5 January 2018
EMA/624094/2017

Public summary of opinion on orphan designation

Bitopertin for the treatment of beta thalassaemia intermedia and major

On 16 October 2017, orphan designation (EU/3/17/1919) was granted by the European Commission to Roche Registration Limited, United Kingdom, for bitopertin for the treatment of beta thalassaemia intermedia and major.

What is beta thalassaemia intermedia and major?

Beta thalassaemia is an inherited disease in which patients are unable to make enough haemoglobin, the iron-rich protein in red blood cells that carries oxygen around the body. Beta thalassaemia major is a severe form of the disease in which patients need frequent blood transfusions. Beta thalassaemia intermedia is a less severe form which may worsen with age. Both types of beta thalassaemia are caused by changes in the gene responsible for producing beta-globin, one of the components of haemoglobin, which result in low levels of haemoglobin in the blood.

Beta thalassaemia intermedia and major are life-long debilitating diseases. They may be life threatening because of severe anaemia (low red blood cell count due to lack of haemoglobin), the need for repeated blood transfusions and the risk of complications associated with them.

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

At the time of designation, beta thalassaemia intermedia and major affected less than 1 in 10,000 people 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, 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 main treatments for beta thalassaemia intermedia and major were blood transfusions and the use of iron chelators (medicines for reducing 'iron overload' - the high iron levels in the body caused by repeated blood transfusions). In some cases, allogeneic haematopoietic stem cell transplantation was used to cure the disease. This is a complex procedure where the bone

*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

marrow of the patient is cleared of cells and replaced with healthy bone marrow cells from a matched donor, allowing the patient to produce red blood cells with normal haemoglobin.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with beta thalassaemia intermedia and major because early results from experimental studies suggest it can increase the production of normal haemoglobin and improve symptoms of the condition, which would reduce the need for blood transfusions. 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?

Normal haemoglobin is made up of both alpha- and beta-globin subunits combined with an iron-containing molecule called 'haem'. Patients with beta thalassaemia intermedia and major cannot make enough beta-globin, and are left with uncombined alpha-globin and haem. Uncombined alpha-globin reduces production of red blood cells by the bone marrow and shortens their life.

Bitopertin blocks a protein called GlyT1 which is needed to make haem. By blocking GlyT1, bitopertin reduces the amount of haem produced, which in turn triggers reduced production of alpha-globin. The damaging effects of alpha-globin on red blood cell production are therefore reduced and the lifespan of red blood cells increased to more normal levels. This is expected to reduce the need for blood transfusions.

What is the stage of development of this medicine?

The effects of bitopertin have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with bitopertin in patients with beta thalassaemia intermedia and major had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for beta thalassaemia intermedia and major 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 7 September 2017 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:

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	Bitopertin	Treatment of beta-thalassaemia intermedia and major
Bulgarian	Битопертин	Лечение на бета таласемия интермедия и майор
Croatian	Bitopertin	Liječenje beta-talasemije intermedije i major
Czech	Bitopertin	Léčení beta thalasémie intermedia a major
Danish	Bitopertin	Behandling af beta-thalassæmia intermedia og major
Dutch	Bitopertin	Behandeling van bètathalassemie intermedia en major
Estonian	Bitopertiin	Keskmise ja raske beetatalasseemia ravi
Finnish	Bitopertiini	Beetatalassemia intermedia-ja major-tyypin hoito
French	Bitopertin	Traitement de la bêta-thalassémie intermédiaire et majeure
German	Bitopertin	Behandlung der Beta-Thalassämie (Intermediäre und Major-Form)
Greek	Βιτοπερτίνη	Θεραπεία της β-μεσογειακής αναιμίας, ενδιάμεσης και μείζονος
Hungarian	Bitopertin	Béta-talasszémia intermedia és major kezelése
Italian	Bitopertin	Trattamento della beta-talassemia intermedia e major
Latvian	Bitopertīns	Vidēji izteiktas un izteiktas bēta talasēmijas ārstēšana
Lithuanian	Bitopertinas	Vidutinio sunkumo ir sunkios β-talasemijos gydymas
Maltese	Bitopertin	Kura tal-beta talassemija intermedja u maġġuri
Polish	Bitopertyna	Leczenie talasemii beta-intermedia i major
Portuguese	Bitopertina	Tratamento da beta talassémia intermédia e major
Romanian	Bitopertin	Tratamentul beta talasemiei intermediare şi majore
Slovak	Bitopertín	Liečba stredne závažnej a závažnej beta talasémie
Slovenian	Bitopertin	Zdravljenje srednje in velike talasemije beta
Spanish	Bitopertina	Tratamiento de la beta talasemia intermedia y mayor
Swedish	Bitopertin	Behandling av beta-thalassaemia intermedia och major
Norwegian	Bitopertin	Behandling av beta-thalassemia intermedia og beta-thalassemia major
Icelandic	Bítópertín	Meðferð á langvinnu járnofhleðslu sem krefst klómeðferðar

[1] At the time of designation