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Voraxaze (*glucarpidase*)

An overview of Voraxaze and why it is authorised in the EU

What is Voraxaze and what is it used for?

Voraxaze is a medicine used to lower the level of methotrexate (a cancer medicine) in the blood of adults and children older than 28 days whose body is not able to remove methotrexate quickly enough or who are at risk of methotrexate toxicity (when methotrexate is harmful to normal cells and organs in the body).

Methotrexate toxicity is rare, and Voraxaze was designated an 'orphan medicine' (a medicine used in rare diseases) on 3 February 2003. Further information on the orphan designation can be found here: ema.europa.eu/medicines/human/orphan-designations/eu-3-02-128.

Voraxaze contains the active substance glucarpidase.

How is Voraxaze used?

Voraxaze can only be obtained with a prescription and should be used under the supervision of a healthcare professional. It is given as a single injection into the vein within 48 to 60 hours of the start of the methotrexate infusion (drip) when the patient is at risk of methotrexate toxicity (based on the level of methotrexate in the blood).

Voraxaze is used with other medicines to treat methotrexate toxicity and supportive measures, such as giving fluids.

For more information about using Voraxaze, see the package leaflet or contact your doctor or pharmacist.

How does Voraxaze work?

Methotrexate stops cells from growing by interfering with the production of DNA. This especially affects fast-growing cells such as cancer cells. However, methotrexate can also be harmful to other normal cells and organs in the body. This harmful effect is called methotrexate toxicity. Methotrexate toxicity is a life-threatening condition.

Glucarpidase, the active substance in Voraxaze, is a protein that can transform methotrexate in the blood into harmless substances. Thus, the amount of methotrexate in the blood is lowered, and the

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risk of toxicity is reduced. Since glucarpidase does not enter cells, it does not stop any methotrexate already inside cancer cells from treating the cancer.

What benefits of Voraxaze have been shown in studies?

Four studies involving patients at risk of methotrexate toxicity found that Voraxaze was effective at achieving a clinically important reduction (CIR) in the level of methotrexate in the blood (in other words, to a level where methotrexate no longer causes harm). The studies looked at 169 patients in whom the level of methotrexate had been measured using a method called high-performance liquid chromatography (HPLC) at least once after the first dose of Voraxaze. Voraxaze was not compared with other treatments.

The first study involved patients who were at risk of methotrexate toxicity due to reduced kidney function or because they had received too much methotrexate intrathecally (by injection into the fluid surrounding the spinal cord). Treatment with Voraxaze achieved a CIR in the level of methotrexate in the blood in 24 out of 28 (85.7%) patients.

Two studies involved patients who were unable to clear methotrexate from their body because of reduced kidney function. In these studies, treatment with Voraxaze achieved a CIR in the methotrexate blood level in 14 out of 27 (51.9%) and 20 out of 30 (66.7%) patients.

In the last study, patients who were unable to clear methotrexate from their body because of reduced kidney function were given Voraxaze alone or with thymidine (another treatment to lower the level of methotrexate). Of these patients, 46 out of 84 patients (54.8%) achieved a CIR in methotrexate levels in the blood. Of the patients who received Voraxaze and thymidine, 50% achieved a CIR in methotrexate, compared with 59.5% of those receiving Voraxaze alone.

Overall, across the four studies, the average level of methotrexate decreased by between 96.8% and 99.3% within 15 minutes of the first dose of Voraxaze. In addition, the level of methotrexate remained stable for 8 to 15 days.

What are the risks associated with Voraxaze?

The most common side effects with Voraxaze (which may affect up to 1 in 10 people) are burning sensation, headache, paraesthesia (sensations like numbness, tingling, pins and needles), flushing and feeling hot.

For the full list of side effects and restrictions of Voraxaze, see the package leaflet.

Why is Voraxaze authorised in the EU?

Methotrexate toxicity is a serious, life-threatening condition that happens when the medicine is not adequately removed by the kidneys and builds up in the blood and the whole body. In patients who are at risk of methotrexate toxicity, Voraxaze causes a rapid and large decrease in the levels of methotrexate in the blood, which remain low for up to 15 days after treatment. Although there are limited data on the safety of Voraxaze, the European Medicines Agency considered that the side effects after one dose of Voraxaze are acceptable given the seriousness of methotrexate toxicity. The Agency therefore decided that Voraxaze's benefits are greater than its risks and it can be authorised for use in the EU.

Voraxaze has been authorised under 'exceptional circumstances'. This is because it has not been possible to obtain complete information about Voraxaze due to the rarity of the condition. Every year,

the Agency will review any new information that becomes available and this overview will be updated as necessary.

What information is still awaited for Voraxaze?

Since Voraxaze has been authorised under exceptional circumstances, the company that markets Voraxaze will provide further data on the safety and effectiveness of Voraxaze in patients who are unable to adequately clear methotrexate from their body.

What measures are being taken to ensure the safe and effective use of Voraxaze?

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Voraxaze have been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Voraxaze are continuously monitored. Suspected side effects reported with Voraxaze are carefully evaluated and any necessary action taken to protect patients.

Other information about Voraxaze

Voraxaze received a marketing authorisation under exceptional circumstances valid throughout the EU on 11 January 2022.

Further information on Voraxaze can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/voraxaze.

This overview was last updated in 01/2022.