HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Elitek safely and effectively. See full prescribing information for Elitek®.
ELITEK® (rasburicase) for injection, for intravenous use
Initial U.S. Approval: 2002

WARNING: HYPERSENSITIVITY REACTIONS, HEMOLYSIS, METHEMOGLOBINEMIA, AND INTERFERENCE WITH URIC ACID MEASUREMENTS
See full prescribing information for complete boxed warning.

- Hypersensitivity Reactions: Elitek can cause serious and fatal hypersensitivity reactions including anaphylaxis. Immediately and permanently discontinue Elitek if a serious hypersensitivity reaction occurs (4, 5.1, 6.2).
- Hemolysis: Do not administer Elitek to patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency. Immediately and permanently discontinue Elitek if hemolysis occurs. Screen patients at higher risk for G6PD deficiency (e.g., patients of African or Mediterranean ancestry) prior to starting Elitek therapy (4, 5.2).
- Methemoglobinemia: Elitek can result in methemoglobinemia in some patients. Immediately and permanently discontinue Elitek if methemoglobinemia occurs (4, 5.3).
- 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 maintain sample in an ice water bath. Assay plasma samples within 4 hours of collection (5.4).

INDICATIONS AND USAGE
Elitek is a recombinant urate-oxidase indicated for initial management of plasma uric acid levels in pediatric and adult 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. (1)

Limitations of use: Elitek is indicated only for a single course of treatment. (1)

DOSE AND ADMINISTRATION
- Administer at 0.2 mg/kg as an intravenous infusion over 30 minutes daily for up to 5 days. (2.1)
- Do not administer as an intravenous bolus. (2.3)

DOSE FORMS AND STRENGTHS
- For injection, 1.5 mg, lyophilized powder in single-dose vial (3)
- For injection, 7.5 mg, lyophilized powder in single-dose vial (3)

CONTRAINDICATIONS
- History of the following reactions to rasburicase: anaphylaxis, severe hypersensitivity, hemolysis, methemoglobinemia. (4)
- Glucose-6-phosphate dehydrogenase (G6PD) deficiency. (4)

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. (6.1)

To report SUSPECTED ADVERSE REACTIONS, contact sanofi-aventis U.S. LLC at 1-800-633-1610 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

USE IN SPECIFIC POPULATIONS
- Pregnancy: May cause fetal harm. (8.1)
- Lactation: Breastfeeding not recommended. (8.2)

See 17 for PATIENT COUNSELING INFORMATION
Revised: 12/2019

FULL PRESCRIBING INFORMATION: CONTENTS
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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 [see Contraindications (4), Warnings and Precautions (5.1), Adverse Reactions (6.2)].

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 [see Contraindications (4), Warnings and Precautions (5.2)].

Methemoglobinemia
Elitek can result in methemoglobinemia in some patients. Immediately and permanently discontinue Elitek in patients developing methemoglobinemia [see Contraindications (4), Warnings and Precautions (5.3)].

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 [see Warnings and Precautions (5.4)].

1 INDICATIONS AND USAGE
Elitek is indicated for the initial management of plasma uric acid levels in pediatric and adult patients with leukemia, lymphoma, and solid tumor malignancies who are receiving antineoplastic therapy expected to result in tumor lysis and subsequent elevation of plasma uric acid.

Limitations of Use
Elitek is indicated only for a single course of treatment [see Warnings and Precautions (5.1)].

2 DOSAGE AND ADMINISTRATION
2.1 Dosage
The recommended dose of Elitek is 0.2 mg/kg as a 30-minute intravenous infusion daily for up to 5 days. Dosing beyond 5 days or administration of more than one course is not recommended.

2.2 Reconstitution Procedure
- Reconstitute the 1.5 mg vial of Elitek with 1 mL of diluent. Reconstitute the 7.5 mg vial of Elitek with 5 mL of diluent. Mix by gentle swirling. Do not shake or vortex.

2.3 Further Dilution and Administration
- Administer Elitek as an intravenous infusion only:
  - Inject the calculated dose of reconstituted Elitek solution into an infusion bag containing the appropriate volume of 0.9% sterile sodium chloride, to achieve a final total volume of 50 mL.
  - Infuse over 30 minutes through a separate line or flush line with at least 15 mL of normal saline prior to and after Elitek infusion.
  - Do not use filters during infusion of reconstituted Elitek drug product.
  - Store reconstituted or diluted solution at 2°C–8°C.
  - Discard unused product solution 24 hours following reconstitution.

