ANTICANCER THERAPIES: CONSIDER ASSOCIATED TLS RISK

Certain anticancer agents have been associated with elevated uric acid or tumor lysis syndrome (TLS)[1-14]

Highly effective anticancer therapies can promote rapid cell death, causing the release and catabolism of nucleic acids, which result in the rise of uric acid levels.[15]

Hyperuricemia is one of 4 metabolic disorders that can lead to TLS, the most common disease-related emergency in hematologic cancers.[16]

Agents treating leukemia or lymphoma associated with risk of increasing uric acid or TLS[1-14]*		
Venetoclax	Obinutuzumab	Carfilzomib
Dasatinib	Blinatumomab	Lenalidomide
Ibrutinib	Bortezomib	Rituximab†
Vincristine sulfate†	Doxorubicin HCl†	Bendamustine HCl‡

*This is not a comprehensive list of agents.
†Components of the R-CHOP regimen.
‡There is an increased risk of severe skin toxicity when bendamustine HCl is used concomitantly with allopurinol.[12]

ELITEK® (rasburicase) is recommended for patients at high or intermediate risk of developing TLS associated with hyperuricemia. Unlike allopurinol, only ELITEK has the mechanism to clear uric acid.[16,17]

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.

VENETOCLAX THERAPY AND TLS

The National Comprehensive Cancer Network (NCCN®) has specifically developed a set of supportive care recommendations for TLS in patients with CLL or SLL who have been prescribed venetoclax therapy[18]

- Venetoclax can cause a rapid reduction of the tumor, thus posing a risk for TLS[1]
- TLS, including fatal events and renal failure requiring dialysis, has occurred in patients with high tumor burden when treated with venetoclax[1]

Risk factors for TLS in patients with CLL or SLL[18]:


Bulky lymph nodes


Elevated uric acid levels at baseline


Reduced renal function (CrCl <80 mL/min)
Renal disease or renal involvement by tumor


Progressive disease after small-molecule inhibitor therapy


Treatment with venetoclax, chemoimmunotherapy, lenalidomide, and obinutuzumab


Spontaneous TLS


Elevated WBC count

This is not a comprehensive list of all potential risk factors.

NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) recommend TLS prophylaxis and monitoring based on tumor burden in patients with CLL/SLL receiving venetoclax[18]:

- **Management of patients with CrCl <80 mL/min and medium tumor burden (any lymph node 5 cm to <10 cm or ALC ≥25 x 10^9/L) as high risk for TLS**
- **Consider rasburicase for patients with both high tumor burden and elevated baseline uric acid***

ALC=absolute lymphocyte count; CLL=chronic lymphocytic leukemia; CrCl=creatinine clearance; SLL=small lymphocytic lymphoma; WBC=white blood cell.

*In patients receiving venetoclax therapy, high tumor burden is defined as any lymph node ≥10 cm or ALC ≥25 x 10^9/L and any lymph node ≥5 cm.[18]

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. Venclexta [prescribing information]. South San Francisco, CA: Genentech USA, Inc.; 2019. **2.** Sprycel [prescribing information]. Princeton, NJ: Bristol-Myers Squibb Company; 2018. **3.** Imbruvica [prescribing information]. Sunnyvale, CA: Pharmacyclics LLC; 2019. **4.** Marqibo [prescribing information]. South San Francisco, CA: Talon Therapeutics; 2019. **5.** Gazyva [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2017. **6.** Blincyto [prescribing information]. Thousand Oaks, CA: Amgen Inc.; 2019. **7.** Velcade [prescribing information]. Cambridge, MA: Millennium Pharmaceuticals, Inc.; 2019. **8.** Adriamycin [prescribing information]. Bedford, OH: Bedford Laboratories; 2012. **9.** Kyprolis [prescribing information]. Thousand Oaks, CA: Onyx Pharmaceuticals, Inc.; 2019. **10.** Revlimid [prescribing information]. Summit, NJ: Celgene Corporation; 2019. **11.** Rituxan [prescribing information]. South San Francisco, CA: Genentech, Inc.; 2020. **12.** Treanda [prescribing information]. North Wales, PA: Teva Pharmaceuticals USA, Inc.; 2019. **13.** Belay Y, Yirdaw K, Enawgaw B. Tumor lysis syndrome in patients with hematological malignancies. *J Oncol.* 2017. https://doi.org/10.1155/2017/9684909. **14.** 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. **15.** Coiffier B, Altman A, Pui C-H, 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. **16.** Howard SC, Jones DP, Pui C-H. The tumor lysis syndrome. *N Engl J Med.* 2011;364(19):1844-1854. **17.** Ueng S. Rasburicase (ELITEK): a novel agent for tumor lysis syndrome. *Proc (Bayl Univ Med Cent).* 2005;18:(3)275-279. **18.** Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma. V4.2020. ©National Comprehensive Cancer Network, Inc. 2020. All rights reserved. Accessed February 20, 2020. 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.

SANOFI GENZYME

 SAUS.RAS.20.02.0751 03/20

ELITEK® rasburicase IV Infusion