

## **Indication and Limitations of Use**

- Voraxaze® (glucarpidase) is indicated for the treatment of toxic plasma methotrexate concentrations ( $>1 \mu\text{mol/L}$ ) in patients with

delayed methotrexate clearance due to impaired renal function

- Voraxaze® is not indicated for use in patients who exhibit the expected clearance of methotrexate (plasma methotrexate concentrations within 2 standard deviations of the mean methotrexate excretion curve specific for the dose of methotrexate administered) or those with normal or mildly impaired renal function because of the potential risk of subtherapeutic exposure to methotrexate

## **Important Safety Information**

### **Adverse Reactions**

- In clinical trials, the common related adverse events (occurring in  $>1\%$  of patients) were paresthesias, flushing, nausea and/or vomiting, hypotension, and headache

### **Warnings and Precautions**

#### **Serious Allergic Reactions**

- Serious allergic reactions, including anaphylactic reactions, may occur

#### **Monitoring Methotrexate Concentration/Interference With Assay**

- Methotrexate concentrations within 48 hours following Voraxaze® administration can only be reliably measured by a chromatographic method due to interference from metabolites. Measurement of methotrexate concentrations within 48 hours of Voraxaze® administration using immunoassays can overestimate the methotrexate concentration

#### **Continuation and Timing of Leucovorin Rescue**

- Leucovorin should not be administered within 2 hours before or after Voraxaze® dose because leucovorin is a substrate for Voraxaze®
- For the first 48 hours after Voraxaze®, administer the same leucovorin dose as given prior to Voraxaze®. Beyond 48 hours after Voraxaze®, administer leucovorin based on the measured methotrexate concentration
- Do not discontinue therapy with leucovorin based on the determination of a single methotrexate concentration below the leucovorin treatment threshold
- Therapy with leucovorin should be continued until the methotrexate concentration has been maintained below the leucovorin treatment threshold for a minimum of 3 days
- Continue hydration and alkalinization of the urine as indicated