

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Fludarabine Phosphate Injection safely and effectively. See full prescribing information for Fludarabine Phosphate Injection.

Fludarabine Phosphate Injection

WARNING: CNS TOXICITY, HEMOLYTIC ANEMIA, AND PULMONARY TOXICITY

See full prescribing information for complete boxed warning.

- Severe central nervous system toxicity occurred in 36% of patients treated with doses approximately four times greater (96 mg/m²/day for 5 to 7 days) than the recommended dose. This toxicity was seen in <0.2% of patients treated at the recommended dose levels (25 mg/m²). (5.1)
- Instances of life-threatening and sometimes fatal autoimmune hemolytic anemia have been reported after one or more cycles of treatment. (5.2)
- In a clinical investigation of the combination of fludarabine phosphate with pentostatin (deoxycoformycin) for the treatment of refractory chronic lymphocytic leukemia (CLL), there was an unacceptably high incidence of fatal pulmonary toxicity. (5.6)

INDICATIONS AND USAGE

Fludarabine Phosphate Injection is a nucleotide metabolic inhibitor indicated for:

- The treatment of adult patients with B-cell chronic lymphocytic leukemia (CLL) who have not responded to or whose disease has progressed during treatment with at least one standard alkylating-agent containing regimen. Benefit in treatment-naïve or non-refractory CLL patients is not established. (1.1)

Important limitations:

- Fludarabine phosphate should not be used in patients with severe renal impairment (creatinine clearance less than 30 mL/min/1.73 m²). (5.7)

DOSAGE AND ADMINISTRATION

Chronic Lymphocytic Leukemia (CLL) (2.1):

- The recommended adult dose is 25 mg/m² administered intravenously over a period of approximately 30 minutes daily for five consecutive days.
- Each 5 day course of treatment should commence every 28 days.

Renal Insufficiency (2.2):

- Adult patients with moderate impairment of renal function (creatinine clearance 30 to 70 mL/min/1.73 m²) should have 20% dose reduction.
- Not indicated in patients with severe renal impairment.

Use of Infusion Solutions (2.3):

- Fludarabine Phosphate Injection contains no antimicrobial preservative and should be used within 8 hours of opening. Care must be taken to assure sterility of infusion solutions. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

DOSAGE FORMS AND STRENGTHS

- A 50 mg/2 mL (25 mg/mL), clear, colorless to almost colorless, sterile solution intended for intravenous administration.

CONTRAINDICATIONS

- None

WARNINGS AND PRECAUTIONS

- Severe bone marrow suppression, notably anemia, thrombocytopenia and neutropenia. Monitor blood counts before and during treatment. (5.2)
- Transfusion-associated graft-versus-host disease. Use only irradiated blood products for transfusions. (5.5)
- Infections. Monitor for infection. (5.3)
- Renal Insufficiency. Reduce dose for moderate renal impairment and monitor closely. Do not administer to patients with severe renal impairment. (5.7)
- Tumor lysis syndrome (TLS). Take precautions for patients at high risk for TLS. (5.4)
- May cause fetal harm when administered to a pregnant woman. Women should be advised to avoid becoming pregnant. (5.9)

ADVERSE REACTIONS

Most common adverse reactions (incidence > 30%) include myelosuppression (neutropenia, thrombocytopenia and anemia), fever, infection, nausea and vomiting, fatigue, anorexia, cough and weakness (6).

To report SUSPECTED ADVERSE REACTIONS, contact Parenta Pharmaceuticals at 1-800-898-9948 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

DRUG INTERACTIONS

- Fludarabine Phosphate Injection in combination with pentostatin is not recommended due to the risk of severe pulmonary toxicity (5.6 and 7.1).

USE IN SPECIFIC POPULATIONS

- Renal clearance represents approximately 40% of the total body clearance. Patients with moderate renal impairment (17 to 41 mL/min/m²) receiving 20% reduced fludarabine phosphate dose had a similar exposure (AUC; 21 versus 20 nM•h/mL) compared to patients with normal renal function receiving the recommended dose (2.2, 5.7 and 8.6)

For Full Prescribing Information and Patient Counseling Information please visit www.parentarx.com.

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