Bullous and Exfoliative Skin Toxicity

Serious and sometimes fatal, bullous, blistering and exfoliative skin toxicity, including cases suggestive of Stevens-Johnson Syndrome/Toxic epidermal necrolysis can occur with AXTLE. Permanently discontinue AXTLE for severe and life-threatening bullous, blistering or exfoliating skin toxicity.

Interstitial Pneumonitis

Serious interstitial pneumonitis, including fatal cases, can occur with AXTLE treatment. Withhold AXTLE for acute onset of new or progressive unexplained pulmonary symptoms such as dyspnea, cough, or fever pending diagnostic evaluation. If pneumonitis is confirmed, permanently discontinue AXTLE.

Radiation Recall

Radiation recall can occur with AXTLE in patients who have received radiation weeks to years previously. Monitor patients for inflammation or blistering in areas of previous radiation treatment. Permanently discontinue AXTLE for signs of radiation recall.

Increased Risk of Toxicity with Ibuprofen in Patients with Renal Impairment

Exposure to pemetrexed is increased in patients with mild to moderate renal impairment who take concomitant ibuprofen, increasing the risks of adverse reactions of AXTLE. In patients with creatinine clearances between 45 mL/min and 79 mL/min, avoid administration of ibuprofen for 2 days before, the day of, and 2 days following administration of AXTLE™. If concomitant ibuprofen use cannot be avoided, monitor patients more frequently for pemetrexed adverse reactions, including myelosuppression, renal, and gastrointestinal toxicity.

Embryo-Fetal Toxicity

Based on findings from animal studies and its mechanism of action, AXTLE can cause fetal harm when administered to a pregnant woman. Advise pregnant women of the potential risk to a fetus. Advise females of reproductive potential to use effective contraception during treatment with AXTLE and for 6 months after the last dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with AXTLE and for 3 months after the last dose.

IMPORTANT SAFETY INFORMATION (CONTINUED)

ADVERSE REACTIONS

- The most common adverse reactions (incidence ≥20%) of pemetrexed, when administered as a single agent are fatigue, nausea, and anorexia.
- The most common adverse reactions (incidence ≥20%) of pemetrexed when administered with cisplatin are vomiting, neutropenia, anemia, stomatitis/pharyngitis, thrombocytopenia, and constipation.
- The most common adverse reactions (incidence ≥20%) of pemetrexed when administered in combination with pembrolizumab and platinum chemotherapy are fatigue/asthenia, nausea, constipation, diarrhea, decreased appetite, rash, vomiting, cough, dyspnea, and pyrexia.

DRUG INTERACTIONS

Effects of Ibuprofen on Pemetrexed

Ibuprofen increases exposure (AUC) of pemetrexed. In patients with creatinine clearance between 45 mL/min and 79 mL/min:

- Avoid administration of ibuprofen for 2 days before, the day of, and 2 days following administration of AXTLE.
- Monitor patients more frequently for myelosuppression, renal, and gastrointestinal toxicity, if concomitant administration of ibuprofen cannot be avoided.

USE IN SPECIFIC POPULATIONS

Pregnancy

Advise pregnant women of the potential risk to a fetus.

Lactation

Advise women not to breastfeed during treatment with AXTLE and for one week after the last dose.

Females and Males of Reproductive Potential

Verify pregnancy status of females of reproductive potential prior to initiating AXTLE.

Because of the potential for genotoxicity, advise females of reproductive potential to use effective contraception during treatment with AXTLE and for 6 months after the last dose; and advise males with female partners of reproductive potential to use effective contraception during treatment with AXTLE and for 3 months after the last dose.

AXTLE may impair fertility in males of reproductive potential.

Pediatric Use

The safety and effectiveness of AXTLE in pediatric patients have not been established.

Geriatric Use

The incidences of Grade 3-4 anemia, fatigue, thrombocytopenia, hypertension, and neutropenia were higher in patients 65 years of age and older as compared to younger patients in at least one of five randomized clinical trials.

Patients with Renal Impairment

Pemetrexed is primarily excreted by the kidneys. Decreased renal function results in reduced clearance and greater exposure (AUC) to pemetrexed compared with patients with normal renal function. No dose is recommended for patients with creatinine clearance less than 45 mL/min.

IMPORTANT SAFETY INFORMATION (CONTINUED)

OVERDOSAGE

No drugs are approved for the treatment of pemetrexed overdose.

Please see full Prescribing Information of AXTLE.

To report SUSPECTED ADVERSE REACTIONS, contact Avyxa Pharma, LLC at 1-888-520-0954 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.