ELITEK® rasburicase IV Infusion

20 YEARS OF POWERFUL PROTECTION

Assessing your patients' risk for **tumor lysis syndrome (TLS)**

Know what to look for in patients receiving treatment for hematologic malignancies

Scan to use an interactive tool for **assessing TLS risk or visit TLSrisk.com**

INDICATION

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

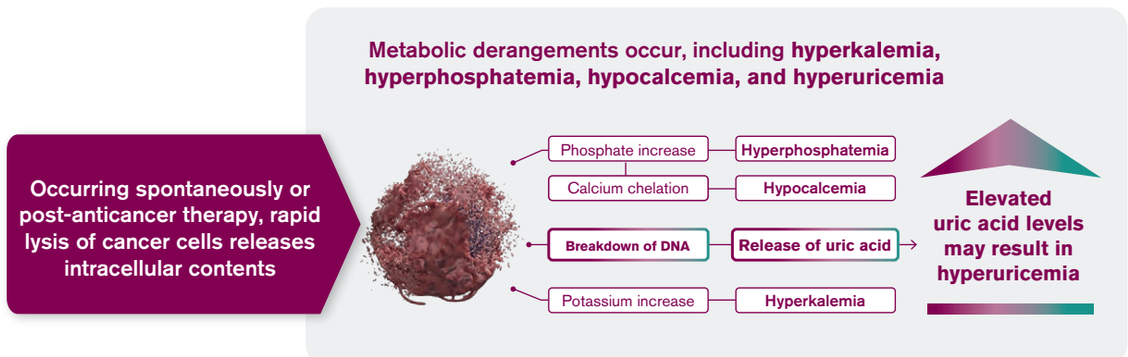
WARNING: HYPERSENSITIVITY REACTIONS, HEMOLYSIS, METHEMOGLOBINEMIA, AND INTERFERENCE WITH URIC ACID MEASUREMENTS

- **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 Important Safety Information throughout, and accompanying full Prescribing Information including Boxed WARNING.

TLS is a common oncologic emergency with **potentially devastating consequences**

TLS is caused by a massive release of intracellular contents into peripheral blood that results in metabolic derangements[1-3]



Untreated TLS may progress to cause acute renal failure, cardiac arrhythmias, loss of muscle control, seizures, or death[3]

TLS is the most common disease-related emergency in hematologic cancers[2]

37% **Incidence of TLS per year from 2010 to 2014[4]**

- In a retrospective analysis, a total of 15,051 cases of TLS were identified among 40,494 patients with hematologic malignancies during this period[4]
- Based on data from the National Inpatient Sample database, the largest publicly available, all-payer inpatient database[4]

Identifying patients at risk may reduce the impact of TLS[3,5]

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).

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

Know what to look for to **help identify patients at risk for TLS**

Patients are at increased risk for TLS if they present with one or more of the following diagnostic criteria[6-15]:

Laboratory risk[6,7]

- Baseline uric acid >7.5 mg/dL
- Baseline creatinine >1.4 mg/dL*
- LDH ≥2x ULN
- Elevated WBC count

Malignancy risk[6]

Patients with (but not limited to) these hematologic malignancies may be at risk for TLS:

- ALL
- MM
- BL
- DLBCL
- CML
- AML
- CLL

Anticancer therapy risk[8-15]

Many anticancer therapies increase the risk for hyperuricemia and TLS. These include, but are not limited to:

- Venetoclax
- Obinutuzumab
- R-CHOP†
- Ibrutinib

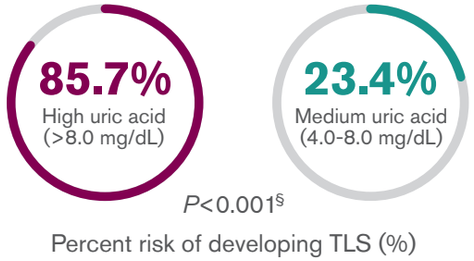
Tumor burden and other risk factors[6,7]

- High tumor burden
- Bulky disease
- Renal disease or renal involvement

This is not a complete list of potential risk factors for TLS.

