10 March 2015
EMA/COMP/365538/2014 Rev.1
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant fusion protein consisting of a modified form of the extracellular domain of human activin receptor IIB linked to the human IgG1 Fc domain for the treatment of beta thalassaemia intermedia and major

First publication	27 August 2014
Rev.1: transfer of sponsorship	10 March 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 29 July 2014, orphan designation (EU/3/14/1300) was granted by the European Commission to IDEA Innovative Drug European Associates Limited, the United Kingdom, for recombinant fusion protein consisting of a modified form of the extracellular domain of human activin receptor IIB linked to the human IgG1 Fc domain for the treatment of beta thalassaemia intermedia and major.

The sponsorship was transferred to Celgene Europe Limited, United Kingdom, in February 2015.

What is beta thalassaemia intermedia and major?

Beta thalassaemia is an inherited disease in which patients are unable to make enough haemoglobin, the protein found in red blood cells that carry 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 beta thalassaemia intermedia and major are caused by defects in the gene responsible for the production of beta-globin, one of the components of haemoglobin, which result in low or no production of beta-globin.

Beta thalassaemia intermedia and major are long-lasting 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.

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

At the time of designation, beta thalassaemia major and minor affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 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 the high iron levels in the body caused by repeated blood transfusions). In some cases, bone-marrow transplantation was used to cure the disease. This is a complex procedure in which the bone marrow of the patient is destroyed and replaced with bone marrow from a matched donor, to allow the patient to produce red blood cells with normal levels of haemoglobin.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with beta thalassaemia intermedia or major because early studies show that it may improve anaemia, an aspect of the condition that is not targeted by currently authorised 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?

In patients with beta-thalassemia, the bone marrow has too many precursor red blood cells that fail to develop into mature red blood cells.

This medicine is an engineered protein that has been designed to attach to certain proteins in the body which slow down (or inhibit) the maturation of red blood cells. By attaching to these 'inhibitory' proteins, it is expected to trap them so they do not have their normal effect on the red blood cells. As a result, production of red blood cells is increased. This is expected to improve the symptoms of patients with beta thalassaemia intermedia and major.

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 and major were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for beta thalassaemia intermedia and 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 12 June 2014 recommending the granting of this designation.

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[*]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.
At the time of designation, this represented a population of 512,900,000 (Eurostat 2014).

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	Recombinant fusion protein consisting of a modified form of the extracellular domain of human activin receptor IIB linked to the human IgG1 Fc domain	Treatment of beta-thalassaemia intermedia and major
Bulgarian	Рекомбинантен фузионен протеин, състоящ се от модифицирана форма на екстрацелуларния домейн на човешки активин рецептор IIB, свързан към Fc домейн на човешки IgG1	Лечение на бета таласемия интермедия и майор
Croatian	Rekombinantni fuzijski protein sačinjen od modificiranog oblika ljudskog aktivinskog receptora IIB povezanog na ljudsku IgG1 Fc domenu	Liječenje beta-talasemije intermedije i major
Czech	Rekombinantní fúzní protein sestávající z modifikované formy extracelulární domény lidského receptoru typu II B pro aktivin navázané na Fc doménu lidského IgG1	Léčení beta thalasémie intermedia a major
Danish	Rekombinant fusionsprotein bestående af en modificeret form af ekstracellulære dele af human activin receptor IIB knyttet til det humane IgG1 Fc domæne.	Behandling af beta-thalassæmia intermedia og major
Dutch	Recombinant fusie-eiwit dat bestaat uit een gemodificeerde vorm van het extracellulaire domein van de humane activinereceptor IIB gekoppeld aan het humane IgG1 Fc-domein	Behandeling van bètathalassemie intermedia en major
Estonian	Rekombinantne liitvalk, mis koosneb inimese IgG1 Fc domeeniga seotud inimese aktiviini retseptori IIB rakuvälise domeeni modifitseeritud vormist	*Intermedia - ja major*-tüüpi beetatalasseemia ravi
Finnish	Ihmisen IgG1 Fc -domeeniin yhdistetystä muunnellusta solun ulkopuolisesta aktiviini IIB -reseptorin domeenimuodosta koostuva rekombinantti fuusioproteiini.	Beetatalassemia intermedia - ja major-tyypin hoito
French	Protéine de fusion recombinante consistant en une forme modifiée du domaine extracellulaire du récepteur IIB de l'activine humaine qui se lie au domaine Fc de l'IgG1 humaine	Traitement de la bêta-thalassémie intermédiaire et majeure
German	Rekombinantes Fusionsprotein, das aus einer modifizierten Form der extrazellulären Domäne des humanen Activin-Rezeptors IIB besteht, der an die Fc-Domäne von humanem IgG1 angekoppelt wurde	Behandlung der Beta-Thalassämie (Intermediäre und Major-Form)
Greek	Ανθρώπινη ανασυνδυασμένη πρωτεΐνη σύντηξης αποτελούμενη από τροποποιημένη μορφή του εξωκυττάριου τμήματος του υποδοχέα της ακτιβίνης IIB συνδεδεμένο με την περιοχή Fc της ανθρώπινης IgG1	Θεραπεία της β-μεσογειακής αναιμίας, ενδιάμεσης και μείζονος

