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Libmeldy (*autologous CD34+ cell enriched population that contains haematopoietic stem and progenitor cells transduced* ex vivo *using a lentiviral vector encoding the human arylsulfatase A gene*)

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

What is Libmeldy and what is it used for?

Libmeldy is a medicine used to treat children with metachromatic leukodystrophy (MLD). MLD is a rare inherited disorder in which there is a change (mutation) in a gene needed to make an enzyme called arylsulfatase A (ARSA), which breaks down substances called sulfatides. As a result, sulfatides build up and damage the nervous system and other organs, causing symptoms such as walking difficulties, gradual mental deterioration and eventual death.

Libmeldy is used in children with MLD who have mutations in the ARSA gene. It is given to

- those with late infantile or early juvenile forms of the disease who have not yet developed symptoms;
- those with early juvenile MLD who have initial symptoms but can still walk independently and have not yet developed mental deterioration.

Libmeldy is a type of advanced therapy medicine called a 'gene therapy'. This type of medicine works by delivering genes into the body. The active substance in Libmeldy is 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 ARSA and can divide to produce other sorts of blood cells.

MLD is rare, and Libmeldy 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: ema.europa.eu/medicines/human/orphan-designations/eu307446.

How is Libmeldy used?

Libmeldy can only be obtained with a prescription and treatment should only be given in a specialist transplant centre.

To prepare Libmeldy, a sample containing stem cells is collected either from the patient's bone marrow or blood. These are modified to make Libmeldy by including a copy of the gene to make ARSA.

Libmeldy 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, busulfan, is given as a so-called conditioning treatment, to clear out existing bone marrow cells so they can be replaced with the modified cells in Libmeldy. Patients are also given other medicines before treatment to reduce the risk of reactions.

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

How does Libmeldy work?

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

Once given back into the patient's vein, Libmeldy 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 working ARSA. These white blood cells spread through the body and produce ARSA, helping to break down sulfatides in the surrounding cells, and so controlling symptoms of the disease. The effects are expected to be long-lasting.

What benefits of Libmeldy have been shown in studies?

The benefits of Libmeldy in treating MLD were shown in a main study involving 20 children with late infantile or early juvenile MLD. ARSA activity increased in all the children to levels above or within the range for healthy children within 3 months of treatment. After 2 years, the overall Gross Motor Function Measure score (a value between 0 and 100 measuring a developing child's ability to make normal movements such as crawling, standing and walking) was 72.5 in the group with late infantile MLD, compared to 7.4 in records of similar untreated children. Similarly, in children with early juvenile MLD, the average score 2 years after treatment with Libmeldy was 76.5, whereas that in previous untreated cases was 36.3. Benefit was greatest in children who had not yet developed symptoms and seemed to be lost in those who could no longer walk independently or had developed mental deterioration.

There was evidence of continuing benefit on follow-up for up to 8 years.

What are the risks associated with Libmeldy?

The most common side effect with Libmeldy (which may affect more than 1 in 10 people) is development of antibodies to ARSA, although this does not seem to affect how well Libmeldy works. As a result of the conditioning treatment with busulfan, low white cell counts, sometimes with fever (a sign of infection), metabolic acidosis (imbalance in the body's acid levels), stomatitis (mouth inflammation), vomiting, hepatomegaly (enlarged liver), veno-occlusive liver disease (when blood vessels to the liver become blocked causing liver damage) and ovarian failure in girls are also very common.

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

Libmeldy must not be used in patients who have had previous gene therapy involving blood stem cells, or in those who cannot be given the medicines needed to prepare them for producing or receiving Libmeldy. For the full list of restrictions, see the package leaflet.

Why is Libmeldy authorised in the EU?

The benefits of Libmeldy in patients with MLD who had not yet developed symptoms were clear, and during the study period patients maintained similar progress to healthy subjects. Benefit was less marked and more variable in those with early juvenile MLD who already have symptoms, so use in this group was restricted to those who can still walk and have not developed decline in mental function.

Although benefit with Libmeldy lasted several years it is not yet clear whether it will persist life-long, and extended follow-up is needed. Because MLD is a rare disease, the studies are necessarily small and the amount of data available on side effects is 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 Libmeldy'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 Libmeldy?

The company that markets Libmeldy will carry out a long-term study to provide further information on the benefits and safety of the medicine, and will take steps to ensure that patients who qualify for the treatment can have the medicine produced quickly so they can be treated as early as possible, before symptoms start or progress. In addition, the company will provide educational materials for healthcare professionals and patients or their carers on how Libmeldy is to be used and monitored, and a patient alert card about their treatment for patients to show when receiving healthcare.

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

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

Other information about Libmeldy

Libmeldy received a marketing authorisation valid throughout the EU on 17 December 2020.

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

This overview was last updated in 12-2020.