22 November 2018
EMA/530846/2018

Public summary of opinion on orphan designation

1-(3-methylbutanoyl)-L-aspartyl-L-threonyl-L-histidyl-L-phenylalanyl-L-prolyl-(L-cystinyl-L-isoleucyl-[(N6-(S)-4-carboxy-4-palmitamidobutanoyl)-L-lysinyl]-L-phenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamide, disulfide, acetate salt for the treatment of beta-thalassaemia intermedia and major

On 24 August 2018, orphan designation (EU/3/18/2058) was granted by the European Commission to IQVIA RDS Ireland Limited, Ireland, for 1-(3-methylbutanoyl)-L-aspartyl-L-threonyl-L-histidyl-L-phenylalanyl-L-prolyl-(L-cystinyl-L-isoleucyl-[(N6-(S)-4-carboxy-4-palmitamidobutanoyl)-L-lysinyl]-L-phenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamide, disulfide, acetate salt (also known as hepcidin mimetic) 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 found 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, while beta thalassaemia intermedia is a less severe form, which may worsen with age. Both types of beta thalassaemia are caused by defects 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 approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 52,000 people*, and is

*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 517,400,000 (Eurostat 2018).

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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 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 this medicine might be of significant benefit for patients with beta thalassaemia intermedia and major because laboratory studies showed it might improve formation of red blood cells and reduce anaemia. 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?

In patients with beta thalassaemia intermedia or major, excess iron can build up in the body damaging organs such as the heart and liver and reducing the formation of red blood cells.

This medicine is a small molecule that mimics the action of the hormone hepcidin. Hepcidin regulates the levels of iron in the body by blocking the uptake of iron from food and by stopping the release of iron from iron-storage cells. Levels of hepcidin are low in patients with thalassaemia. By acting in the same way as hepcidin, the medicine is expected to improve iron regulation and to decrease the damaging effect of iron on the formation of red blood cells, thus improving anaemia and the symptoms of the condition.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with the medicine in patients with beta thalassaemia intermedia or major were planned.

At the time of submission, the medicine was not authorised anywhere in the EU for beta thalassaemia intermedia or major. Orphan designation of the medicine had been granted in the United States for beta thalassaemia.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 19 July 2018 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	1-(3-methylbutanoyl)-L-aspartyl-L-threonyl-L-histidyl-L-phenylalanyl-L-prolyl-(L-cystinyl-L-isoleucyl-[(N6-(S)-4-carboxy-4-palmitamidobutanoyl)-L-lysinyl]-L-phenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamide, disulfide, acetate	Treatment of beta-thalassaemia intermedia and major
Bulgarian	1-(3-метилбутаноил)-Ь-аспартил-Ь-треонил-Ь-хистидил-Ь-фенилаланил-Ь-пролил-(Ь-цистинил-Ь-изолевцил-[(N6-(S)-4-карбокси-4-палмитамидобутаноил)-Ь-лизинил]-Ь-фенилаланил-Ь-глутамил-Ь-пролил-Ь-аргинил-Ь-серинил-Ь-лизинил-Ь-глицинил-Ь-цистинил)-Ь-лизинамид, дисулфид, ацетат	Лечение на бета таласемия интермедия и майор
Croatian	1-(3-metilbutanoil)-L-aspartil-L-treonil-L-histidil-L-fenilalanil-L-prolil-(L-cistinil-L-izoleucil-[(N6-(S)-4-karboksi-4-palmitamidobutanoil)-l-lizinil]-L-fenilalanil-L-glutamil-L-prolil-L-arginil-L-serinil-L-lizinil-L-glicinil-L-cistinil)-L-lisinamid, disulfid, acetat	Liječenje beta-talasemije intermedije i major
Czech	1-(3-methylbutanoyl)-L-aspartyl-L-threonyl-L-histidyl-L-fenylalanyl-L-prolyl-(L-cystinyl-L-leucyl-[(N6-(S)-4-karboxy4-palmitamidobutanoyl)-L-lysinových]-L-fenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinových-L-glycinyl-L-cystinyl)-L-lysinamid, disulfid, acetát	Léčení beta thalasémie intermedia a major
Danish	1-(3-methylbutanoyl)-L-aspartyl-L-threonyl-L-histidyl-L-phenylalanyl-L-prolyl-(L-cystinyl-L-isoleucyl-[(N6-(S)-4-carboxy-4-palmitamidobutanoyl)-L-lysinyl]-L-phenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamid, disulfid, acetat	Behandling af beta-thalassæmia intermedia og major
Dutch	1-(3-methylbutanoyl)-L-aspartyl-L-threo-L-histidyl-L-fenylalanyl-L-prolyl-(L-cystinyl-L-isoleucyl-[(N6-(S)-4-carboxy-4-palmitamidobutanoyl)-L-lysinyl]-L-fenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamide, disulfide, acetaat	Behandeling van bètathalassemie intermedia en major
Estonian	1-(3-metüülbutanoüül)-L-aspartüül-L-treonüül-L-histidüül-L-fenüülalanüül-L-prolüül-(L-tsüstinüül-L-isoleutsüül-[(N6-(S)-4-karboksü-4-palmitamidobutanoüül)-L-lüsinüül]-L-fenüülalanüül-L-glutamüül-L-prolüül-L-arginüül-L-serüül-L-lüsinüül-L-glütsinüül-L-tsüstiinüül)-L-lüsiinamiidi, disulfiid, atsetaat	Keskmise ja raske beetatalasseemia ravi

