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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Estetrol for the treatment of neonatal encephalopathy

On 20 April 2017, orphan designation (EU/3/17/1865) was granted by the European Commission to Mithra Pharmaceuticals S.A., Belgium, for estetrol for the treatment of neonatal encephalopathy.

What is neonatal encephalopathy?

Neonatal encephalopathy refers to brain damage that occurs around the time of birth in babies who are not premature. Symptoms include reduced level of consciousness, seizures (fits), difficulty breathing, low muscle tone and poor reflexes. It is often caused by low levels of oxygen in the blood.

Neonatal encephalopathy is a long-term debilitating disease due to its effects on mental and physical development, and can often be life-threatening in the most severe cases.

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

At the time of designation, neonatal encephalopathy affected less than 1 in 10,000 people per year in the European Union (EU). This was equivalent to a total of fewer than 52,000 people*, and is below the ceiling for orphan designation. 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, babies with neonatal encephalopathy received therapeutic hypothermia, whereby the baby's body is cooled down to a body temperature lower than normal (hypothermia) to reduce extent of damage.

The sponsor has provided sufficient information to show that estetrol might be of significant benefit for babies with neonatal encephalopathy because laboratory studies indicate that estetrol could improve symptoms and general well-being of patients affected by the condition. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

*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 515,700,000 (Eurostat 2017).

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

How is this medicine expected to work?

Lower levels of oxygen in the brain increase the production of reactive oxygen species which can trigger mechanisms (oxidative stress) that damage cells and ultimately lead to their death.

Results from laboratory studies indicate that estetrol may help protect against oxidative stress. The medicine is therefore expected to help prevent further damage and relieve the baby's symptoms.

What is the stage of development of this medicine?

The effects of estetrol have been evaluated in experimental models.

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

At the time of submission, estetrol was not authorised anywhere in the EU for neonatal encephalopathy 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 15 March 2017 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	Estetrol	Treatment of neonatal encephalopathy
Bulgarian	Естетрол	Лечение на неонатална енцефалопатия
Croatian	Estetrol	Liječenje neonatalne encefalopatije
Czech	Estetrol	Léčba neonatální encefalopatie
Danish	Estetrol	Behandling af neonatal encephalopati
Dutch	Estetrol	Behandeling van neonatale encephalopathie
Estonian	Estetrool	Neonataalse entsefalopaatia ravi
Finnish	Estetroli	Neonataalisen enkefalopatian hoito
French	Estetrol	Traitement de l'encéphalopathie néonatale
German	Estetrol	Behandlung der neonatalen Enzephalopathie
Greek	Εστετρόλη	Θεραπεία της νεογνικής εγκεφαλοπάθειας
Hungarian	Estetrol	Újszülöttkori enkefalopátia kezelésére
Italian	Estetrol	Trattemento dell'encefalopatia neonatale
Latvian	Estetrols	Neonatālas encefalopātijas ārstēšana
Lithuanian	Estetrolis	Naujagimių encefalopatijos gydymas
Maltese	Estetrol	Kura tal-enċefalopatija fi trabi tat-twelid
Polish	Estetrol	Leczenie encefalopatii noworodka
Portuguese	Estetrol	Tratamento da encefalopatia neonatal
Romanian	Estetrol	Tratamentul encefalopatiei neonatale
Slovak	Estetrol	Liečba neonatálnej encefalopatie
Slovenian	Estetrol	Zdravljenje neonatalne encefalopatije
Spanish	Estetrol	Tratamiento de la encefalopatia neonatal
Swedish	Estetrol	Behandling av neonatal encefalit
Norwegian	Estetrol	Behandling av neonatal encefalopati
Icelandic	Estetról	Meðferð nýbura heilakvilla

[1] At the time of designation