RASBURICASE powder and solvent for concentrate for solution for infusion (Fasturtec®) for severe, refractory, tophaceous gout

The Pan Mersey Area Prescribing Committee does not recommend the prescribing of RASBURICASE powder and solvent for concentrate for solution for infusion (Fasturtec®) for severe, refractory, tophaceous gout.

BLACK

Rasburicase is licensed for the treatment and prophylaxis of acute hyperuricaemia, in order to prevent acute renal failure, in adults, children and adolescents (aged 0 to 17 years) with haematological malignancy with a high tumour burden and at risk of a rapid tumour lysis or shrinkage at initiation of chemotherapy.[1]

Rasburicase is a tariff excluded drug and funding falls with NHS England for its licensed indication. However, it has been confirmed that for the "off label" use of rasburicase for the treatment of severe, refractory, tophaceous gout, commissioning responsibility lies with local CCGs.

An application was submitted for the above "off label" indication as there are no further treatment options to reduce uric acid for these patients as described above.

The Pan Mersey Area recommendation was made on the following grounds:

- There is very little evidence, limited to a small number of case series, for the use of this drug in the indication as described above to justify a local decision to recommend prescribing of this drug.[2-6]

Note: Patients who are not eligible for treatment under this statement may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. In this situation, follow locally defined processes.

Supporting information

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Effectiveness

In some patients with chronic gout, xanthine oxidase inhibitors and uricosuric agents fail to work and control uric acid levels which results in the development of tophi depositing in different areas of soft tissue. The development of tophi can be severely debilitating. The human body is not able to break down uric acid which results in the formation of tophi. Rasburicase is a form of recombinant urate-oxidase that catalyses the oxidation of uric acid to allantoin, which is water soluble and can be excreted in the urine.[1] The use of rasburicase is therefore based on mechanism of action. There are a small number of case series that describe its use in patients who are allergic to allopurinol or are refractory.[2-6] The case studies results demonstrated that rasburicase reduces serum uric acid levels and had the potential to reduce the size of tophi, however the evidence is poor.[2-6]

From the available reviews, the main paper that is discussed is Richette et al.[2] The study had 10 patients included and rasburicase use was evaluated.

Different experimental applications of rasburicase; 0.2 mg/kg daily (group 2, n=5) vs 0.2mg/kg monthly (group 1, n=4) in patients with tophaceous gout not treatable by allopurinol. In the treatment group proposed to Pan Mersey (group 1) the dose and schedule proposed was 200 micrograms/kg by intravenous infusion administered every 4 weeks. Uric acid levels declined progressively during the six months significantly from baseline (p=0.001) in group 1. In 2 of the 4 patients of group 1 there was a change in tophus area. In group 2, rapid reduction of uric acid was seen but at 2 months, levels were not significantly lower than baseline and there was no reduction in tophi. Monthly injections were the most efficacious based on evidence available.

SAFETY [1,2]

Rasburicase is prescribed and administered as an intravenous infusion in secondary care only.

There is risk of development of antibodies to this drug and therefore the risk of infusion related reactions may increase the longer the patient is on the drug.

The most common side effects with rasburicase (seen in more than 1 patient in 10) are nausea (feeling sick), vomiting, headache, fever and diarrhoea. Risk of infusion related reactions including anaphylaxis have also been observed.

Rasburicase is contraindicated and must not be used in patients with a deficiency in (low levels of) glucose 6 phosphate dehydrogenase (G6PD) or other metabolic disorders known to cause haemolytic anaemia (low haemoglobin levels caused by the abnormal breakdown of red blood cells).

Likely acute flare up of gout as with any drugs that rapidly lower serum uric acid levels.

Refer to SPC for full safety information.

Cost[7]

Dose: 200 micrograms per kilogram.
Frequency: Monthly IV infusion
Pack Cost: 1.5mg powder in vial, 3 vials =£208.39.
7.5mg powder in vial, 1 vial =£347.32

Patient factors

It is rare to have such severe disease and so patient numbers are likely to be small.
Severe, tophaceous gout which is refractory to standard treatments affects all joints and is severely debilitating.
The uncontrolled raised uric acid level also poses significant cardiovascular risk to the patients and increases the risk of myocardial infarction.
Acute flares will be managed with the use of corticosteroids, colchicine and etoricoxib where clinically appropriate.

Prescribing information

Rasburicase is not recommended for the treatment of severe, refractory, tophaceous gout.

Supporting information

References

1. Sanofi. Summary of Product Characteristics -Fasturtec 1.5 mg/ml powder and solvent for concentrate for solution for infusion, January 2016. Accessed 05 June 2019 at: http://www.medicines.org.uk/emc/medicine/4604

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7. NHSBA Dictionary of Medicine and Devices (dm+d Browser). Accessed 15 July 2019