12 December 2016
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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

5-[4-[2-(5-(1-hydroxyethyl)-2-pyridinyl)ethoxy]benzyl]-2,4-thiazolidinedione hydrochloride for the treatment of adrenoleukodystrophy

On 18 November 2016, orphan designation (EU/3/16/1770) was granted by the European Commission to Minoryx Therapeutics S.L., Spain, for 5-[4-[2-(5-(1-hydroxyethyl)-2-pyridinyl)ethoxy]benzyl]-2,4-thiazolidinedione hydrochloride (also known as MIN-102) 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 located 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 them from accumulating in tissues.

In the brain and spinal cord, the build-up of VLCFAs damages the protective sheath (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 functioning properly and reduces their ability to produce 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 513,700,000 (Eurostat 2016).

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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 treat the adrenal insufficiency.

How is this medicine expected to work?

This medicine is expected to work in patients with ALD by attaching to and activating receptors called 'PPAR gamma receptors', which are found inside cells and regulate the function of mitochondria and anti-inflammatory responses. Mitochondria are components within cells that generate energy. Activating PPAR gamma receptors will improve the function of mitochondria and reduce inflammation seen in ALD. These effects are expected to protect cells from damage and slow the progression of the disease.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of the medicine in experimental models was ongoing.

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

At the time of submission, the medicine was not authorised anywhere in the EU for ALD or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 October 2016 recommending the granting of this designation.

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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, on the medicine's rare disease designations page.

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	5-[4-[2-(5-(1-hydroxyethyl)-2-pyridinyl)ethoxy]benzyl]-2,4-thiazolidinedione hydrochloride	Treatment of adrenoleukodystrophy
Bulgarian	5-[4-[2-(5-(1-хидроксиетил)-2-пиридинил)етокси]бензил]-2,4-тиазолидиндион хидрохлорид	Лечение на аденолевкодистрофия
Croatian	5-[4-[2-(5-(1-hidroksietil)-2-piridinil)etoksi]benzil]-2,4-tiazolidindion hidroklorid	Liječenje adrenoleukodistrofije
Czech	5-[4-[2-(5-(1-hydroxyethyl)-2-pyridinyl)ethoxy]benzyl]-2,4-thiazolidinedione hydrochlorid	Léčba adrenoleukodystrofie
Danish	5-[4-[2-(5-(1-hydroxyethyl)-2-pyridinyl)ethoxy]benzyl]-2,4-thiazolidindion-hydrochlorid	Behandling af adrenoleukodystrofi
Dutch	5-[4-[2-(5-(1-hydroxyethyl)-2-pyridinyl)ethoxy]benzyl]-2,4-thiazolidinedion hydrochloride	Behandeling van adrenoleukodystrofie
Estonian	5-[4-[2-(5-(1-hüdroksüetüül)-2-püridinüül)etoksü]bensüül]-2,4-tiasolidiindioon vesinikkloriid	Adenoleukodüstroofia ravi
Finnish	5-[4-[2-(5-(1-hydroksietyyli)-2-pyridinyyli)etoksi]bentsyyli]-2,4-tiatsolidiinidioni-hydrokloridi	Adrenoleukodystrofian hoito
French	5-[4-[2-(5-(1-hydroxyéthyl)-2-pyridinyl)éthoxy]benzyl]-2,4-thiazolidinedione chlorhydrate	Traitement de l'adrénoleucodystrophie
German	5-[4-[2-(5-(1-hydroxyethyl)-2-pyridinyl)ethoxy]benzyl]-2,4-thiazolidindion-Hydrochlorid	Behandlung der Adrenoleukodystrophie
Greek	5-[4-[2-(5-(1-υδροξυαιθυλ)-2-πυριδινυλο)αιθοξυ]βενζυλ]-2,4-θειαζολιδινοδιόνη υδροχλωρική	Θεραπεία της αδρενολευκοδυστροφίας
Hungarian	5-[4-[2-(5-(1-hidroxietil)-2-piridinil)etoxi]benzil]-2,4-thiazolidindion hidroklorid	Adrenoleukodisztrófia kezelése
Italian	5-[4-[2-(5-(1-idrossietil)-2-piridinil)etossi]benzil]-2,4-tiazolidinedione cloridrato	Trattamento dell'adrenoleucodistrofia
Latvian	5-[4-[2-(5-(1-hidroksietil)-2-piridinil)etoksi]benzil]-2,4-tiazolidinediona hidrohlorīds	Adrenoleikodistrofijas ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	5-[4-[2-(5-(1-hidroksietil)-2-piridinil)etoksi]benzil]-2,4-tiazolidindiono hidrochloridas	Adrenoleukodistrofijos gydymas
Maltese	5-[4-[2-(5-(1-idrossitil)-2-piridinil)etossi]benzil]-2,4-kloridrat tat-tiazolidinedjon	Kura tal-adrenolewkodistrofija
Polish	5-[4-[2-(5-(1-hydroksyetylo)-2-pirydynylo)etoksy]benzylo]-2,4-tiazolidynodion chlorowodorek	Leczenie adrenoleukodystrofii
Portuguese	Cloridrato de 5-[4-[2-(5-(1-hidroxietil)-2-piridinil)etoxi]benzil]-2,4-tiazolidinodiona	Tratamento da adrenoleucodistrofia
Romanian	Clorhidrat de 5-[4-[2-(5-(1-hidroxietil)-2-piridinil)etoxi]benzil]-2,4-tiazolidindionă	Tratmentul adrenoleucodistrofiei
Slovak	5-[4-[2-(5-(1-hydroxyetyl)-2-pyridyl)etoxy]benzyl]-2,4-tiazolidíndión hydrochlorid	Liečba adrenoleukodystrofie
Slovenian	5-[4-[2-(5-(1-hidroksietil)-2-piridinil)etoksi]benzil]-2,4-tiazolidindiona hidroklorid	Zdravljenje adrenolevkodistrofije
Spanish	Cloridrato de 5-[4-[2-(5-(1-hidroxietil)-2-piridinil)etoxi]benzil]-2,4-tiazolidinodiona	Tratamiento de la adrenoleucodistrofia
Swedish	5-[4-[2-(5-(1-hydroxietyl)-2-pyridinyl)etoxi]bensyl]-2,4-tiazolidindion - hydroklorid	Behandling av adrenoleukodystrofi
Norwegian	5-[4-[2-(5-(1-hydroksyetyl)-2-pyridinyl)etoksy]benzyl]-2,4-tiazolidindionhydroklorid	Behandling av adrenoleukodystrofi
Icelandic	5-{4-[2-(5-(-(hýdroxýetýl)-2-pýridýnýl)etoxý]benzyl]-2,4-tíazólidíndíón-hýdróklóríð	Meðferð við nýrnahettu hvtavefskyrkingi