3 DOSAGE FORMS AND STRENGTHS
- For injection: 1.5 mg, lyophilized powder in single-dose vial for reconstitution
- For injection: 7.5 mg, lyophilized powder in single-dose vial for reconstitution

4 CONTRAINDICATIONS
Elitek is contraindicated in individuals deficient in glucose-6-phosphate dehydrogenase (G6PD) [see Boxed Warning, Warnings and Precautions (5.2, 5.3)].

Elitek is contraindicated in patients with a history of anaphylaxis or severe hypersensitivity to rasburicase or in patients with development of hemorrhagic reactions or methemoglobinemia with rasburicase [see Boxed Warning, Warnings and Precautions (5.1, 5.2, 5.3)].

Elitek is contraindicated in patients with deficiency of cytochrome b5 reductase (formerly known as methemoglobin reductase) or of other enzymes with antioxidant activity are at increased risk for methemoglobinemia or hemolytic anemia. Immediately and permanently discontinue Elitek administration in any patient identified as having developed methemoglobinemia. Institute appropriate monitoring and support measures (e.g., transfusion support, methylene-blue administration) [see Boxed Warning, Contraindications (4)].

5.4 Laboratory Test Interference
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. Special sample handling procedure must be followed to avoid ex vivo uric acid degradation [see Boxed Warning, Drug Interactions (7)].

6 ADVERSE REACTIONS
The following clinically significant adverse reactions are discussed in greater detail in other sections of the prescribing information:
- Anaphylaxis [see Boxed Warning, Contraindications (4), Warnings and Precautions (5.1)]
- Hemolysis [see Boxed Warning, Contraindications (4), Warnings and Precautions (5.2)]
- Methemoglobinemia [see Boxed Warning, Contraindications (4), Warnings and Precautions (5.3)]

6.1 Clinical Trials Experience
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 data below reflect exposure to Elitek in 265 pediatric and 82 adult patients enrolled in one active-controlled trial (Study 1), two uncontrolled trials (Studies 2 and 3), and an uncontrolled safety trial (n=82). Additional data were obtained from an expanded access program of 356 patients, for whom data collection was limited to serious adverse reactions. Among these 703 patients 63% were male, the median age was 10 years (range 10 days to 88 years), 73% were Caucasian, 9% African, 4% Asian, and 14% other/unknown.

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 (28%), abdominal pain (20%), constipation (20%), diarrhea (20%), mucusitis (15%), and rash (13%). In Study 1, an active control study, the following adverse reactions occurred more frequently in Elitek-treated subjects than in allopurinol-treated subjects: vomiting, fever, nausea, diarrhea, and headache. Although the incidence of rash was similar in the two arms, severe rash was reported only in one Elitek-treated patient.

Further studies, including one active-controlled study (Study 4) and four supportive studies, have been conducted in adult patients. In these studies, Elitek was administered to a total of 434 adult patients (58% male, 42% female; median age 56 years [range 18 years to 89 years]; 52% Caucasian, 7% African, 14% Asian, 28% other/unknown). Of these 434 patients, 275 adult patients with leukemia, lymphoma, or solid tumor malignancies at risk for hyperuricemia and tumor lysis syndrome (TLS) were randomized in an open label trial receiving either Elitek alone, Elitek in combination with allopurinol, or allopurinol alone (Study 4).

A drug-related adverse reaction in Study 4 of any grade was experienced in 4.3% of Elitek-treated patients, 5.4% of Elitek/Allopurinol-treated patients, and 1.1% of allopurinol-treated patients.

Table 1 presents the per-patient incidence of adverse reactions by study arm in Study 4.

<table>
<thead>
<tr>
<th>Adverse Reaction</th>
<th>Elitek</th>
<th>Elitek/Allopurinol</th>
<th>Allopurinol</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n=92)</td>
<td>(n=92)</td>
<td>(n=91)</td>
</tr>
<tr>
<td>Overall incidence</td>
<td>10%</td>
<td>10%</td>
<td>10%</td>
</tr>
</tbody>
</table>

Table 1: Per-Patient Incidence of Selected Adverse Reactions by Study Arm in Study 4

Adverse Reaction

<table>
<thead>
<tr>
<th>Grade</th>
<th>Elitek</th>
<th>Elitek/Allopurinol</th>
<th>Allopurinol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grades 1, 2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grades 3, 4</td>
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<tr>
<td>Grades 3, 4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Overall incidence ≥10% in any Elitek arm and the difference between any Elitek arm versus the allopurinol arm ≥5%.

