

*American Hospital Formulary  
Service (AHFS) Drug Information\**

**1. AHFS DRUG INFORMATION  
CLASSIFICATION NUMBER**

44.00 Enzymes

**2. GENERIC NAME**

Rasburicase

**3. INDICATION<sup>1</sup>**

*ELITEK*<sup>®</sup> is indicated for the initial management of plasma uric acid levels in pediatric 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.

**4. SUPPLY**

**a. Two different strengths of ELITEK are available:**

*ELITEK* is supplied in colorless, glass vials: a 3-mL vial containing 1.5 mg of *ELITEK* and a 10-mL vial containing 7.5 mg of *ELITEK*.

Each 3-mL vial contains 1.5 mg rasburicase, 10.6 mg mannitol, 15.9 mg L-alanine, and between 12.6 and 14.3 mg of dibasic sodium phosphate. Each 10-mL vial contains 7.5 mg rasburicase, 53 mg mannitol, 79.5 mg L-alanine, and between 63 and 71.5 mg dibasic sodium phosphate.

**b. These 2 vials are supplied as follows:**

For the 3-mL vial containing 1.5 mg of *ELITEK*:

One carton (NDC 0024-5150-10) containing 3 single-use vials, each containing 1.5 mg of rasburicase; and 3 ampules, each containing 1 mL Water for Injection, USP, and 1 mg Poloxamer 188.

For the 10-mL vial containing 7.5 mg of *ELITEK*:

One carton (NDC 0024-5151-75) containing 1 single-use vial that contains 7.5 mg of rasburicase; and 1 ampule that contains 5 mL Water for Injection, USP, and 5 mg Poloxamer 188.

**c. Describe the diluent for parenteral administration:**

The diluent for reconstitution is supplied in two clear, glass ampules:

The 2-mL ampule contains 1.0 mL Water for Injection, USP, and 1.0 mg Poloxamer 188.

The 5-mL ampule contains 5 mL Water for Injection, USP, and 5 mg Poloxamer 188.

**5. BIOLOGICS LICENSE APPLICATION (BLA)  
NUMBER AND DATE OF FDA APPROVAL**

BLA application number, BL-103946/0; date of FDA approval, July 2002.

**6. PHYSICAL PROPERTIES OF THE CHEMICAL ENTITY<sup>1</sup>**

**a. Macroscopic appearance:**

*ELITEK* is a sterile, white to off-white, lyophilized powder intended for intravenous (IV) administration following reconstitution.

**b. Solubility:**

*ELITEK*, reconstituted with diluent, is a clear, colorless solution.

**7. CHEMICAL PROPERTIES<sup>1</sup>**

**a. Describe any structural similarities of the drug to other available compounds or groups of compounds:**

*ELITEK* is a recombinant urate-oxidase enzyme produced by a genetically modified *Saccharomyces cerevisiae* strain. The cDNA coding for rasburicase was cloned from a strain of *Aspergillus flavus*. Rasburicase is a tetrameric protein with identical subunits of a molecular mass of 34 kDa. The molecular formula of the monomer is C<sub>1523</sub>H<sub>2383</sub>N<sub>417</sub>O<sub>462</sub>S<sub>7</sub>. The monomer, made up of a single 301 amino acid polypeptide chain, has no intra- or inter-disulfide bridges and is N-terminal acetylated.

**b. Describe any structural differences and their consequences when compared with these compounds:**

NOT APPLICABLE

\* This AHFS Drug Information is adapted from a document created by Interlink Healthcare Communications, based on the Product Information Form by the American Society of Health-System Pharmacists, Inc. Permission to use the Product Information Form for the AHFS Drug Information as modified by Interlink Healthcare Communications was granted by the American Society of Health-System Pharmacists, Inc. The answers to questions were not supplied by the Society, nor were they intended to imply the endorsement of the American Society of Health-System Pharmacists, Inc.

