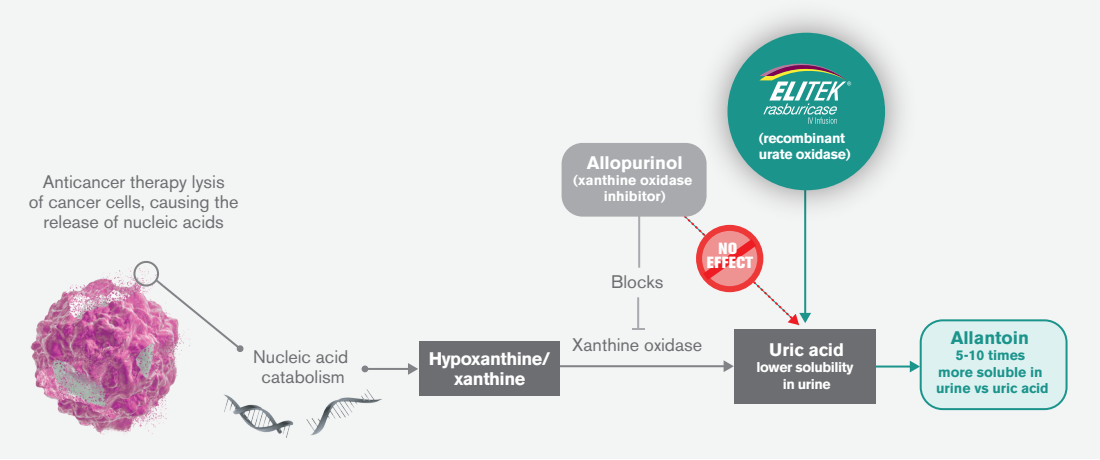
ELITEK® rasburicase IV Infusion

MECHANISM OF ACTION

ELITEK is the only antihyperuricemic agent that has the mechanism to clear existing uric acid[1,2]

- Allopurinol blocks the formation of new uric acid but has no mechanism to clear uric acid



Consider ELITEK as your preferred choice for clearing both existing and newly formed uric acid[1]

ELITEK is indicated for the initial management of plasma uric acid levels in patients with leukemia, lymphoma, and solid tumor malignancies who are receiving anticancer therapy expected to result in tumor lysis and subsequent elevation of plasma uric acid. ELITEK is indicated only for a single course of treatment.

Important Safety Information

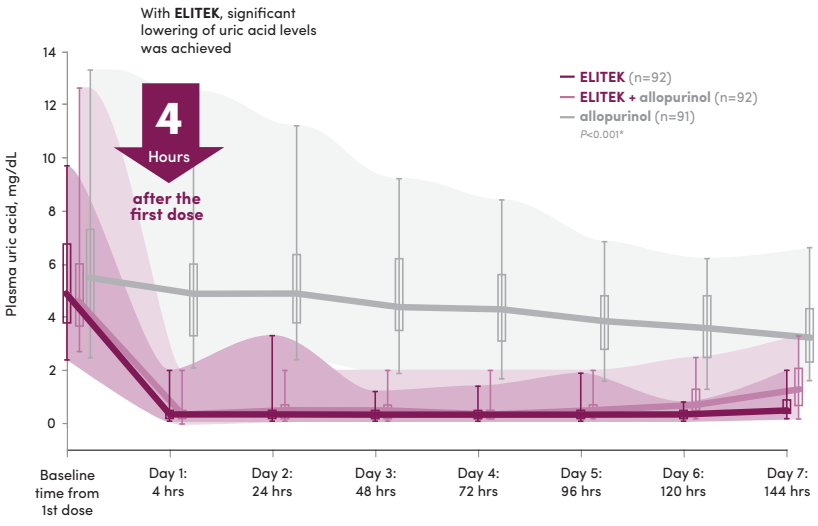
WARNING: HYPERSENSITIVITY REACTIONS, HEMOLYSIS, METHEMOGLOBINEMIA, AND INTERFERENCE WITH URIC ACID MEASUREMENTS

- **Hypersensitivity Reactions: ELITEK can cause serious and fatal hypersensitivity reactions including anaphylaxis. Immediately and permanently discontinue ELITEK in patients who experience a serious hypersensitivity reaction.**
- **Hemolysis: Do not administer ELITEK to patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Immediately and permanently discontinue ELITEK in patients developing hemolysis. Screen patients at higher risk for G6PD deficiency (e.g., patients of African or Mediterranean ancestry) prior to starting ELITEK.**
- **Methemoglobinemia: ELITEK can result in methemoglobinemia in some patients. Immediately and permanently discontinue ELITEK in patients developing methemoglobinemia.**
- **Interference with Uric Acid Measurements: ELITEK enzymatically degrades uric acid in blood samples left at room temperature. Collect blood samples in prechilled tubes containing heparin and immediately immerse and maintain sample in an ice water bath. Assay plasma samples within 4 hours of collection.**

Please see additional Important Safety Information throughout, and accompanying full Prescribing Information, including Boxed WARNING.