*Events were reported and graded according to NCI-CTC version 3.0 and presented as preferred terms MedDRA version 10.1.

Hypersensitivity reactions occurred in 4.3% of Elitek-treated patients and 1.1% of Elitek/allopurinol-treated patients in Study 4. Clinical manifestations of hypersensitivity included arthralgia, injection site irritation, peripheral edema, and rash.

The following serious adverse reactions occurred at a difference in incidence of ≥2% in patients receiving Elitek compared to patients receiving allopurinol in randomized studies (Study 1 and Study 4): pulmonary hemorrhage, respiratory failure, supraventricular arrhythmias, ischemic coronary artery disorders, and abdominal and gastrointestinal infections.

The incidence of anaphylaxis, hemolysis, and methemoglobinemia was less than 1% of the 887 Elitek-treated patients entered on these clinical trials.
6.2 Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. Elitek can elicit antiprotein antibodies that bind to rasburicase and in some instances inhibit the activity of rasburicase in vitro [see Boxed Warning, Warnings and Precautions (5.1)].

In clinical trials of pediatric patients with hematologic malignancies, 24/218 patients tested (11%) developed antibodies to rasburicase by day 28 following Elitek administration as assessed by quantitative ELISA. Using quasi-quantitative immunoassays in rasburicase-naïve adult patients with hematologic malignancies, 47/280 (18%) patients were positive for anti-rasburicase immunoglobulin G (IgG), 21/260 (8%) patients were positive for anti-rasburicase neutralizing IgG, and 16/260 (6%) patients were positive for anti-rasburicase immunoglobulin M (IgM) from day 14 to 24 months after 5 daily doses of Elitek.

The incidence of antibody responses detected is highly dependent on the sensitivity and specificity of the assay, which have not been fully evaluated. Additionally, the observed incidence of antibody positivity in an assay may be influenced by several factors, including serum sampling, timing and methodology, concomitant medications, and underlying disease. Therefore, comparison of the incidence of antibodies to Elitek with the incidence of antibodies to other products may be misleading.

6.3 Postmarketing Experience

The following adverse reactions have been identified from clinical trials and/or postmarketing surveillance. Because they are reported voluntarily from a population of unknown size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. Central nervous system disorders: convulsion, muscle contractions involuntary. Immune system disorders: cases of anaphylaxis with fatal outcome have been reported.

7 DRUG 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 immediately. Blood must be collected into prechilled tubes containing heparin anticoagulant. Immediately immerse plasma samples for uric acid measurement 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 four hours of collection [see Boxed Warning].

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Based on findings in animals, Elitek may cause fetal harm when administered to pregnant women. In animal reproduction studies, intravenous administration of rasburicase to pregnant rabbits during organogenesis at 5 times the human exposure (based on AUC) at the recommended human dose of 0.2 mg/kg resulted in adverse developmental outcomes, including structural abnormalities, embryo-fetal mortality, and alterations to growth (see Data). The limited available data with Elitek use in pregnant women are insufficient to evaluate a drug-associated risk of major birth defects, miscarriage, or adverse maternal/fetal outcomes. Consider the benefits and risks of Elitek and possible risks to the fetus when prescribing Elitek to a pregnant woman.

The estimated background risk of major birth defects and miscarriage in the indicated population is unknown. All pregnancies have a background risk of birth defect, miscarriage, or other adverse outcomes. In a maternal-fetal toxicology study in rabbits, the estimated background risk of major birth defects and miscarriages in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data

Animal data

In clinical administration of rasburicase at doses of 10, 20, or 50 mg/kg/day (approximately 14, 34, and 100 times the exposure at the recommended human dose of 0.2 mg/kg) to pregnant rats from gestation days 6 to 16, no evidence of fetal toxicity was observed. The fetal weight and relative organ weight were similar in the control and the rasburicase-treated groups at doses of 10 and 50 mg/kg/day (approximately 100 times and 500 times the exposure at the recommended human dose). Other observed findings included maternal deaths and postpartum loss, abortion, decreased uterine weight, decreased fetal body weights, and heart rate fluctuations. No abnormalities in fetal development were observed at any dose levels. In a study using rabbits, the doses of 10 and 50 mg/kg/day (approximately 100 and 500 times the exposure at the recommended human dose) caused abortions, malformations, and fetal deaths. The fetal weight and relative organ weight were similar in the control and the rasburicase-treated groups at doses of 10 and 50 mg/kg/day (approximately 100 times and 500 times the exposure at the recommended human dose).