**c. List the amount of active ingredient in the vial containing 1.5 mg of ELITEK and the volume of solution after reconstitution:**

To each vial containing 1.5 mg of *ELITEK*<sup>®</sup> (rasburicase), 1 mL of the provided reconstitution solution (diluent) is added to provide a final concentration of 1.5 mg/mL prior to dilution for IV infusion.

**d. List the amount of active ingredient in the vial containing 7.5 mg of ELITEK and the volume of solution after reconstitution:**

To each vial containing 7.5 mg of *ELITEK*, 5 mL of the provided reconstitution solution (diluent) is added to provide a final concentration of 1.5 mg/mL prior to dilution for IV infusion.

**e. List the recommended storage conditions for the commercially available product:**

The lyophilized drug product and the solution for reconstitution should be stored at 2°C–8°C (36°F–46°F). Do not freeze. Protect from light.

**f. List the expiration dating period for the commercially available product:**

36 months

**g. List the recommended storage conditions for the final diluted product:**

Refer to **e** and **f** above.

## 8. PHARMACOLOGIC CLASSIFICATION

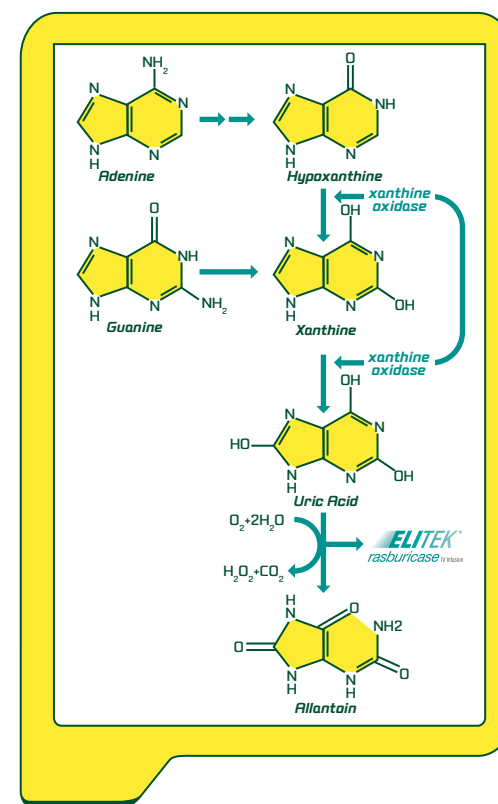
**a. Pharmacologic class:**

*ELITEK* is a protein formulation for IV infusion.<sup>1</sup>

**b. Mechanism of action:**

In humans, uric acid is the final step in the catabolic pathway of purines. Rasburicase catalyzes enzymatic oxidation of uric acid into an inactive and soluble metabolite (allantoin). Rasburicase is only active at the end of the purine catabolic pathway.<sup>1</sup> Uric acid levels in the blood may become elevated in patients with specific malignancies as a result of rapid cell turnover from the cancer itself or because of rapid cell lysis associated with chemotherapy. As large numbers of malignant cells die, they release their contents into the bloodstream. Among these released cellular contents are the nucleic acids DNA and RNA, whose purine components and additional purine metabolites are rapidly catabolized to produce high levels of uric acid. Treatment with *ELITEK* eliminates circulating uric acid by converting it to allantoin; *ELITEK* is active only at the end of the purine catabolic pathway, and therefore does not alter the earlier steps of purine metabolism (Figure 1).<sup>1</sup>

Figure 1. Mechanism of action of *ELITEK*.



**c. Pharmacokinetic data for absorption, distribution, metabolism, and excretion of the drug<sup>1</sup>:**

Pharmacokinetics of rasburicase were evaluated in two studies that enrolled patients with lymphoid leukemia (B and T cell), non-Hodgkin's lymphoma (including Burkitt's lymphoma), or acute myelogenous leukemia. *ELITEK* exposure, as measured by  $AUC_{0-24hr}$  and  $C_{max}$ , tended to increase linearly with doses over a limited dose range (0.15 mg/kg to 0.20 mg/kg). The overall elimination half-life was 18 hours. No accumulation of rasburicase was observed between days 1 and 5 of dosing. *ELITEK* mean volume of distribution was 110 mL/kg to 127 mL/kg in pediatric patients. There are insufficient data to characterize pharmacokinetics in adult patients.