[1] At the time of designation

Language	Active ingredient	Indication
Finnish	1-(3-metyylibutanoyyli)-L-aspartyyli-L-treonyyli-L-histidyyli-L-fenyylialanyyli-L-prolyyli-(L-kystinyyli-L-isoleusyyli-[(N6-(S)-4-karboksi-4-palmitamidobutanoyl)-L-lysinyyli]-L-fenyylialanyyli-L-glutamyyli-L-prolyyli-L-arginyyli-L-serinyyli-L-lysinyyli-L-glysinyyli-L-kystinyyli)-L-lysinamidi, disulfidi, asetaatti	Beetatalassemia intermedia- ja major-tyypin hoito
French	1-(3-methylbutanoyl)-L-aspartyl-L-threonyle-L-histidyl-L-phenylalanyl-L-prolyl-(L-cystéinyl-L-isoleucyl-[(N6-(S)-4-carboxy-4-palmitamidobutanoyl)-L-lysinyl]-L-phenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamide, disulfure, acetate	Traitement de la bêta-thalassémie intermédiaire et majeure
German	1-(3-methylbutanoyl)-L-aspartyl-L-threonyl-L-histidyl-L-phenylalanyl-L-prolyl-(L-Cystinyl-L-isoleucyl-[(N6-(S)-4-carboxy-4-Palmitamidobutanoyl)-L-lysinyl]-L-phenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamid, Disulfid, Acetat	Behandlung der Beta-Thalassämie (Intermediäre und Major-Form)
Greek	1-(3-μεθυλβουτανοϋλ)-L-ασπαρτυλ- L -θρεονυλ-L-ιστιδυλο-L-φαινυλαλανυλ-L-προλυλ-(L-κυστίνης-L-ισολευκυλο-[(N6-(S)-4-καρβοξυ-4-παλμιταμιδοβουτανοϋλ)-L-λυσινυλο]-L-φαινυλαλανυλ-L-γλουταμυλο-L-προλυλ-L-αργινυλ-L-σερινυλ-L-λυσινυλο-L-γλυκινυλο-L-κυστίνης)-L-λυσιναμίδιο, δισουλφιδίου, οξικό	Θεραπεία της β-μεσογειακής αναιμίας, ενδιάμεσης και μείζονος
Hungarian	1-(3-metil-butanoil)-L-aszpartil-L-treonil-L-hisztidil-L-fenilalanil-L-prolil-(L-cisztinil-L-izoleucil-[(N6-(S)-4-karboxi-4-palmitamidobutanoil)-L-lizinil]-L-fenil-alanil-L-glutamil-L-prolil-L-arginil-L-szerinil-L-lizinil-L-glicinil-L-cisztinil)-L-lizin-amid, diszulfid, acetát	Béta-talasszémia intermedia és major kezelése
Italian	1-(3-methylbutanoyl)-L-aspartil-L-treonilL-istidil-L-fenilalanile-L-prolil-(L-cystinyl-L-isoleucyl-[(N6-(S)-4-carbossi-4-palmitamidobutanoil)-L-lisinil]-L-fenilalanil-L-glutamil-L-prolil-L-arginil-L-serinil-L-lisinil-L-glicinil-L-cistinil)-L-lisinammide, solfuro, acetato	Trattamento della beta-talassemia intermedia e major
Latvian	1-(3-metilbutanoil)-L-aspartil-L-treonil-L-histidil-L-fenilalanil-L-propil-(L-cistinil-L-izoleicil-[(N6-(S)-4-karboksi-4-palmitamidobutanoil)-L-lizinil]-L-fenilalanil-L-glutamil-L-prolil-L-arginil-L-serinil-L-lizinil-L-glicinil-L-cistinil)-L-lizinamīds, disulfīds, acetāts	Vidēji izteiktas un izteiktas bēta talasēmijas ārstēšana
Lithuanian	1-(3-metilbutanoil)-L-aspartil-L-treonil-L-histidil-L-fenilalanil-L-propil-(L-cistinil-L-isoleucil-[(N6-(S)-4-karboksi-4-palmitamidobutanoil)-L-lizinil]-L-fenilalanil-L-glutamil-L-prolil-L-arginil-L-serinil-L-lizinil-L-glicinil-L-cistinil)-L-lizinamido, disulfido, acetatas	Vidutinio sunkumo ir sunkios β-talasemijos gydymas

