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Skysona (*elivaldogene autotemcel*)

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

What is Skysona and what is it used for?

Skysona is a medicine used to treat children under 18 years of age with early cerebral adrenoleukodystrophy (CALD). CALD is a rare inherited disorder in which there is a change (mutation) in the *ABCD1* gene. The mutation prevents the production of an enzyme called ALDP (adrenoleukodystrophy protein), which breaks down fatty substances in the body called very long-chain fatty acids (VLCFAs). As a result, VLCFAs build up and lead to inflammation and destruction of the protective sheath (myelin) that insulates and improves the way the nerves function. CALD is seen almost exclusively in males.

Skysona is given when a donor for a haematopoietic stem cell transplantation (a procedure where the patient's bone marrow is cleared of cells and replaced with healthy bone marrow cells) is not available.

Skysona is a type of advanced therapy medicine called 'gene therapy'. This type of medicine works by delivering genes into the body. The active substance in Skysona, elivaldogene autotemcel, is made of stem cells (CD34+ cells), derived from the patient's own bone marrow or blood, that have been modified to contain a copy of the gene to make a functional ALDP and can divide to produce other sorts of blood cells.

CALD is rare, and Skysona was designated an 'orphan medicine' (a medicine used in rare diseases) on 13 April 2007. Further information on the orphan designation can be found here: https://www.ema.europa.eu/en/medicines/human/orphan-designations/eu3121003

How is Skysona used?

Skysona can only be given to the patient whose cells were used to make the medicine. It is a single treatment given as an infusion (drip) into a vein, and the dose depends on the patient's weight. A few days before treatment, another medicine, such as busulfan, is given as a so-called conditioning treatment to clear out existing bone marrow cells and replace them with the modified cells in Skysona.

Skysona can only be obtained with a prescription, and treatment should only be given in a specialist centre by a physician with experience in haematopoietic stem cell transplantation and the treatment of patients with nervous system disorders.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000 An agency of the European Union

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

How does Skysona work?

To make Skysona, the CD34+ cells (cells that can make white blood cells) are extracted from the blood or bone marrow. A gene allowing them to make ALDP is inserted into the CD34+ cells using a type of virus called a lentivirus, which has been genetically altered to carry the ALDP gene into cells while not causing a viral disease in humans.

Once given back into the patient's vein, Skysona is transported in the bloodstream to the bone marrow, where the CD34+ cells start to grow and make normal white blood cells that can produce ALDP. These white blood cells spread through the body and produce ALDP, which helps to break down fatty substances in the surrounding cells and control symptoms of the disease. The effects are expected to be long lasting.

What benefits of Skysona have been shown in studies?

The benefits of Skysona in treating CALD were shown in a main study involving 30 boys aged 4 to 14 years with early CALD.

After two years, 90% of the treated boys showed no signs of major nerve damage, such as loss of ability to speak, loss of ability to feed themselves, dependence on wheelchair, blindness or incontinence. This could be compared with 29% in a similar group of untreated boys from a separate study.

Also, around 96% of the boys experienced a stable Gross Neurological Function Measure score (a value measuring a developing child's ability to make normal movements such as crawling, standing and walking) after two years. There was evidence of continuing benefit after up to 8 years.

What are the risks associated with Skysona?

The most common side effect with Skysona (which may affect more than 1 in 10 people) is pancytopenia (low blood cell counts).

For the full list of side effects of Skysona, see the package leaflet.

When using Skysona, the restrictions for a conditioning treatment and mobilisation agents must be taken into account. For the full list of restrictions, see the package leaflet.

Why is Skysona authorised in the EU?

Skysona was shown to stabilise disease by preventing further inflammation and destruction of the myelin of nerve cells in patients with CALD two years after treatment, based on results of a main study. Although the beneficial effects with Skysona lasted several years, it is not yet clear whether it can persist for life, and extended follow-up is needed. Because CALD is a rare disease, the studies are small, and the available data on side effects are limited and will also need long-term follow-up. However, side effects seen to date were in line with those expected for this type of treatment. Given the seriousness of the condition and the lack of existing treatments, the European Medicines Agency decided that Skysona's benefits are greater than its risks, and it can be authorised for use in the EU.

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

The company that markets Skysona will carry out and submit the results of two long-term studies to provide further information on the benefits and safety of the medicine. In addition, the company will provide educational materials for healthcare professionals and patients or their carers on how Skysona is to be used and how patients should be monitored. Patients will also receive a patient alert card about their treatment to show when receiving healthcare.

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

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

Other information about Skysona

Skysona received a marketing authorisation valid throughout the EU on 16 July 2021.

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

This overview was last updated in 07-2021.