**d. Drug-drug interactions<sup>1</sup>:**

Refer to **Drug interactions (b)** under **Precautions** on page 4.

## 9. DOSAGE AND ADMINISTRATION<sup>1</sup>

**a. Recommended dose and schedule:**

The recommended dose and schedule of *ELITEK*<sup>®</sup> (rasburicase) is 0.15 mg/kg or 0.20 mg/kg as a single daily dose for 5 days. Because the safety and effectiveness of other schedules have not been established, dosing beyond 5 days or administration of more than one course of *ELITEK* is not recommended. Chemotherapy should be initiated 4 hours to 24 hours after the first dose of *ELITEK*. **DO NOT ADMINISTER AS A BOLUS INFUSION.** *ELITEK* should be administered as an IV infusion over 30 minutes.

**b. Reconstitution procedure:**

Determine the number of vials of *ELITEK* needed to achieve the proper dosage, based on the individual patient's weight and the dose per kilogram. *ELITEK* must be reconstituted in the diluent provided.

To each 1.5 mg vial of *ELITEK*, add 1 mL of the provided reconstitution solution (diluent) and mix by swirling very gently. **Do not shake or vortex.**

To each 7.5 mg vial of *ELITEK*, add 5 mL of the provided reconstitution solution (diluent) and mix by swirling very gently. **Do not shake or vortex.**

Reconstituted *ELITEK* should be inspected visually for particulate matter and discoloration prior to administration, and discarded if particulate matter is visible or if product is discolored.

**c. Further dilution and administration:**

Using aseptic technique and syringes of appropriate volume, remove the predetermined dose of *ELITEK* from the reconstituted vials and inject into an infusion bag containing the appropriate volume of 0.9% sterile sodium chloride to achieve a final total volume of 50 mL. This final solution for injection is to be infused over 30 minutes. **No filters should be used for the infusion.**

The reconstituted *ELITEK* contains no preservatives and must be administered within 24 hours of reconstitution. The reconstituted or diluted solution can be stored up to 24 hours at 2°C–8°C. Discard any unused product.

*ELITEK* should be infused through a different line than that used for the infusion of other concomitant medications. If use of a separate line is not possible, the line should be flushed with at least 15 mL of saline solution prior to and after infusion with *ELITEK*.

See **DOSAGE AND ADMINISTRATION**, including **BOXED WARNINGS**, in full Prescribing Information.

Please see accompanying full Prescribing Information including Boxed Warnings.

## 10. SAFETY INFORMATION

**a. Adverse Reactions:**

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates.

The data described below reflect exposure to *ELITEK* in 703 patients (63% male, 37% female; median age 10 years [range 10 days to 88 years]; 73% Caucasian, 9% African, 4% Asian, 14% other/unknown). *ELITEK* was studied for adverse reactions, regardless of severity, in 347 patients (265 pediatric and 82 adults) enrolled in one active-controlled trial (Study 1), two uncontrolled trials (Studies 2 and 3), and one uncontrolled safety trial (n=82). Additionally, an expanded access experience enrolled 356 patients, for whom reliably collected data were limited to serious adverse reactions.