8.2 Lactation

Risk Summary

There are no available data on the presence of rasburicase in human breast milk, the effects on the breast-fed child, or the effects on milk production. Because of the potential for serious adverse reactions in the breast-fed child, advises patients that breastfeeding is not recommended during treatment with Elitek, and for 2 weeks after the last dose.

8.4 Pediatric Use

The safety and effectiveness of Elitek have been established in pediatric patients ages 1 month to 17 years for intravenous administration [see Warnings and Precautions (5.1)] and age, gender, baseline liver enzymes and creatinine clearance did not impact the pharmacokinetics of rasburicase. A cross-study comparison revealed that after administration of rasburicase at 0.15 or 0.20 mg/kg, the geometric mean values of body-weight normalized clearance were approximately 40% lower in Japanese (n=20) than that in Caucasians (n=22).

10.5 mg/dL (patients < 10 mg/dL) or ≤ 7.5 mg/dL (patients ≥ 10 mg/dL). 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 0.2 mg/kg/dose (total daily dose 0.2–0.4 mg/kg/day). Initiation of dosing was permitted at any time between 4 to 48 hours before the start of antitumor therapy and could be repeated 5 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 mg/dL and ≥ 28 mg/dL). The primary study objective was to demonstrate a greater reduction in uric acid concentration over 96 hours (AUC<sub>0–96 hr</sub>) in the Elitek group as compared to the allopurinol group. Uric acid AUC<sub>0–96 hr</sub> was defined as the area under the curve for plasma uric acid levels (mg/hr/mL), 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>0–96 hr</sub> calculations [see Warnings and Precautions (5.4)].

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 therapy (n=24, data not reported for 3 patients). The uric acid AUC<sub>0–24 hr</sub> was significantly lower in the Elitek group (128 ± 4.6 hr/mL) as compared to the allopurinol group (328 ± 5.26 hr/mL). All but one patient in the Elitek arm had reduction of maintenance dose 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.

Study 2

Study 2 was a multi-institutional, single-arm study conducted in 89 pediatric and 18 adult patients with hematologic malignancies. Patients received Elitek at a dose of 0.15 mg/kg/day. The primary efficacy outcome was the proportion of patients with maintained plasma uric acid concentration at 48 hours when maintenance of uric acid concentration was defined as: 1) achievement of uric acid concentration ≤ 5.5 mg/dL (patients < 13 years) or ≤ 7.5 mg/dL (patients ≥ 13 years) within a designated time point (48 hours) from initiation of Elitek and maintained until 24 hours after the last administration of Elitek; and 2) control of uric acid levels (≥ 3 mg/dL) 24 hours after the last administration of Elitek for allopurinol or other agents.

The study population demographics were: age < 13 years (76%), males (61%), Caucasian (91%), ECOG performance status=0 (92%), and leukemia (89%). The proportion of patients with maintenance of uric acid concentration at 48 hours in Study 2 was 99% (106/107).

11 DESCRIPTION

Elitek (rasburicase) is a recombinant urate-oxidase produced by a genetically modified Saccharomyces cerevisiae strain. The cDNA coding for rasburicase was cloned from a strain of Aspergillus flavus.
The study population demographics were: age of patients with maintained plasma uric acid concentration at 48 hours as defined for Study 2 above. (n=12) or 0.2 mg/kg/day (n=119). The primary efficacy objective was determination of the proportion of patients with a per-patient change in plasma uric acid concentration by 4 hours after the first dose was a decrease ≥8 mg/dL in 200 patients. The median uric acid concentration at baseline, at 4 hours following the first dose of Elitek, and the per-patient fall in plasma uric acid concentration from baseline to 4 hours, were calculated in those patients in both the per-patient and 4-hour post-treatment values.

The proportion of patients with maintenance of uric acid concentration at 48 hours in Study 3 was 92% in the 0.15 mg/kg group (n=12) and 95% in the 0.2 mg/kg group (n=119).

Figure 1: Box and Whisker Plot of Uric Acid Concentration at Designated Time Blocks – Elitek Administration Began Immediately After Baseline

Figure 1 is a box and whisker plot of plasma uric acid levels inclusive of 261 of the 265 Elitek-treated patients from Studies 1, 2, and 3. Of the 261 evaluable patients, plasma uric acid concentration was maintained (see Study 2 for the definition of uric acid concentration maintenance) by 4 hours for 92% of patients (245/261), by 24 hours for 95% of patients (245/261), by 48 hours for 97% of patients (245/261), by 72 hours for 99% of patients (245/261), and by 96 hours for 100% of patients (245/261). 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 96 hours for 98% of patients (60/61), and by 96 hours for 100% (61/61).

