UNI-LAB

PEMETREXED Trexed®

100 mg & 100 mg Lyophilized Powder for Injection for I.V. infusion

Antineoplastic (Folic Acid Analogue)

FORMULATION

PEMETREXED 100 mg

Each vial contains PEMETREXED 100 mg

eq. to PEMETREXED .... 100 mg or 100 mg

PHARMACODYNAMICS

PEMETREXED PEMETREXED is an anti-cancer lyophilized powder

PHARMACOKINETICS

Non- Small Cell Lung Cancer Combination with Cisplatin

Pemetrexed is rapidly and extensively distributed in tissues. Binding to the other treatment of patients with locally advanced or metastatic nonsquamous non- small cell lung cancer PEMETREXED is moderate (about 81% bound to plasma proteins) in patients with impaired renal function.

Non- Small Cell Lung Cancer (Unlabeled)

Pemetrexed is rapidly and extensively distributed in the treatment of patients with locally advanced or metastatic nonsquamous non- small cell lung cancer PEMETREXED is moderate (about 81% bound to plasma proteins) in patients with impaired renal function.

DOSAGE AND ADMINISTRATION

Non- Small Cell Lung Cancer

Recommended Dosage of PEMETREXED is 500 mg/m² administered as an intravenous infusion over 10 minutes on day 1 of each 21-day cycle. The recommended dose of PEMETREXED is 500 mg/m² administered as an intravenous infusion over 10 minutes on Day 1 of each 21-day cycle. The recommended dose of folic acid is 350 µg to 1 mg administered orally once daily for 7 days beginning 2 days before the first dose of PEMETREXED. Patients should receive a prophylactic dose of dexamethasone (or equivalent) the day before, the day of, and the day after PEMETREXED administration. The patient must be premedicated with a vitamin B12 intramuscular dose (1 mg) within 10 weeks before the first dose of PEMETREXED. The patient must be premedicated with a vitamin B12 intramuscular dose (1 mg) within 10 weeks before the first dose of PEMETREXED. Patients must also receive oral 12 dexamethasone tablets (4 mg) the day before, the day of, and the day after PEMETREXED administration. Folic acid 350 µg to 1 mg, and the dose of vitamin B12, 1 mg, IM. The first patients' cycle dose of folic acid is 350 µg and the dose of vitamin B12 is 1 mg.

Dosage Adjustment

Dose should be adjusted for patients who have creatinine clearance of less than 45 ml/min or creatinine. Pretreatment with dexamethasone (or equivalent) reduces the incidence and severity of skin reactions. In clinical trials, dexamethasone 4 mg orally given twice daily the day before, the day of, and the day after PEMETREXED administration.

Laboratory Monitoring and Dose Modification Recommendations Pemetrexed Monotherapy

Monitoring

Hematological counts, including platelet counts, should be performed on all patients receiving PEMETREXED. Patients should be monitored for nadir and recovery, which occurred in this study within about one week after the drug administration. Patients should not begin a new cycle of treatment unless the ANC is 1500 cells/mm³, the platelet count is 100,000 cells/mm³ and creatinine clearance is 45 ml/min. Periodic chemistry tests including liver function should be performed.

Dose Modifications

Hematologic Toxicity

Any Grade 3 or 4 hematologic toxicity recommended dose reduction by 25% in subsequent cycles. Hematologic toxicity should be delayed, given the following hematologic toxicity: Hemoglobin (Grade 3 or 4 anemia) ..... 75% of previous dose, Grade 3 or 4 neutropenia ..... 50% of previous dose, Grade 3 or 4 thrombocytopenia ..... 50% of previous dose

Grade 3 Non-hematologic Toxicity

Discontinuing treatment after Grade 3 or 4 non-hematologic toxicity, for which no dose reduction is needed.

Dose Modifications for Pemetrexed Combination Therapy with Cisplatin

Dose Modifications for Pemetrexed Combination Therapy with Cisplatin and Leucovorin Recommended Dose Modifications Grade 3 Toxicity

Grade 3 Toxicities Recommended Dose Modifications Grade 3 Toxicities

Neutropenia ..... 50% of previous dose

Thrombocytopenia ..... 50% of previous dose

Diarrhea ..... 50% of previous dose

Stomatitis ..... 50% of previous dose

Other ..... 50% of previous dose

Dose Modifications for Pemetrexed Monotherapy

Dose Modifications for Pemetrexed Monotherapy Grade 3 or 4 Toxicities Grade 3 or 4 Toxicities

Neutropenia ..... 50% of previous dose

Thrombocytopenia ..... 50% of previous dose

Diarrhea ..... 50% of previous dose

Stomatitis ..... 50% of previous dose

Other ..... 50% of previous dose

Dose Modifications for Pemetrexed Combination Therapy with Cisplatin

Dose Modifications for Pemetrexed Combination Therapy with Cisplatin Grade 3 or 4 Toxicities Grade 3 or 4 Toxicities

Neutropenia ..... 50% of previous dose

Thrombocytopenia ..... 50% of previous dose

Diarrhea ..... 50% of previous dose

Stomatitis ..... 50% of previous dose

Other ..... 50% of previous dose

Cisplatin Dose Modifications

Cisplatin Dose Modifications Grade 3 or 4 Toxicities Grade 3 or 4 Toxicities

Neutropenia ..... 50% of previous dose

Thrombocytopenia ..... 50% of previous dose

Diarrhea ..... 50% of previous dose

Stomatitis ..... 50% of previous dose

Other ..... 50% of previous dose

Folic Acid Dose Modifications

Folic Acid