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Upstaza (eladocagene exuparvovec)

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

What is Upstaza and what is it used for?

Upstaza is a gene therapy medicine that is used in adults and children aged 18 months and older with severe aromatic L-amino acid decarboxylase (AADC) deficiency with a genetically confirmed diagnosis.

AADC deficiency is an inherited disease that affects the nervous system leading to symptoms such as developmental delays, weak muscle tone and inability to control the movement of the limbs.

AADC deficiency is rare, and Upstaza was designated an 'orphan medicine' (a medicine used in rare diseases) on 18 November 2016. Further information on the orphan designation can be found here: ema.europa.eu/medicines/human/orphan-designations/eu3161786.

Upstaza is a type of advanced therapy medicine called a 'gene therapy product'. This is a type of medicine that works by delivering genes into the body.

Upstaza contains eladocagene exuparvovec, a functional version of the AADC gene within a modified virus (adeno-associated viral vector). The virus used in this medicine is not known to cause a disease in humans.

How is Upstaza used?

Upstaza can only be obtained with a prescription and must be given in an operating room under anaesthetic by a doctor who is experienced in brain surgery. It is given by infusion into the brain. After infusion the patient has a brain scan. The doctor will monitor recovery and check for any side effects from the surgery and treatment.

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

How does Upstaza work?

AADC deficiency is caused by mutations in the gene that produces the AADC enzyme. This enzyme is needed to produce dopamine, a neurotransmitter that is important for controlling movement. Patients with AADC deficiency do not have a properly working version of the enzyme, resulting in very little or no dopamine production in the brain. The medicine consists of a virus that contains a working version of the AADC gene. When given to the patient, it is expected that the virus will carry the AADC gene

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into nerve cells, enabling them to produce the missing enzyme. This in turn is expected to enable the cells to produce the dopamine they need to work properly, thus improving symptoms of the condition.

What benefits of Upstaza have been shown in studies?

Benefits of Upstaza were shown in three main studies involving 28 children aged 1.5 to 8.5 years with severe AADC deficiency confirmed by a genetic test. The main measures of effectiveness were head control and the ability to sit unassisted. The studies showed that around 70% (14 out of 20) of patients were able to control head movement and around 65% (12 out of 20) of patients could sit unassisted two years after treatment. Data from scientific literature showed that patients with severe AADC deficiency who had not received any treatment could not achieve these developmental milestones.

What are the risks associated with Upstaza?

The most common side effect with Upstaza (which may affect more than 1 in 10 people) is dyskinesia (uncontrollable movements).

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

Why is Upstaza authorised in the EU?

Three main studies have shown that Upstaza is effective at improving the ability to control head movement and to sit in patients with AADC deficiency. Because AADC deficiency is a very rare disease, the study was small but the short-term data available indicated that Upstaza could be effective at achieving important developmental milestones in children. Although the data on the safety of Upstaza are limited, the side effects seen to date are considered manageable. The European Medicines Agency decided that Upstaza's benefits are greater than its risks and it can be authorised for use in the EU, also in adults with AADC deficiency, given the seriousness of the condition and the lack of existing treatments.

Upstaza has been authorised under 'exceptional circumstances'. This means that, because the indication is encountered so rarely, it has not been possible to obtain full information about the medicine. Every year, the European Medicines Agency will review any new information that becomes available and this overview will be updated as necessary.

What information is still awaited for Upstaza?

Since Upstaza has been authorised under exceptional circumstances, the company that markets Upstaza will provide additional data from ongoing studies and carry out a new study to further characterise the long-term safety and effectiveness of Upstaza.

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

The company that markets Upstaza must ensure that hospitals where Upstaza is given have appropriate expertise, facilities and training.

The company must provide educational materials for healthcare professionals and patients about the surgical procedure and possible side effects.

The company must also provide additional data to further show that Upstaza is consistently manufactured with the same quality standards.

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

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

Other information about Upstaza

Upstaza received a marketing authorisation valid throughout the EU on 18 July 2022.

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

This overview was last updated in 07-2022.