14.2 Studies in Adults
A total of 342 adults with either leukemia, lymphoma, or other hematologic malignancy received Elitek in five studies (one randomized study, Study 4, and four uncontrolled studies). Across the five studies, Elitek was administered at a dose of 0.15 mg/kg/day (n=38) or 0.2 mg/kg/day (n=204).

Study 4 was a randomized (1:1:1), multi-center, open-label study conducted in patients with leukemia, lymphoma, and solid tumor malignancies at risk for hyperuricemia and TLS. A total of 275 adult patients received at least one dose of study drug. The median age was 56 years, 62% were males, 60% were Caucasian, 29% had lymphoma; 16% were hyperuricemic (uric acid >7.5 mg/dL) at study entry. Patients in Arm A received Elitek 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 and allopurinol administered approximately 12 hours apart) (n=92). Patients in Arm C received oral allopurinol for 5 days (n=91). Elitek was administered at the dose of 0.2 mg/kg/day as a 30-minute infusion once daily. Allopurinol was administered orally at the dose of 300 mg once a day. Patients were eligible for the study if they were either at high risk or potential risk for TLS. The major endpoint of this study was the uric acid response rate defined as the proportion of patients with plasma uric acid levels ≤7.5 mg/dL from day 3 to day 7, after initiation of antihyperuricemic treatment.

The response rate in Arm A was significantly greater than in Arm C (p=0.0009). The response rate was higher for arm B compared to arm C; this difference was not statistically significant.

Table 2: Summary of Response Rates

<table>
<thead>
<tr>
<th></th>
<th>Arm A Elitek n=92</th>
<th>Arm B Elitek/Allopurinol n=92</th>
<th>Arm C Allopurinol n=91</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response Rate % (95% CI)</td>
<td>87% (80%, 94%)</td>
<td>78% (70%, 87%)</td>
<td>66% (56%, 76%)</td>
</tr>
<tr>
<td>Nonsponse Rate %</td>
<td>13%</td>
<td>22%</td>
<td>34%</td>
</tr>
<tr>
<td>Failed to control uric acid</td>
<td>0</td>
<td>0</td>
<td>11%</td>
</tr>
</tbody>
</table>

Table 2: Summary of Response Rates (continued)

<table>
<thead>
<tr>
<th></th>
<th>Arm A Elitek n=92</th>
<th>Arm B Elitek/Allopurinol n=92</th>
<th>Arm C Allopurinol n=91</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hyperuricemic treatment extended beyond 5 days</td>
<td>0</td>
<td>6.5%</td>
<td>4.4%</td>
</tr>
<tr>
<td>Missing uric acid samples</td>
<td>13%</td>
<td>15%</td>
<td>19%</td>
</tr>
</tbody>
</table>

There were no patients with documented failure to control uric acid in arms A or B. In arm C, 34% of patients did not have a uric acid response; 11% due to failure to control uric acid and 4.4% due to the need for extended antihyperuricemic treatment.

Figure 2: Uric Acid Concentration Over Time – Patient Population Box and Whisker Plot

Tumor Lysis Syndrome (TLS)
Clinical TLS was defined by changes in at least two or more laboratory parameters for hyperuricemia, hyperkalemia, hyperphosphatemia and hypocalcemia and at least one of the following events occurring within 7 days of treatment: renal failure/injury; need for renal dialysis, and/or serum creatinine increase >1.5 ULN, arrhythmia or seizure. Clinical TLS occurred in 3% of Elitek-treated patients, 3% of Elitek/allopurinol-treated patients, and 4% of allopurinol-treated patients.

16 HOW SUPPLIED/STORAGE AND HANDLING
How Supplied
NDC 0024-5150-10: One carton contains 3 single-dose vials each containing 1.5 mg of rasburicase and 3 ampules each containing 1 mL diluent.
NDC 0024-5151-75: One carton contains 1 single-dose vial containing 7.5 mg of rasburicase and 1 ampule containing 5 mL diluent.

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

17 PATIENT COUNSELING INFORMATION
Hypersensitivity Reactions
Instruct patients to notify their physician immediately if any of the following occur: allergic reaction, bronchospasm, chest pain or tightness, dyspnea, hypoxia, hypotension, shock or urticaria [see Boxed Warning, Warnings and Precautions (5.1)].

Lactation
Advise females not to breastfeed during treatment with Elitek and for at least 2 weeks after the last dose [see Use in Specific Populations (8.2)].

Manufactured by:
sanofi-aventis U.S. LLC
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