



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Pioglitazone for the treatment of adrenoleukodystrophy

On 19 February 2014, orphan designation (EU/3/14/1245) was granted by the European Commission to Minoryx Therapeutics S.L., Spain, for pioglitazone 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' 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 mainly males, is caused by abnormalities in a gene called *ABCD1* which is responsible for the production of the protein needed to break down the fatty substances and prevent them from accumulating in tissues.

In the brain and spinal cord, the build-up of the fatty acids 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 approximately 0.35 in 10,000 people in the European Union (EU). This was equivalent to a total of around 18,000 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 511,100,000 (Eurostat 2014).



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 complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow) had been used in some patients. Corticosteroids were also used to treat the adrenal insufficiency.

How is this medicine expected to work?

Pioglitazone is a medicine that has been used for several years in the treatment of diabetes. It is expected to work in patients with ALD by attaching to and activating receptors called 'PPAR gamma receptors', which are found inside cells including nerve cells. Pioglitazone is expected to protect nerve cells from damage by improving the function of certain structures within nerve cells called mitochondria. This is expected to 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 pioglitazone in experimental models was ongoing.

At the time of submission of the application for orphan designation, no clinical trials with pioglitazone 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 9 January 2014 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

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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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	Pioglitazone	Treatment of adrenoleukodystrophy
Bulgarian	Пиоглитазон	Лечение на аденолевкодистрофия
Czech	Pioglitazon	Léčba adrenoleukodystrofie
Croatian	Pioglitazon	Liječenje adrenoleukodistrofije
Danish	Pioglitazon	Behandling af adrenoleukodystrofi
Dutch	Pioglitazon	Behandeling van adrenoleukodystrofie
Estonian	Pioglitason	Adenoleukodüstroofia ravi
Finnish	Pioglitasoni	Adrenoleukodystrofian hoito
French	Pioglitazone	Traitement de l'adrénoleucodystrophie
German	Pioglitazon	Behandlung der Adrenoleukodystrophie
Greek	Πιογλιταζόνη	Θεραπεία της αδρενολευκοδυστροφίας
Hungarian	Pioglitazon	Adrenoleukodisztrófia kezelése
Italian	Pioglitazone	Trattamento dell'adrenoleucodistrofia
Latvian	Pioglitazons	Adrenoleikodistrofijas ārstēšana
Lithuanian	Pioglitazonas	Adrenoleukodistrofijos gydymas
Maltese	Pioglitazone	Kura tal-adrenolewkodistrofija
Polish	Pioglitazon	Leczenie adrenoleukodystrofii
Portuguese	Pioglitazona	Tratamento da adrenoleucodistrofia
Romanian	Pioglitazonă	Tratamentul adrenoleucodistrofiei
Slovak	Pioglitazón	Liečba adrenoleukodystrofie
Slovenian	Pioglitazon	Zdravljenje adrenolevkodistrofije
Spanish	Pioglitazona	Tratamiento de la adrenoleucodistrofia
Swedish	Pioglitazon	Behandling av adrenoleukodystrofi
Norwegian	Pioglitazon	Behandling av adrenoleukodystrofi
Icelandic	Píóglitazón	Meðferð við adrenal hvítavefkyrkingi

¹ At the time of designation