Language	Active ingredient	Indication
Maltese	1-(3-methylbutanoyl)-L-aspartyl-L-threonylL-histidylL-phenylalanyl-L-prolyl-(L-cystinyl-L-isoleucyl-[(N6-(S)-4-carboxy-4-palmitamidobutanoyl)-L-lysinyl]-L-phenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lisinyl-L-glycinyl-L-cystinyl)-L-lisinamide, disulfide, aċetat	Kura tal-beta talassemija intermedja u maġġuri
Polish	1-(3-metylobutanoilo)-L-aspartylo-L-treonylo-L-histydylo-L-fenyloalanylo-L-prolilo-(L-cystynylo-L-izoleucylo-[(N6-(S)-4-karboksy-4-palmitamidobutanoilo)-L-lysnylo]-L-fenyloalanylo-L-glutamyl-L-prolilo-L-arginyl-L-sinylo-L-lizynylo-L-glicynylo-L-cystynylo)-L-lizynoamid, disiarczek, octan	Leczenie talasemii beta-intermedia i major
Portuguese	1-(3-metilbutanoil)-L-aspartil-L-treonil-L-histidil-L-fenilalanil-L-prolil-(L-cistinil-L-isoleucil-[(N6-(S)-4-carboxi-4-palmitamidobutanoil)-L-lisinil]-L-fenilalanil-L-glutamil-L-prolil-L-arginil-L-serinil-L-lisinil-L-glicinil-L-cistinil)-L-lisinamida, dissulfureto, acetato	Tratamento da beta talassémia intermédia e major
Romanian	1-(3-metilbutanoil)-L-aspartil-L-treonil-L-histidil-L-fenilalanil-L-prolil-(L-cistinil-L-izoleucil-[(N6-(S)-4-carboxi-4-palmitamidobutanoil)-L-lizinil]-L-fenilalanil-L-glutamil-L-prolil-L-arginil-L-serinil-L-lizinil-L-glicinil-L-cistinil)-L-lisinamidă, disulfură, acetat	Tratamentul beta talasemiei intermediare şi majore
Slovak	1-(3-metylbutanoyl)-L-aspartyl-L-treonyl-L-histidyl-L-fenylalanyl-L-prolyl-(L-cystinyl-L-leucyl-[(N6-(S)-4-karboxy 4-palmitamidobutanoyl)-L-lysinových]-L-fenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinových-L-glycín-L-cystinyl)-L-lyzinamid, disulfid, acetát	Liečba stredne závažnej a závažnej beta talasémie
Slovenian	1-(3-metilbutanoil)-L-asparti-L-treonil-L-histidil-L-fenilalanil-L-prolil)-L-cistinil-L-izoleucil-[(N6-(S)-4-palmitamidobutanoil)-L-lizinil]-L-fenilalanil-L-glutamil-L-prolin-L-arginil-L-serinil-L-lizinil-L-glicinil-L-cistinil)-L-lizinamida, disulfid, acetat	Zdravljenje srednje in velike talasemije beta
Spanish	1-(3-metilbutanoil)-L-aspartil-L-treonil-L-histidil-L-fenilalanil-L-prolil)-L-cistinil-L-isoleucil-[(N6-(S)-4-carboxi-4-palmitamidobutanoil)-L-lisinil]-L-fenilalanil-L-glutamil-L-prolil-L-arginil-L-serinil-L-lisinil-L-glicinil-L-cistinil)-L-lisinamida, disulfuro, acetato	Tratamiento de la beta talasemia intermedia y mayor
Swedish	1-(3-metylbutanoyl)-L-aspartyl-L-treonyl-L-histidyl-L-fenylalanyl-L-prolyl)-L-cystinyl-L-isoleucyl-[(N6-(S)-4-karboxi-4-palmitamidobutanoyl)-L-lysinyl]-L-fenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamid, disulfid, acetat	Behandling av beta-thalassaemia intermedia och major
Norwegian	1-(3-metylbutanoyl)-L-aspartyl-L-treonyl-L-histidyl-L-fenylalanyl-L-prolyl)-L-cystinyl-L-isoleucyl-[(N6-(S)-4-karboksy-4-palmitamidobutanoyl)-L-lysinyl]-L-fenylalanyl-L-glutamyl-L-prolyl-L-arginyl-L-serinyl-L-lysinyl-L-glycinyl-L-cystinyl)-L-lysinamid, disulfid, acetat	Behandling av beta-thalassemia intermedia og beta-thalassemia major

Language	Active ingredient	Indication
Icelandic	1-(3-metýlbútanóýl)-L-aspartýl-L-treónýl-L-histidýl-L-fenýlalanýl-L-prólýl)-L-cýstinýl-L-ísóleucýl-[(N6-(S)-4-karboxý-4-palmitamidóbútanóýl)-L-lýsinýl]-L-fenýlalanýl-L-glútamýl-L-prólyl-L-arginýl-L-serinýl-L-lýsinýl-L-glýkínýl-L-cýstínýl)-L-lýsinamíð, dísúlfíð, asetat	Meðferð á langvinnu járnofhleðslu sem krefst klómeðferðar