20 April 2015
EMA/COMP/440579/2012 Rev.3
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Metreleptin for the treatment of Lawrence syndrome

First publication	28 August 2012
Rev.1: transfers of sponsorship	25 April 2014
Rev.2: sponsor's change of address	1 October 2014
Rev.3: transfer of sponsorship	20 April 2015

Disclaimer

Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.

On 17 July 2012, orphan designation (EU/3/12/1024) was granted by the European Commission to Aptiv Solutions (UK) Limited, United Kingdom, for metreleptin for the treatment of Lawrence syndrome.

The sponsorship was transferred to Bristol-Myers Squibb / AstraZeneca EEIG, United Kingdom, in February 2014 then to AstraZeneca AB, Sweden, in April 2014 and subsequently to Aegerion Pharmaceuticals Limited, United Kingdom, in March 2015.

What is Lawrence syndrome?

Lawrence syndrome (also known as acquired generalised lipodystrophy) is a condition characterised by loss of subcutaneous (under the skin), adipose (fatty) tissue in large areas of the body, especially the face and extremities.

Patients with Lawrence syndrome usually develop loss of fat during childhood or adolescence. Fat loss is usually gradual over months or years, but in some patients, fat can disappear over a few weeks. The disease leads to severe complications, including high levels of fats called triglycerides circulating in the blood, insulin resistance (when the body is unable to recognise insulin, a hormone that helps regulate blood sugar levels), diabetes, liver cirrhosis (scarring) and pancreatitis (inflammation of the pancreas).

Lawrence syndrome is a long-term debilitating and life-threatening condition because of its severe complications including diabetes, hypertriglyceridemia (high blood triglyceride levels), acute

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

pancreatitis (inflammation of the pancreas), and severe disease of major organs such as the heart, kidneys and liver.

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

At the time of designation, Lawrence syndrome affected approximately 0.1 in 10,000 people in the European Union (EU)[*]. This was equivalent to a total of around 5,100 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, no methods were authorised in the EU for the treatment of Lawrence syndrome. Patients with the condition were advised to follow a low-fat diet.

How is this medicine expected to work?

Metreleptin is similar to a human hormone called leptin, which plays a key role in regulating body fat. In Lawrence syndrome, metreleptin is expected to increase fat breakdown in the blood, muscles and liver, and improve insulin function, thereby correcting some abnormalities in patients with this condition such as insulin resistance. However, the medicine is not expected to restore adipose tissue.

Metreleptin is made by a method known as 'recombinant DNA technology': it is made by bacteria that have received a gene (DNA) which makes them able to produce metreleptin.

What is the stage of development of this medicine?

The effects of metreleptin have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with metreleptin including patients with Lawrence syndrome were ongoing.

At the time of submission, metreleptin was not authorised anywhere in the EU for Lawrence syndrome. Orphan designation of metreleptin had been granted in the United States of America for metabolic disorders secondary to lipodystrophy.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 June 2012 recommending the granting of this designation.

[*]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 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 507,700,000 (Eurostat 2011).

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:

Aegerion Pharmaceuticals Limited
Lakeside House
1 Furzeground Way
Stockley Park East
Uxbridge UB11 1BD
United Kingdom
Tel. +44 208 622 4100
Fax +44 208 622 3592

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	Metreleptin	Treatment of Lawrence syndrome
Bulgarian	Метрелептин	Лечение на синдрома на Lawrence
Croatian	Metreleptin	Liječenje Lawrenceovog sindroma
Czech	Metreleptin	Léčba Lawrencova syndromu
Danish	Metreleptin	Behandling af Lawrence-syndrom
Dutch	Metreleptine	Behandeling van Lawrence syndroom
Estonian	Metreleptiin	Lawrence sündroomi ravi
Finnish	Metreleptiini	Lawrencen oireyhtymän hoito
French	Métréleptine	Traitement du syndrome de Lawrence
German	Metreleptin	Behandlung des Lawrence-syndroms
Greek	Μετρελεπτίνη	Θεραπεία του συνδρόμου Lawrence syndrome
Hungarian	Metreleptin	Lawrence-szindróma kezelése
Italian	Metreleptina	Trattamento della sindrome di Lawrence
Latvian	Metreleptīns	Lawrence sindroma ārstēšana
Lithuanian	Metreleptinas	Lawrence sindromo gydymas
Maltese	Metreleptin	Kura tas-sindrome ta' Lawrence
Polish	Metreleptyna	Leczenie zespołu Lawrence'a
Portuguese	Metreleptina	Tratamento da síndrome de Lawrence
Romanian	Metreleptină	Tratamentul sindromului Lawrence
Slovak	Metreleptin	Liečba Lawrencovho syndrómu
Slovenian	Metreleptin	Zdravljenje Lawrencovega sindroma
Spanish	Metreleptina	Tratamiento de síndrome de Lawrence
Swedish	Metreleptin	Behandling av Lawrences syndrom
Norwegian	Metreleptin	Behandling av Lawrence syndrom
Icelandic	Metreleptín	Meðferð á Lawrenceheilkenni

[1] At the time of transfer of sponsorship