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EMA/COMP/313675/2016
Committee for Orphan Medicinal Products

# Public summary of opinion on orphan designation

## Temsirolimus for the treatment of adrenoleukodystrophy

On 30 May 2016, orphan designation (EU/3/16/1669) was granted by the European Commission to Centro de Investigación Biomédica en Red (CIBER), Spain, for temsirolimus 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 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 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?

Autophagy (or cell degradation) is an important process for degrading components of cells. In patients with ALD this function is impaired and the result is the accumulation of certain altered proteins that contribute to the worsening of the disease.

Temsirolimus acts by blocking mTOR, a protein involved in controlling autophagy. By blocking mTOR, the medicine is expected to improve autophagy and thereby reduce the accumulation of altered proteins and slow progression of the disease.

## What is the stage of development of this medicine?

The effects of temsirolimus have been evaluated in experimental models.

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

At the time of submission, temsirolimus was authorised in the EU for advanced renal-cell carcinoma (a type of kidney cancer) and mantle-cell lymphoma (a blood cancer).

At the time of submission, temsirolimus 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 21 April 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 | Temsirolimus | Treatment of adrenoleukodystrophy |
| Bulgarian | Темсиролимус | Лечение на аденолевкодистрофия |
| Croatian | Temsirolimus | Liječenje adrenoleukodistrofije |
| Czech | Temsirolimusum | Léčba adrenoleukodystrofie |
| Danish | Temsirolimus | Behandling af adrenoleukodystrofi |
| Dutch | Temsirolimus | Behandeling van adrenoleukodystrofie |
| Estonian | Temsirolimus | Adenoleukodüstroofia ravi |
| Finnish | Temsirolimuusi | Adrenoleukodystrofian hoito |
| French | Temsirolimus | Traitement de l'adrénoleucodystrophie |
| German | Temsirolimus | Behandlung der Adrenoleukodystrophie |
| Greek | Temsirolimus | Θεραπεία της αδρενολευκοδυστροφίας |
| Hungarian | Temsirolimus | Adrenoleukodisztrófia kezelése |
| Italian | Temsirolimus | Trattamento dell'adrenoleucodistrofia |
| Latvian | Temsirolimuss | Adrenoleikodistrofijas ārstēšana |
| Lithuanian | Temsirolimuzas | Adrenoleukodistrofijos gydymas |
| Maltese | Temsirolimus | Kura tal-adrenolewkodistrofija |
| Polish | Temsirolimus | Leczenie adrenoleukodystrofii |
| Portuguese | Temsirolimus | Tratamento da adrenoleucodistrofia |
| Romanian | Temsirolimus | Tratmentul adrenoleucodistrofiei |
| Slovak | Temsirolimus | Liečba adrenoleukodystrofie |
| Slovenian | Temsirolimus | Zdravljenje adrenolevkodistrofije |
| Spanish | Temsirolimus | Tratamiento de la adrenoleucodistrofia |
| Swedish | Temsirolimus | Behandling av adrenoleukodystrofi |
| Norwegian | Temsirolimus | Behandling av adrenoleukodystrofi |
| Icelandic | Temsírólímus | Meðferð við adrenal hvtavefskyrkingi |

[1] At the time of designation