[1] At the time of designation

Language	Active ingredient	Indication
Hungarian	A humán IgG1 Fc doménhez kötődő humán aktivin receptor módosított IIB extracelluláris doménjéből álló rekombináns fúziós fehérje	Béta-talasszémia intermedia és major kezelése
Italian	Proteina ricombinante di fusione costituita da una forma modificata del dominio extracellulare del recettore dell'activina umana di tipo IIB legata al dominio Fc di IgG1 umana	Trattamento della beta-talassemia intermedia e major
Latvian	Rekombinants fūzijas proteīns, ko veido cilvēka aktivīna IIB receptora ekstracelulārā domēna modificēta forma, kas savienota ar cilvēka IgG1 Fc domēnu	Vidēji izteiktas un izteiktas bēta talasēmijas ārstēšana
Lithuanian	Rekombinantinis sulietas baltymas, sudarytas iš modifikuotos formos ekstraląstelinio žmogaus aktivino IIB receptoriaus domeno, sujungto su žmogaus IgG1 Fc domenu	Vidutinio sunkumo ir sunkios β-talasemijos gydymas
Maltese	Proteina ta' fużjoni rikombinanti li tikkonsisti minn għamla modifikata tal-qasam ekstraċellulari tar-riċettur uman għal activin IIB magħqud mal-qasam IgG1 Fc uman	Kura tal-beta talassemija intermedja u maġġuri
Polish	Rekombinowane białko fuzyjne składające się ze zmodyfikowanej postaci zewnątrzkomórkowej domeny receptora ludzkiej aktywiny typu IIB połączonego z domeną Fc ludzkiej IgG1	Leczenie talasemii beta-intermedia i major
Portuguese	Proteína de fusão recombinante composta por uma forma modificada do domínio extracelular do receptor IIB da activina humana ligada ao domínio Fc da IgG1 humana	Tratamento da beta talassémia intermédia e major
Romanian	Proteină de fuziune recombinantă constând dintr-o formă modificată a domeniului extracelular al receptorului activinei umane de tip IIB legată de domeniul Fc al IgG1 umane	Tratamentul beta talasemiei intermediare şi majore
Slovak	Rekombinantný fúzny proteín zložený z modifikovanej formy extracelulárnej časti ľudského receptora pre aktivín IIB viazaného na Fc doménu ľudského IgG1	Liečba stredne závažnej a závažnej beta talasémie
Slovenian	Rekombinantna fuzijska beljakovina, sestavljena iz prilagojene oblike zunajcelične domene humanega receptorja IIB za aktivin, vezanega na domeno Fc humanega IgG1	Zdravljenje srednje in velike talasemije beta
Spanish	Proteína recombinante de fusión constituida por una forma modificada del dominio extracelular del receptor humano de activina tipo IIB unida al dominio Fc de la IgG1 humana	Tratamiento de la beta talasemia intermedia y mayor
Swedish	Rekombinant fusionsprotein bestående av en modifierad form av den extracellulära domänen av human aktivinreceptor IIB länkad till den humana IgG1 Fc-domänen	Behandling av beta-thalassaemia intermedia och major

Language	Active ingredient	Indication
Norwegian	Rekombinant fusjonsprotein som består av en modifisert form av det ekstracellulære domenet for human aktivinreseptor IIB, bundet til det humane IgG1 Fc-domenet	Behandling av beta-thalassemia intermedia og beta-thalassemia major
Icelandic	Raðbrigða samrunaprótein sem er samsett úr breyttri mynd af utanfrumu léni aktivín viðtaka IIB manna sem er tengt við IgG1 Fc lén manna	Meðferð á beta-Miðjarðarhafsblóðleysi intermedia og beta-Miðjarðarhafsblóðleysi major