VORAXAZE® ▼(glucarpidase) 1,000 units powder for solution for injection.

Please consult Summary of Product Characteristics (SmPC) before prescribing.

Presentation & composition: White to off-white powder for solution for injection.

Indication: To reduce toxic plasma methotrexate concentration in adults and children (aged 28 days and older) with delayed methotrexate elimination.

Dosage: A single dose of 50 units per kilogram (kg) by bolus intravenous (IV) injection over 5 minutes. Once diagnosis of delayed methotrexate (MTX) elimination or risk of toxicity is established, glucarpidase should be administered without delay, the optimal window is within 48-60 hours from the start of the high dose MTX (HDMTX) infusion. Folinic acid should not be administered within the 2 hours before or after glucarpidase administration. No dose adjustment is recommended for patients with renal impairment. No dose adjustment is required for the paediatric population.

Administration: Glucarpidase is intended for use under medical supervision. In order to take into account all MTX doses and infusion durations that could be administered to a patient, it is recommended to utilise local or national treatment protocols or guidelines if available, to determine when glucarpidase should be administered.

Recommendations for intervention with glucarpidase are considered when plasma MTX levels are greater than 2 standard deviations of the mean expected MTX excretion curve. Administration of Glucarpidase should optimally occur within 60 hours from the start of the HDMTX infusion as life threatening toxicities may not be preventable beyond this time point. Recommendations for intervention with glucarpidase are detailed below:

MTX Dose:	**≤ 1 g/m²**	**1-8 g/m²**	**8-12 g/m²**
Infusion duration:	Over 36-42 hours	Over 24 hours	Over ≤ 6 hours
Hours following start of MTX infusion	Threshold plasma MTX concentration (µM)		
24 hours	-	-*	≥ 50
36 hours	-	≥ 30	≥ 30
42 hours	-	≥ 10	≥ 10
48 hours	≥ 5	≥ 5	≥ 5

* Start supportive care when ≥ 120 µM.

As a further guide for patients receiving short infusion MTX regimens, glucarpidase administration may be considered as detailed below:

MTX Dose:	**3-3.5 g/m²**	**5 g/m²**
Hours following start of MTX infusion	Threshold plasma MTX concentration (µM)	
24 hours	≥ 20	-
36 hours	-	≥ 10
48 hours	≥ 5	≥ 6

Contraindications: Hypersensitivity to active substance or excipients (lactose, trometamol, zinc acetate dihydrate).

Warnings & Precautions:
Traceability:
In order to improve the traceability of biological medicinal products, the tradename and the batch number of the administered product should be clearly recorded.

Paediatric population:
No formal evaluation of the effect of age on the pharmacokinetics of glucarpidase has been performed.

It is important to measure baseline plasma MTX concentrations and renal function and to continue to monitor these throughout treatment with high dose MTX therapy. A high performance chromatography (HPLC) method is recommended for measuring MTX concentrations following glucarpidase administration. Glucarpidase does not reverse pre-existing renal damage or renal failure that occurs as a consequence of MTX administration, but instead removes MTX to reduce the risk of sustaining further renal toxicity. As such, other supportive care, including hydration and alkalinisation of the urine, should be started at the onset of MTX administration and continued in accordance with local treatment guidelines. Allergic type hypersensitivity reactions are possible following administration of glucarpidase, see SmPC.

Interactions: Glucarpidase can decrease folinic acid concentration, which may decrease the effect of folinic acid rescue unless it is dosed as recommended. Glucarpidase may also reduce the concentrations of other folate analogs or folate analog metabolic inhibitors.

Fertility, Pregnancy and lactation: It is unknown whether glucarpidase causes harmful effects during pregnancy and/or on the foetus/newborn child or whether it can affect reproductive capacity. There is no data for the use of Glucarpidase in pregnant women. Glucarpidase should only be given to a pregnant woman if clearly needed. It is unknown whether glucarpidase/metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded. It is unknown whether glucarpidase affects fertility.

Driving and machines: Glucarpidase has no or negligible influence on the ability to drive and use machines.

Undesirable effects:
Uncommon: Nervous system disorders (burning sesation, headache, paraesthesia), Vascular disorders (flushing), General disorders (feeling hot). **Rare**: Immune system disorders (hypersensitivity), Nervous system disorders (hypoesthesia, somnolence, tremor), Vascular disorders (hypotension), Gastrointestinal disorders (abdominal pain upper, diarrhoea, nausea, vomiting), Skin and subcutaneous tissue disorders (pruritis, rash and General disorders (pyrexia, rebound effect). **Very rare**: Immune system disorders (anaphylactic reaction), Cardiac disorders (tachycardia), Skin and subcutaneous tissue disorders (including drug eruption, skin reaction), Renal disorders (crystalluria) and General disorders (infusion site reaction). See SmPC for further details.

Legal classification: POM

NHS Price: £25385.00

UK (Great Britain) Marketing Authorisation number: PLGB 18442/0002

Marketing Authorisation Holder: Protherics Medicines Development Limited, Blaenwaun Ffostrasol Llandysul Ceredigion, SA44 5JT

Job code: UK-VRX-2200024

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Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to vigilance@btgsp.com