Patients with high uric acid levels (>8.0 mg/dL) are at high risk of developing TLS[16]

Relationship between uric acid level and development of TLS[16‡]



Even patients with normal uric acid levels may be at significant risk[16]

- Patients with a 25% increase in uric acid from baseline are also at high risk of developing TLS[1]

Preventing a rise in uric acid is essential for protecting patients against TLS associated with hyperuricemia[16]

*Indicator of renal impairment.
†R=rituximab, C=cyclophosphamide, H=doxorubicin hydrochloride (hydroxydaunomycin), O=vincristine sulfate (Oncovin®), P=prednisone.
‡Results are from a retrospective analysis conducted to determine the relationship between uric acid levels and TLS in 1198 patients with a hematologic malignancy who were admitted for inpatient chemotherapy.[16]
§Medium vs high uric acid level.[16]

ALL=acute lymphoblastic leukemia; AML=acute myeloid leukemia; BL=Burkitt lymphoma; CLL=chronic lymphocytic leukemia; CML=chronic myeloid leukemia; DLBCL=diffuse large B-cell lymphoma; LDH=lactate dehydrogenase; MM=multiple myeloma; ULN=upper limit of normal; WBC=white blood cell.

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ELITEK is the only antihyperuricemic agent that has the **mechanism to clear new and existing uric acid**

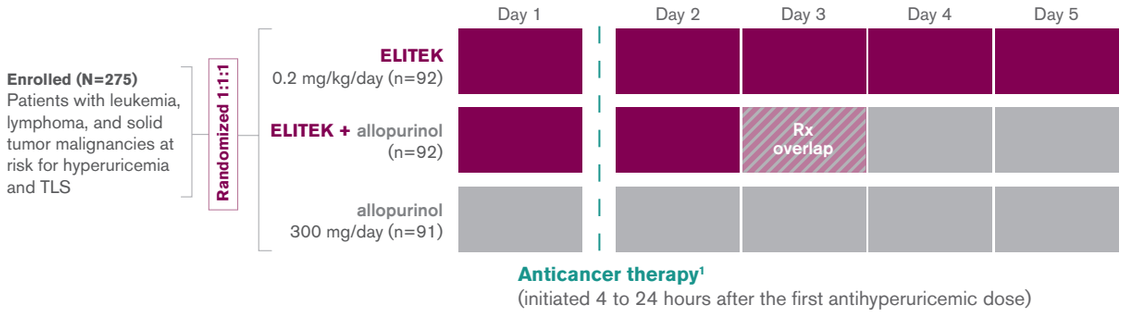
Mechanism of action: ELITEK vs allopurinol[5,17]

Unlike allopurinol, which only blocks the formation of new uric acid, ELITEK has the mechanism to rapidly lower new and existing uric acid[17]

Prophylactic use of ELITEK was proven to prevent rising uric acid levels in a head-to-head trial against allopurinol[1,18]

Antihyperuricemic therapy was initiated prior to anticancer therapy in all 3 arms[1,18]

Pivotal trial design: phase 3, randomized, multicenter, open-label study[1,18]



Primary endpoint: Response rate defined as the proportion of adult patients with plasmic uric acid levels maintained at ≤7.5 mg/dL between 3 and 7 days after initiation of antihyperuricemic treatment. 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 levels in 78% of patients (*P*=not significant vs allopurinol).[1]

IMPORTANT SAFETY INFORMATION (cont'd)

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.

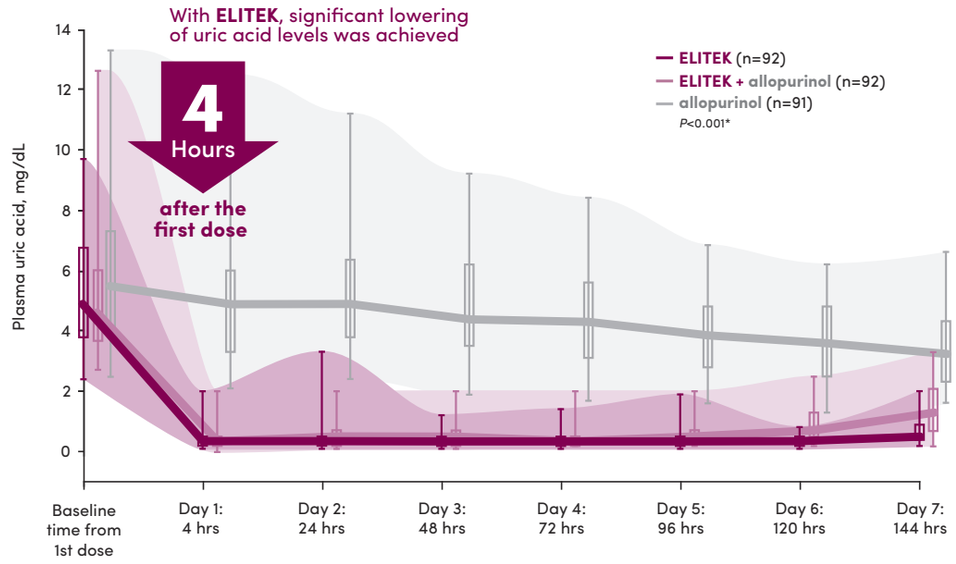
Please see Important Safety Information throughout, and accompanying full Prescribing Information including Boxed WARNING.

