EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Ataluren for the treatment of mucopolysaccharidosis type I

On 19 November 2014, orphan designation (EU/3/14/1380) was granted by the European Commission to PTC Therapeutics, Limited, United Kingdom, for ataluren for the treatment of mucopolysaccharidosis type I.

What is mucopolysaccharidosis type I?

Mucopolysaccharidosis type I (MPS I) is one of a group of inherited diseases caused by the lack of certain enzymes in lysosomes (structures in the body's cells that break down nutrients and other substances) that are needed to break down substances in the body called glycosaminoglycans (GAGs). In MPS I the enzyme that is lacking is called α-L-iduronidase. Since patients with MPS I cannot break GAGs down properly, they gradually build up in various organs in the body and damage them. This can cause a range of symptoms including impaired vision, developmental delay, mental disability, progressive joint stiffness and skeletal problems, breathing difficulties, enlarged liver and heart disease. The condition varies in severity, with the mildest form known as Scheie syndrome and the most severe as Hurler syndrome.

MPS I is a seriously debilitating and life-threatening disease that leads to multiple disabilities and can result in premature death.

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

At the time of designation, MPS I affected less than 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 5,000 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).

What treatments are available?

At the time of designation, the medicine Aldurazyme (laronidase) was authorised in the EU to treat the symptoms of MPS I that are not connected with the brain or nerves, by supplying patients with a

*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).

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version of the missing enzyme (enzyme replacement therapy). Some patients were treated with haematopoietic stem cell transplantation, a complex procedure where the patient receives blood stem cells from a matched donor; the stem cells are able to develop into normal blood cells that can produce the missing enzyme.

The sponsor has provided sufficient information to show that ataluren might be of significant benefit for patients with MPS I because early experimental studies suggest that it can reduce symptoms connected with the brain and nerves that are not helped by current treatments. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

How is this medicine expected to work?

The lack of the enzyme α-L-iduronidase in patients with MPS I is due to various mutations (defects) in the gene responsible for producing the enzyme. In about 70% of patients these take the form of certain defects (called nonsense mutations) in the gene which prematurely stop the production of a normal enzyme. Ataluren works in these patients by enabling the protein-making apparatus in cells to move past the defect, allowing the cells to produce a functional α-L-iduronidase.

What is the stage of development of this medicine?

The effects of ataluren have been evaluated in experimental models.

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

At the time of submission, ataluren was authorised as Translarna in the EU for treatment of patients with another orphan condition, Duchenne muscular dystrophy, where this was due to a nonsense mutation. The medicine was not authorised anywhere in the EU for MPS I 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 October 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

Sponsor's contact details:

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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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Ataluren	Treatment of mucopolysaccharidosis type I
Bulgarian	Аталурен	Лечение на мукополизахаридоза тип I
Croatian	Ataluren	Liječenje mukopolisaharidoze tipa I
Czech	Ataluren	Léčba mukopolysacharidozy typu I
Danish	Ataluren	Behandling af mucopolysaccharidose type I
Dutch	Ataluren	Behandeling van mucopolysacharidose type I
Estonian	Ataluren	I-tüüpi mukopolüsahharidoosi ravi
Finnish	Ataluereeni	Tyypin I mukopolysakkaridoosin hoito
French	Ataluren	Traitement de la mucopolysaccharidose de type I
German	Ataluren	Behandlung der Mukopolysaccharidose Typ I
Greek	Αταλουρένη	Θεραπεία βλεννοπολυσακχαρίδωσης, τύπου I
Hungarian	Ataluren	ɨ 1-es típusú mucopolisaccharidosis kezelése
Italian	Ataluren	Trattamento della mucopolisaccaridosi di tipo I
Latvian	Atalurēns	I tipa mukopolisaharidozes ārstēšana
Lithuanian	Atalurenas	Mukopolisacharidozės(I tipo) gydymas
Maltese	Ataluren	Kura tal-mukopolisakkaridożi tat-tip I
Polish	Ataluren	Leczenie mukopolisacharydozy typu I
Portuguese	Atalurene	Tratamento da mucopolissacaridose, tipo I
Romanian	Ataluren	Tratamentul mucopolizaharidozei de tip I
Slovak	Ataluren	Liečba mukopolysacharidózy typu I
Slovenian	Ataluren	Zdravljenje mukopolisaharidoze vrste I
Spanish	Ataluren	Tratamiento de la mucopolisacaridosis tipo I
Swedish	Ataluren	Behandling av mukopolysackaridos typ I
Norwegian	Ataluren	Behandling av mukopolysakkaridose type I
Icelandic	Atalúren	Meðferð við slímsykrukvilla gerð I

[1] At the time of designation