Among the 703 patients for whom serious adverse reactions were assessed, the most serious adverse reactions caused by *ELITEK* were allergic reactions including anaphylaxis (<1%), rash (1%), hemolysis (<1%), and methemoglobinemia (<1%) (see **BOXED WARNINGS** and **WARNINGS**, in full Prescribing Information). The commonly observed serious adverse reactions were fever (5%), neutropenia with fever (4%), respiratory distress (3%), sepsis (3%), neutropenia (2%), and mucositis (2%). The following additional serious adverse reactions were observed in ≤1% of patients regardless of causality: acute renal failure, arrhythmia, cardiac failure, cardiac arrest, cellulitis, cerebrovascular disorder, chest pain, convulsions, cyanosis, diarrhea, dehydration, hot flushes, ileus, infection, intestinal obstruction, hemorrhage, myocardial infarction, paresthesia, pancytopenia, pneumonia, pulmonary edema, pulmonary hypertension, retinal hemorrhage, rigors, thrombosis, and thrombophlebitis.

Among the 347 patients for whom all adverse reactions regardless of severity were assessed, the most frequently observed adverse reactions (incidence ≥10%) were vomiting (50%), fever (46%), nausea (27%), headache (26%), abdominal pain (20%), constipation (20%), diarrhea (20%), mucositis (15%), and rash (13%). In Study 1, an active control study, the following adverse events occurred more frequently in *ELITEK*-treated subjects than allopurinol-treated subjects: vomiting, fever, nausea, diarrhea, and headache. Although the incidence of rash was similar in the two arms, severe rash (NCI CTC, Grade 3 or 4) was reported only in one *ELITEK*-treated patient.

## 11. CONTRAINDICATIONS<sup>1</sup>

*ELITEK* is contraindicated in individuals deficient in glucose-6-phosphate dehydrogenase (G6PD) (see **BOXED WARNINGS**, **Hemolysis** and **WARNINGS**, **Hemolysis**, in full Prescribing Information).

*ELITEK* is contraindicated in patients with a known history of anaphylaxis or hypersensitivity reactions, hemolytic reactions, or methemoglobinemia reactions to *ELITEK* or any of the excipients (see **BOXED WARNINGS** and **WARNINGS**, in full Prescribing Information).

## 12. BOXED WARNINGS

**Anaphylaxis**

*ELITEK* may cause severe hypersensitivity reactions including anaphylaxis. *ELITEK* should be immediately and permanently discontinued in any patient developing clinical evidence of a serious hypersensitivity reaction (see **WARNINGS**, **Anaphylaxis** and **ADVERSE REACTIONS**, **Immunogenicity**).

**Hemolysis**

*ELITEK* administered to patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency can cause severe hemolysis. *ELITEK* administration should be immediately and permanently discontinued in any patient developing hemolysis. It is recommended that patients at higher risk for G6PD deficiency (eg, patients of African or Mediterranean ancestry) be screened prior to starting *ELITEK* therapy (see **CONTRAINDICATIONS** and **WARNINGS**, **Hemolysis**).

**Methemoglobinemia**

*ELITEK* use has been associated with methemoglobinemia. *ELITEK* administration should be immediately and permanently discontinued in any patient identified as having developed methemoglobinemia (see **WARNINGS**, **Methemoglobinemia**).

**Interference with Uric Acid Measurements**

*ELITEK* will cause enzymatic degradation of the uric acid within blood samples left at room temperature, resulting in spuriously low uric acid levels. To ensure accurate measurements, blood must be collected into prechilled tubes containing heparin anticoagulant and immediately immersed and maintained in an ice water bath; plasma samples must be assayed within 4 hours of sample collection (see **PRECAUTIONS**, **Laboratory Test Interactions**).

## 13. PRECAUTIONS<sup>1</sup>

**a. General:**

Patients on *ELITEK*<sup>®</sup> (rasburicase) should receive intravenous hydration according to standard medical practice for the management of plasma uric acid in patients at risk for tumor lysis syndrome.

**b. Drug interactions:**

No studies of interactions with other drugs have been conducted in humans.

Rasburicase does not metabolize allopurinol, cytarabine, methylprednisolone, methotrexate, 6-mercaptopurine, thioguanine, etoposide, daunorubicin, cyclophosphamide, or vincristine *in vitro*. No metabolic-based drug interactions are therefore anticipated with these agents in patients.

