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Public summary of opinion on orphan designation

Dimethyl fumarate for the treatment of adrenoleukodystrophy

On 9 January 2020, orphan designation EU/3/19/2236 was granted by the European Commission to Consorcio Centro de Investigación Biomédica en Red, M.P, Spain, for dimethyl fumarate for the treatment of adrenoleukodystrophy.

What is adrenoleukodystrophy?

Adrenoleukodystrophy (ALD) is an inherited disease in which there is a build-up of fatty substances known as 'very long chain fatty acids' (VLCFAs) in tissues around the body, mainly in the brain and spinal cord and in the adrenal glands, the small glands above the kidneys.

The condition, which affects mostly males, is caused by abnormalities in a gene called *ABCD1* which is responsible for the production of the protein needed to break down VLCFAs and prevent their build-up in tissues.

In the brain and spinal cord, the build-up of VLCFAs leads to toxic forms of oxygen causing damage and inflammation to the protective insulation (myelin) around the nerves, causing a wide range of neurological problems that usually worsen over time. In the adrenal glands, the build-up prevents the glands from working properly and producing hormones such as cortisol. Symptoms of the condition include behavioural problems, problems with vision, hearing and coordination, seizures (fits) and dementia.

ALD is a life-threatening and long-term debilitating condition due to the progressive damage to the brain and nerves.

What is the estimated number of patients affected by the condition?

At the time of designation, ALD affected less than 0.4 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 21,000 people*, and is below the ceiling for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

*Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed on the basis of data from the European Union (EU 28), Norway, Iceland and Liechtenstein. This represents a population of 518,400,000 (Eurostat 2019).

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What treatments are available?

At the time of designation, there was no satisfactory treatment authorised in the EU for ALD. Haematopoietic (blood) stem-cell transplantation (a procedure where the patient's bone marrow is cleared of cells and replaced by stem cells from a donor to form new bone marrow that produces healthy blood cells) had been used in some patients. Corticosteroids were also used to replace hormones that the adrenal glands normally produce.

How is this medicine expected to work?

Dimethyl fumarate, which is authorised for treating multiple sclerosis, is thought to work by activating a protein called Nrf2, which can reduce inflammation and protect cells against toxic forms of oxygen. The medicine is expected to reduce damage to the nerves and improve neurological symptoms of the condition.

What is the stage of development of this medicine?

The effects of dimethyl fumarate have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with dimethyl fumarate in patients with ALD had been started.

At the time of submission, dimethyl fumarate was authorised in the EU for multiple sclerosis and for psoriasis.

Dimethyl fumarate was not authorised anywhere in the EU for the treatment of ALD or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 5 December 2019, recommending the granting of this designation.

Opinions on orphan medicinal product designations are based on the following three criteria:

- the seriousness of the condition;
- the existence of alternative methods of diagnosis, prevention or treatment;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the EU) or insufficient returns on investment.

Designated orphan medicinal products are products that are still under investigation and are considered for orphan designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of quality, safety and efficacy is necessary before a product can be granted a marketing authorisation.

For more information

Sponsor's contact details:

Contact details of the current sponsor for this orphan designation can be found on EMA website.

For contact details of patients' organisations whose activities are targeted at rare diseases see:

- Orphanet, a database containing information on rare diseases, which includes a directory of patients' organisations registered in Europe;
- European Organisation for Rare Diseases (EURORDIS), a non-governmental alliance of patient organisations and individuals active in the field of rare diseases.

Translations of the active ingredient and indication in all official EU languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Dimethyl fumarate	Treatment of adrenoleukodystrophy
Bulgarian	Диметилфумарат	Лечение на аденолевкодистрофия
Croatian	Dimetil fumarate	Liječenje adrenoleukodistrofije
Czech	Dimethyl-fumarát	Léčba adrenoleukodystrofie
Danish	Dimethylfumarat	Behandling af adrenoleukodystrofi
Dutch	Dimethylfumaraat	Behandeling van adrenoleukodystrofie
Estonian	Dimetüülfumaraat	Adenoleukodüstroofia ravi
Finnish	Dimetyylifumaraatti	Adrenoleukodystrofian hoito
French	Fumarate de diméthyle	Traitement de l'adrénoleucodystrophie
German	Dimethylfumarat	Behandlung der Adrenoleukodystrophie
Greek	Φουμαρικό διμεθύλιο	Θεραπεία της αδρενολευκοδυστροφίας
Hungarian	Dimetil-fumarát	Adrenoleukodisztrófia kezelése
Italian	Dimetilfumarato	Trattamento dell'adrenoleucodistrofia
Latvian	Dimetilfumarāts[2]	Adrenoleikodistrofijas ārstēšana
Lithuanian	Dimetilfumaratas	Adrenoleukodistrofijos gydymas
Maltese	Dimethyl fumarate	Kura tal-adrenolewkodistrofija
Polish	Fumaran dimetylu	Leczenie adrenoleukodystrofii
Portuguese	Fumarato de dimetilo	Tratamento da adrenoleucodistrofia
Romanian	Dimetil fumarat	Tratmentul adrenoleucodistrofiei
Slovak	Dimetylfumarát	Liečba adrenoleukodystrofie
Slovenian	Dimetil fumarat	Zdravljenje adrenolevkodistrofije
Spanish	Dimetilfumarato	Tratamiento de la adrenoleucodistrofia
Swedish	Dimetylfumarat	Behandling av adrenoleukodystrofi
Norwegian	Dimetylfumarat	Behandling av adrenoleukodystrofi
Icelandic	Dímetýl fúmarat	Meðferð við adrenal hvtavefskyrkingi

[1] At the time of designation
[2] Active substance aligned with translation the already authorised medicine Tecfidera (Latvia)