



Positive Quality Intervention: Use of Rasburicase (Elitek) for Treatment of Tumor Lysis Syndrome

Description: The purpose of this PQI is to identify appropriate dosing and utilization of rasburicase based on uric acid levels

Background: Rasburicase is an FDA approved intravenous medication for the management of serum uric acid levels in the setting of anticancer therapy that is expected to result in tumor lysis.^{1,2}

While rasburicase breaks down uric acid that has already formed in the body, allopurinol prevents the formation of additional uric acid. The two medications work concomitantly to actively decrease elevated uric acid levels while also preventing hyperuricemia in the future.³

In general, the risk of a patient developing TLS is higher with hematologic malignancies. Risk stratification can be found in the modified chart below, adapted from TLS stratification⁵ and prophylaxis¹⁰ references.^{5,10,12}

Type of Malignancy	High Risk	Intermediate Risk	Low Risk
Non-Hodgkin Lymphoma (NHL) ⁵	Burkitt lymphoma	DLBCL	Indolent NHL
Acute lymphoblastic leukemia (ALL) ¹⁰	WBC \geq 100,000 OR WBC <100,000 and/or LDH \geq 2X ULN	WBC <100,000 and LDH <2X ULN	WBC <100,000
Acute myeloid leukemia (AML) ¹⁰	WBC \geq 100,000, monoblastic	WBC >25,000 but <100,000 OR WBC <25,000 and LDH \geq 2X ULN	WBC <25,000 and LDH <2X ULN
Chronic lymphocytic leukemia (CLL) ^{10,12}	Venetoclax use (lymph node \geq 10 cm or ALC \geq 25,000 and lymph node \geq 5 cm)	WBC 10,000 – 100,000 and treatment with targeted and/or biologic Therapy (ex. Fludarabine or Venetoclax) (lymph node 5-<10 cm or ALC \geq 25,000)	WBC < 10,000 and using only alkylating agents Venetoclax use (all lymph nodes < 5 cm and ALC < 25,000)
Other hematologic malignancies (chronic myeloid leukemia, multiple myeloma) and solid tumors (small cell lung cancer) ⁵	---	Rapid proliferation with expected rapid response to therapy	Remainder of patients

While FDA approved dosing of rasburicase is weight-based (0.2 mg/kg daily for up to 5 days), several studies have been performed that evaluated the use of single, fixed doses of rasburicase.^{1,4,6,7,8,9} Trifilio and colleagues demonstrated that rasburicase 3 mg effectively lowered uric acid levels to \leq 7 mg/dL in 72% of patients at 24 hours; uric acid levels continued to decrease without additional doses of rasburicase. Of note, patients with higher baseline uric acid levels (defined as \geq 12 mg/dL) were found to be at risk of rasburicase failure. This patient population may require a higher initial dose of rasburicase at 6 mg, or a repeated dose of 3 mg if uric acid levels begin to rise again.⁶ McBride and colleagues found similar success with the 3 mg dose in their study. However, it is worth noting that patients who received 3 mg of rasburicase had lower baseline uric acid levels compared to the patients who received 6 mg of rasburicase.⁷

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PQI Process:

- Confirm the patient has an order/prescription for allopurinol
- Confirm the patient is maintaining adequate oral hydration or initiated on IV hydration
- Baseline and follow-up TLS labs (potassium, serum creatinine, uric acid, phosphorus, calcium, lactate dehydrogenase) should be obtained pre- and post-rasburicase administration
- Rasburicase dosing may vary per institution guidelines/policies
 - Patients with malignancies that are classified as having a high risk for TLS may require upfront dosing of rasburicase
 - Consider rasburicase 3 mg for patients with baseline uric acid <12 mg/dL
 - Encourage use of allopurinol and aggressive hydration prior to initiation of rasburicase
 - Consider rasburicase 6 mg for patients with baseline uric acid ≥12 mg/dL OR consider an initial dose of 3 mg and monitor the patient's uric acid levels closely to determine if a repeat dose of 3 mg is warranted
 - If warranted, repeated rasburicase dosing can be considered 24 hours after the initial dose
- Ensure uric acid levels obtained after rasburicase administration are immediately put on ice. If left at room temperature, the enzymatic activity of rasburicase will continue to break down uric acid and can result in a falsely low uric acid level

Patient Centered Activities:

- Patient Education
 - Although rare, hypersensitivity reactions have been reported with rasburicase
 - Methemoglobinemia can occur as a result of rasburicase administration
 - Hemolysis can occur after rasburicase administration in patients with G6PD deficiency
 - Counsel patients to maintain increased oral hydration

References:

1. Elitek (rasburicase) [prescribing information]. Bridgewater, NJ: Sanofi-Aventis; July 2019.
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Supplemental Information

Table 1: Diagnosis of Tumor Lysis (Cairo-Bishop Classification)^{3,5}

Laboratory Tumor Lysis	Clinical TLS
Two or more of the following occurring in a patient with cancer within <u>3 days prior</u> to or <u>7 days following</u> initiation of cancer treatment: <ul style="list-style-type: none"> • Uric acid ≥ 8 mg/dL or 25% increase from baseline • Potassium ≥ 6 mmol/L (6 mg/L) or 25% increase from baseline • Phosphate ≥ 4.5 mg/dL or 25% increase from baseline • Calcium ≤ 7 mg/dL or 25% decrease from baseline 	Laboratory tumor lysis plus one of the following: <ul style="list-style-type: none"> • Serum creatinine ≥ 1.5 x ULN • Cardiac arrhythmia/sudden death • Seizure

Image 1: TLS Risk Assessment regarding tumor mass¹¹

TLS Risk Assessment

- Measures of serum potassium, phosphorus, calcium, creatinine, uric acid, and urine output

Risk of TLS With ≤ 1 Abnormal Laboratory Value

	Negligible Risk		Low Risk		Intermediate Risk		High Risk	
Cancer mass ^a	Small or resected localized tumor	Medium mass	Medium mass	Large mass	Medium mass	Large mass	Medium mass	Large mass
Cell lysis potential	–	Low	Medium	Low	Medium/unknown	Medium/unknown	High	High
Preexisting nephropathy, dehydration, acidosis, hypotension, or nephrotoxin exposure	–	None	None	–	Yes	–	–	–

- Patients with ≥ 2 abnormal laboratory values, without clinical symptoms, have laboratory TLS and are considered to be at high risk for clinical TLS if there is concomitant hyperkalemia, hypocalcemia, or acute kidney injury

^aSmall mass, all ≤ 2 cm; medium mass, ≤ 2 bulky (5-10 cm); large mass, many bulky (5-10 cm) or ≥ 1 very bulky (>10 cm).
Howard SC et al. *N Engl J Med* 2011;364(10):1844-54.

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