In preclinical *in vivo* studies, rasburicase did not affect the activity of isoenzymes CYP1A, CYP2A, CYP2B, CYP2C, CYP2E, and CYP3A, suggesting no induction nor inhibition potential. Clinically relevant P450-mediated drug-drug interactions are therefore not anticipated in patients treated with the recommended *ELITEK* dose and dosing schedule.

**c. Laboratory test interactions:**

At room temperature, *ELITEK* causes enzymatic degradation of the uric acid in blood/plasma/serum samples potentially resulting in

spuriously low plasma uric acid assay readings. The following special sample handling procedure must be followed to avoid *ex vivo* uric acid degradation:

Uric acid must be analyzed in plasma. Blood must be collected into prechilled tubes containing heparin anticoagulant. Samples must be immediately immersed in an ice water bath. Plasma samples must be prepared by centrifugation in a precooled centrifuge (4°C). Finally, the plasma must be maintained in an ice water bath and analyzed for uric acid within 4 hours of collection (see **BOXED WARNINGS**, **Interference With Uric Acid Measurements**, in full Prescribing Information).

**d. Carcinogenesis, mutagenesis, impairment of fertility:**

Long-term studies in animals to evaluate carcinogenic potential have not been performed.

*ELITEK* was nongenotoxic in the Ames, unscheduled DNA synthesis, chromosome analysis, mouse lymphoma, and micronucleus tests.

*ELITEK* did not affect reproductive performance or fertility in male or female rats at doses 8-fold higher than the human dose when corrected for differences in body surface area.

**e. Pregnancy category C:**

Rasburicase is teratogenic in rabbits and rats. Pregnant rabbits were dosed with rasburicase at levels of 2 mg/kg, 10 mg/kg, or 20 mg/kg (equivalent to 10, 50, and 100 times the human equivalent dose). Mortality occurred at 2 mg/kg and 20 mg/kg, abortions at 10 mg/kg and clinical signs of toxicity appeared at all dose levels. At doses equal to or greater than 10 mg/kg, decreases were observed in uterine weight and viable fetuses while increases were observed in the number of fetal resorptions and post-implantation loss. Additionally, fetal body weights were decreased while increases occurred in heart and great vessel malformation at all dose levels. In offspring of pregnant rats given 50 mg/kg (equivalent to 250 times the human dose), multiple heart and great vessel malformations were observed.

There are no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human response, *ELITEK* should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

**f. Nursing mothers:**

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, a decision should be made whether to discontinue nursing or to discontinue *ELITEK*, taking into account the importance of the drug to the mother.

**g. Pediatric use:**

The efficacy and safety of *ELITEK* were studied in 246 pediatric patients ranging in age from 1 month to 17 years. There were an insufficient number of patients in the 0–6 months age group (n=7) to determine whether they respond differently than older children.

These patients were pooled into the <2 years of age group (n=24). Children <2 years of age had a higher mean uric acid  $AUC_{0-96hr}$  than those age 2 years–17 years (150 ± SE 16 mg•hr/dL vs 108 ± SE 4 mg•hr/dL, respectively).

In addition, the data suggest that children <2 years of age had a lower rate of success at achieving maintenance uric acid concentration by 48 hours (83% [95% CI of 62 to 95] vs 93% [95% CI of 89 to 91], respectively). Children <2 years old also experienced more toxicity.

The following adverse events were observed more frequently in children < 2 years of age compared with those age 2 years–17 years, respectively: vomiting (75% vs 55%), diarrhea (63% vs 20%), fever (50% vs 38%), and rash (38% vs 10%).

**h. Geriatric use:**

Five of the 19 adults among the 265 patients enrolled in clinical studies of *ELITEK*<sup>®</sup> (rasburicase) were age 65 or greater. Therefore, there are insufficient data to determine whether geriatric subjects, or adults in general, respond differently from pediatric subjects.

