Glucarpidase (Voraxaze®) for the Treatment of Methotrexate-induced Renal Dysfunction

Introduction:
Glucarpidase is an orphan medicine that is commissioned by NHS England for the urgent treatment of methotrexate-induced renal dysfunction. It is unlicensed in the UK and only available on a named-patient basis.

Background:
Methotrexate is an anti-folate medicine used in the treatment of autoimmune conditions and some cancers. When used in high doses precipitation of methotrexate and its metabolites in the renal tubules can lead to life-threatening acute renal dysfunction. A delay in the excretion of methotrexate results in elevated plasma concentrations and the potential for additional life-threatening toxicities.

Patients receiving high dose methotrexate will receive aggressive fluid resuscitation to improve methotrexate solubility, alongside folinate rescue to counteract the effects of methotrexate. In some patients, however, severe and fatal nephrotoxicity may occur.

Glucarpidase works by rapidly hydrolysing methotrexate into inactive non-cytotoxic metabolites that can be cleared by alternative routes of elimination.

Indication:
Treatment of methotrexate-induced renal dysfunction in patients receiving high-dose methotrexate chemotherapy (doses > 1g/m²) who:

- develop a significant deterioration in renal function after the start of treatment (serum creatinine ≥ 1.5xULN and rising, or the presence of oliguria)
- have toxic plasma methotrexate levels (>1micromole/L)
- have been treated with rescue measures
- are at risk of life-threatening methotrexate-induced toxicities
- have had optimisation of all other supportive measures e.g. fluids, folinic acid

All of the above criteria must be met in order for glucarpidase to be funded by NHS England. The decision to use glucarpidase must be approved by a consultant oncologist or haematologist.

Dose:
A single dose of 50 units/kg administered via IV injection over 5 minutes.

Administration:
Reconstitute each vial with 5ml of sodium chloride 0.9%. Roll and tilt the vial gently to mix. Flush the line before and after use.

Caution:
Severe allergic reaction (including anaphylaxis) may occur. Monitor the patient and ask them to report any signs and symptoms of an infusion reaction e.g. fever, chills, flushing, rash, hives, itching, throat tightness or breathing problems, tingling, numbness or headache.
Do not administer calcium folinate within 2 hours of glucarpidase.

Do not co-prescribe medicines that reduce methotrexate excretion e.g. NSAIDS, ciprofloxacin, co-trimoxazole, penicillin, probenecid, proton pump inhibitors & piperacillin-tazobactam.

**Ordering information:**
Glucarpidase is not stocked at GHNHSFT. Glucarpidase is manufactured in the USA and distributed by WEP Clinical on a named-patient basis. Blueteq funding is not required.

Glucarpidase vials are ordered in multiples of 2 up to a maximum of 6 vials. Each vial contains 1000 units and must be stored between 2 – 8°C. The price for 2 vials is £34,160.

It is anticipated that delivery turnaround will be within 24 hours.

Order via a member of the pharmacy cancer services team (ext. 2537 or 3367) during normal working hours or via the on call pharmacist outside of normal working hours.

**Useful information:**
Glucarpidase reduces methotrexate levels by >98% within 15 minutes.

No dose adjustment is required in patients with renal impairment. There is no information on the use of glucarpidase in patients with hepatic impairment.

**Monitoring:**
Samples taken within 48 hours of administration of glucarpidase will be unreliable for determining methotrexate levels. For the 48 hours post administration of glucarpidase work out the dose of calcium folinate based on the methotrexate level prior to glucarpidase administration. Continue calcium folinate treatment once methotrexate levels <0.1 for a minimum of 3 days.

**References:**


Correspondence with WEP Clinical, November 2020

Glucarpidase Emergency Supply Form, WEP Clinical