ELITEK SIGNIFICANTLY AND RAPIDLY LOWERED URIC ACID LEVELS COMPARED WITH ALLOPURINOL

96% of ELITEK adult patients (N=275) achieved uric acid levels ≤2 mg/dL within 4 hours after their first dose vs 0% with allopurinol[3,4]



*Plasma uric acid AUC from Day 1 through Day 7 was significantly lower for ELITEK and ELITEK + allopurinol than for allopurinol alone ($P<0.001$).[3]

Study design: Phase 3, randomized, multicenter, open-label, 3-arm study in 275 patients with leukemia, lymphoma, and solid tumor malignancies at risk for hyperuricemia and TLS. Patients were randomized 1:1:1 to 1 of 3 arms. Patients in Arm A received ELITEK 0.2 mg/kg/d for 5 days (n=92). Patients in Arm B received ELITEK from Day 1 through Day 3, followed by oral allopurinol from Day 3 through Day 5 (overlap on Day 3: ELITEK 0.2 mg/kg/d and allopurinol 300 mg/d administered approximately 12 hours apart) (n=92). Patients in Arm C received oral allopurinol 300 mg/d for 5 days (n=91). Anticancer therapy was initiated 4 to 24 hours after the first antihyperuricemic dose in each arm.[3,4]

Primary endpoint: Response rate defined as the proportion of patients with plasmic uric acid levels maintained at ≤7.5 mg/dL between 3 and 7 days after initiation of antihyperuricemic treatment.[4]

87% of patients receiving ELITEK prophylactically maintained uric acid levels ≤7.5 mg/dL vs 66% of patients receiving allopurinol ($P=0.001$). ELITEK + allopurinol maintained normal uric acid in 78% of patients (P=NS vs allopurinol).[3]

The difference in the mechanism of action of ELITEK vs allopurinol contributes to more rapid uric acid reduction[1,3,4]

Per-patient incidence of selected adverse reactions by study arm in Study 4: All Grades ARs in Study 4 (ELITEK alone; ELITEK plus oral allopurinol; oral allopurinol alone) were nausea (57.6%, 60.9%, 54.9%), peripheral edema (50%, 43.5%, 42.9%), vomiting (38%, 37%, 30.8%), anxiety (23.9%, 17.4%, 17.6%), abdominal pain (21.7%, 33.7%, 25.3%), hypophosphatemia (17.4%, 22.8%, 16.5%), hyperbilirubinemia (16.3%, 14.1%, 7.7%), pharyngolaryngeal pain (14.1%, 20.7%, 9.9%), sepsis (12%, 7.6%, 4.4%), fluid overload (12%, 6.5%, 3.3%), increased ALT (10.9%, 27.2%, 17.6%), and hyperphosphatemia (9.8%, 15.2%, 8.8%).[4]

ALT=alanine aminotransferase; AR=adverse reaction.

Important Safety Information (cont'd)

CONTRAINDICATIONS

ELITEK is contraindicated in patients with a history of anaphylaxis or severe hypersensitivity to rasburicase or in patients with development of hemolytic reactions or methemoglobinemia with rasburicase. ELITEK is contraindicated in individuals deficient in glucose-6-phosphate dehydrogenase (G6PD).

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥20%), when used concomitantly with anticancer therapy, are vomiting, nausea, fever, peripheral edema, anxiety, headache, abdominal pain, constipation, diarrhea, hypophosphatemia, pharyngolaryngeal pain, and increased alanine aminotransferase.

USE IN SPECIFIC POPULATIONS

- **Pregnancy:** Consider the benefits and risks of ELITEK and possible risks to the fetus when prescribing ELITEK to a pregnant woman
- **Lactation:** Because of the potential for serious adverse reactions in the breastfed child, advise patients that breastfeeding is not recommended during treatment with ELITEK and for 2 weeks after the last dose

Please see accompanying full Prescribing Information, including Boxed WARNING.

References: 1. Ueng S. Rasburicase (Elitek): a novel agent for tumor lysis syndrome. *Proc (Bayl Univ Med Cent).* 2005;18:(3)275-279. **2.** Coiffier B, Altman A, Pui CH, Younes A, Cairo MS. Guidelines for the management of pediatric and adult tumor lysis syndrome: an evidence-based review. *J Clin Oncol.* 2008;28(16):2767-2778. **3.** Cortes J, Moore JO, Maziarz RT, et al. Control of plasma uric acid in adults at risk for tumor lysis syndrome: efficacy and safety of rasburicase alone and rasburicase followed by allopurinol compared with allopurinol alone–results of a multicenter phase III study. *J Clin Oncol.* 2010;28(27):4207-4213. **4.** ELITEK [prescribing information]. Bridgewater, NJ: sanofi-aventis U.S. LLC.

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