Unlike allopurinol, ELITEK maintained normal uric acid levels in 100% of assessable adult patients

Documented failure rate in hyperuricemic and nonhyperuricemic adult patients[18]

- The ELITEK, ELITEK + allopurinol, and allopurinol arms had 13%, 15%, and 19% missing uric acid samples, respectively. The uric acid failure status in those patients is unknown[18]
- 18% of adult patients (n=275) were hyperuricemic (>7.5 mg/dL) at baseline and therefore considered at high risk of developing TLS[1]

96% of adult patients who received ELITEK achieved uric acid levels ≤2 mg/dL within 4 hours after their first dose vs 0% with allopurinol[1,18]



*Plasma uric acid area under the curve from Day 1 through Day 7 was significantly lower for ELITEK and ELITEK + allopurinol than for allopurinol alone.[1]

Per-patient incidence of selected adverse reactions in Study 4[18]

All-grade adverse reactions 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 alanine aminotransferase (10.9%, 27.2%, 17.6%), and hyperphosphatemia (9.8%, 15.2%, 8.8%).

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Help protect patients by **effectively assessing their risk for TLS**

The following factors can help identify a patient at risk for TLS:

- Baseline uric acid >7.5 mg/dL and/or a 25% increase in baseline uric acid[1,6]
- Patients on certain anticancer therapies, including venetoclax and R-CHOP[8-13]
- Bulky disease, high tumor burden, and other patient risk factors[6,7]

Preventing a rise in uric acid is essential to protecting patients from TLS associated with hyperuricemia[16]

Want additional resources about ELITEK and the risk of TLS?

Scan or visit ELITEKPro.com to **access additional resources**

Scan to use an interactive tool for **assessing TLS risk or visit TLSrisk.com**

IMPORTANT SAFETY INFORMATION (cont'd)

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

References: 1. 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. **2.** Howard SC, Jones DP, Pui CH. The tumor lysis syndrome. *N Engl J Med*. 2011;364(19):1844-1854. **3.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for B-Cell Lymphomas. V.1.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed March 8, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **4.** Pathak R, Giri S, Aryal M. Recent trends in the incidence and outcomes of tumor lysis syndrome in hematological malignancies: data from 2010-2014 National Inpatient Sample. *Blood*. 2017;130(suppl1):3390. **5.** 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;26(16):2767-2778. **6.** Wilson FP, Berns JS. Onco-nephrology: tumor lysis syndrome. *Clin J Am Soc Nephrol*. 2012;7(10):1730-1739. **7.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. V.2.2022. © National Comprehensive Cancer Network, Inc. 2022. All rights reserved. Accessed February 1, 2022. To view the most recent and complete version of the guideline, go online to NCCN.org. NCCN makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way. **8.** Bose P, Qubaiah O. A review of tumour lysis syndrome with targeted therapies and the role of rasburicase. *J Clin Pharm Ther*. 2011;36(3):299-326. **9.** Venclexta [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; 2021. **10.** Rituxan [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2021. **11.** Doxorubicin hydrochloride [prescribing information]. New York, NY: Pfizer Labs; 2013. **12.** Marqibo [prescribing information]. East Windsor, NJ: Acrotech Biopharma LLC; 2020. **13.** Belay Y, Yirdaw K, Enawgaw B. Tumor lysis syndrome in patients with hematological malignancies. *J Oncol*. 2017. doi:10.1155/2017/9684909 **14.** Gazyva [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2022. **15.** Imbruvica [prescribing information]. Horsham, PA: Janssen Biotech, Inc.; 2020. **16.** Cairo MS. Prevention and treatment of hyperuricemia in hematological malignancies. *Clin Lymphoma*. 2002;3(suppl1):S26-S31. **17.** Ueng S. Rasburicase (Elitek): a novel agent for tumor lysis syndrome. *Proc (Bayl Univ Med Cent)*. 2005;18(3):275-279. **18.** ELITEK [prescribing information]. Bridgewater, NJ: sanofi-aventis U.S. LLC.

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