**14. COMPARISONS**

**a. Therapeutic comparisons with other drugs or treatment regimens:**

Study 1 was a randomized, open-label, controlled study conducted at 6 institutions, in which 52 pediatric patients were randomized to receive either *ELITEK* (n=27) or allopurinol (n=25). The dose of allopurinol varied according to local institutional practice. *ELITEK* was administered as an intravenous infusion over 30 minutes once (n=26) or twice (n=1) daily at a dose of 0.20 mg/kg/dose (total daily dose 0.20 mg/kg/day–0.40 mg/kg/day). Initiation of dosing was permitted at any time between 4 hours to 48 hours before the start of antitumor therapy and could be continued for 5 days to 7 days after initiation of antitumor therapy. Patients were stratified at randomization on the basis of underlying malignant disease (leukemia or lymphoma) and baseline serum or plasma uric acid levels (<8.0 mg/dL and ≥8.0 mg/dL). The primary study objective was to demonstrate a greater reduction in uric acid concentration over 96 hours (AUC<sub>0-96hr</sub>) in the *ELITEK* group as compared to the allopurinol group. Uric acid AUC<sub>0-96hr</sub> was defined as the area under the curve for plasma uric acid levels (mg•hr/dL), measured from the last value prior to the first dose of *ELITEK* until 96 hours after that first dose. Plasma uric acid levels were used for all uric acid AUC<sub>0-96hr</sub> calculations (see **PRECAUTIONS, Laboratory Test Interactions**, in full Prescribing Information).<sup>1</sup>

The demographics of the two study arms (*ELITEK* vs allopurinol) were as follows: age < 13 years (82% vs 76%), males (59% vs 72%), Caucasian (59% vs 72%), ECOG performance status 0 (89% vs 84%), and leukemia (74% vs 76%). The median interval, in hours, between initiation of *ELITEK* and of antitumor treatment was 20 hours, with a range of 70 hours before to 10 hours after the initiation of antitumor treatment (n=24, data not reported for 3 patients).<sup>1</sup>

The uric acid AUC<sub>0-96hr</sub> was significantly lower in the *ELITEK* group (128 ± SE 14 mg•hr/dL) as compared to the allopurinol group (328 ± SE 26 mg•hr/dL). All but one patient in the *ELITEK* arm had reduction and maintenance of uric acid levels to within or below the normal range during the treatment. The incidence of renal dysfunction was similar in the two study arms; one patient in the allopurinol arm developed acute renal failure.<sup>1</sup>

**b. Other studies:**

Studies 2 and 3 were both open-label, nonrandomized, noncomparative studies consisting of a dose validation and accrual phase, in which 107 patients received *ELITEK* at a dosage of 0.15 mg/kg/day, and 131 patients received *ELITEK* at dosages of 0.15 mg/kg/day (n=12) and 0.20 mg/kg/day (n=119).

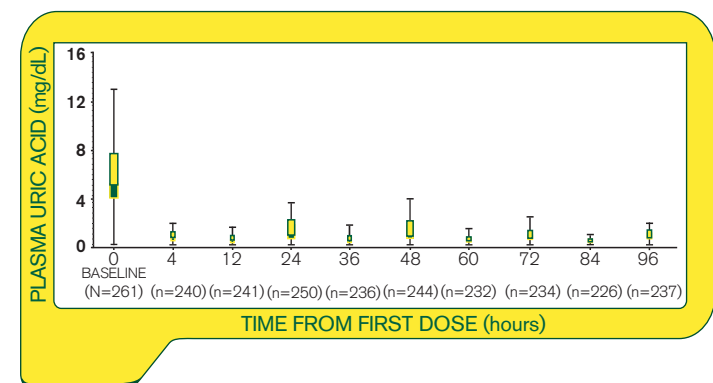
**Table 1.** Reduction of uric acid after *ELITEK* treatment in pooled studies.<sup>1</sup>

	Patients with uric acid ≥8 mg/dL at baseline (n=61)	Patients with uric acid <8 mg/dL at baseline (n=200)
Median (range) plasma uric acid concentration at baseline (mg/dL)	10.6 (8.1–36.4)	4.6 (0.2–7.9)
Decrease in uric acid concentration by 4 hours after first dose (mg/dL)	9.1 (0.3–19.3)	4.1 (0.1–7.6)
Decrease in uric acid at 4 hours post first dose (%)	86	89

In the pooled studies, *ELITEK* reduced uric acid levels by 86% in patients with hyperuricemia (plasma uric acid ≥8 mg/dL) 4 hours after the first dose. *ELITEK* reduced uric acid levels by 89% in patients at risk of hyperuricemia (plasma uric acid <8 mg/dL) 4 hours after the first dose.<sup>1</sup> In the controlled trial, *ELITEK* achieved an 86% reduction in uric acid concentration by 4 hours after the first dose, while allopurinol achieved only a 12% reduction 4 hours after the first dose.<sup>2</sup> The uric acid AUC<sub>0-96hr</sub> was significantly lower in the *ELITEK* group (128 ± SE 14 mg•hr/dL) as compared to the allopurinol group (328 ± SE 26 mg•hr/dL).<sup>1</sup>

Figure 2 is a box and whisker plot of plasma uric acid levels inclusive of 261 of the 265 *ELITEK*<sup>®</sup> (rasburicase)-treated patients from Studies 1, 2, and 3. Of the 261 evaluable patients, plasma uric acid concentration was maintained by 4 hours for 92% of patients (240/261), by 24 hours for 93% of patients (245/261), by 48 hours for 97% of patients (254/261), by 72 hours for 99% of patients (260/261), and by 96 hours for 100% of patients (261/261). Of the subset of 61 patients whose plasma uric acid level was elevated at baseline (≥8 mg/dL), plasma uric acid concentration was maintained by 4 hours for 72% of patients (44/61), by 24 hours for 80% of patients (49/61), by 48 hours for 92% of patients (56/61), by 72 hours for 98% of patients (60/61), and by 96 hours for 100% (61/61).<sup>1</sup>

**Figure 2.** Box-and-whisker-plot of uric acid concentration at designated time blocks. *ELITEK* administration began immediately after baseline.<sup>1</sup>



**c. Benefits of ELITEK:**

The benefits of *ELITEK* include: the ability to manage plasma uric acid levels; a rapid onset of action; decreased time to control of uric acid; ability to start chemotherapy as soon as 4 hours after the first dose; no need for dosing adjustments due to renal impairment; and no anticipated drug interactions with chemotherapy agents. *ELITEK* has a favorable profile in terms of duration of treatment, dosing frequency, and half-life when compared with allopurinol (Table 2).<sup>1</sup>

**Table 2.** Summary of dosing information for *ELITEK* and allopurinol.

Feature	<i>ELITEK</i> <sup>1</sup>	<i>Allopurinol</i> <sup>3,4</sup>
Route of administration	IV	IV and oral
Duration of treatment	5 days	4 to 13 days
Dosing frequency	Once daily (long half-life)	1 to 4 times daily for IV formulation; 3 times daily for oral formulation (short half-life)

**References:**

- ELITEK*<sup>®</sup> (rasburicase) Prescribing Information, sanofi-aventis.
- Goldman SC, Holcenberg JS, Finklestein JZ, et al. A randomized comparison between rasburicase and allopurinol in children with lymphoma or leukemia at high risk for tumor lysis. *Blood*. 2001;97:2998-3003.
- Aloprim<sup>™</sup> (allopurinol sodium) for Injection Prescribing Information. Boca Raton, FL: Nabi; 2003. Distributed by Bioniche Pharma.
- Zyloprim<sup>®</sup> (allopurinol) Prescribing Information. San Diego, CA: Prometheus Laboratories Inc.; 2003.

**FPO  
FOR PI POSITIONING**

Please see accompanying full Prescribing Information including Boxed Warnings.

