



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

16 September 2019  
EMADOC-628903358-1042

## Public summary of opinion on orphan designation

2-(2-{[2-(1H-benzimidazol-2-yl)ethyl]amino}ethyl)-N-[(3-fluoropyridin-2-yl)methyl]-1,3-oxazole-4-carboxamide trihydrochloride for the treatment of beta-thalassaemia intermedia and major

On 28 June 2019, orphan designation EU/3/19/2170 was granted by the European Commission to Vifor France S.A., France, for 2-(2-{[2-(1H-benzimidazol-2-yl)ethyl]amino}ethyl)-N-[(3-fluoropyridin-2-yl)methyl]-1,3-oxazole-4-carboxamide trihydrochloride (also known as VIT-2763) 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 approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 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).

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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. This represents a population of 518,400,000 (Eurostat 2019).



## **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 the medicine might be of significant benefit for patients with beta-thalassaemia intermedia and major. This is because results from laboratory studies suggest it can reduce anaemia, a symptom that existing treatments do not address. 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?**

The medicine blocks a protein, ferroportin, which transports iron from inside the cells into the bloodstream. This is expected to reduce iron levels in the blood and to decrease the damaging effect of high blood iron levels 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, no clinical trials with the medicine 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 the treatment of beta-thalassaemia intermedia and major or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a Positive opinion on 23 May 2019, 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](#).

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<sup>1</sup>, Norwegian and Icelandic

Language	Active ingredient	Indication
English	2-(2-{[2-(1H-benzimidazol-2-yl)ethyl]amino}ethyl)-N-[(3-fluoropyridine-2-yl)methyl]-1,3-oxazole-4-carboxamide trihydrochloride	Treatment of beta-thalassaemia intermedia and major
Bulgarian	2-(2-{[2-(1H-бензимидазол-2-ил)етил]амино}етил)-N-[(3-флуоропиридин-2-ил)метил]-1,3-оксазол-4-карбоксамид трихидрохлорид	Лечение на бета таласемия интермедия и майор
Croatian	2-(2-{[2-(1H-benzimidazol-2-il)etil]amino}etil)-N-[(3-fluoropiridin-2-il)metil]-1,3-oksazol-4-karboksamid trihidroklorid	Liječenje beta-talasemije intermedije i major
Czech	2-(2-{[2-(1H-benzimidazol-2-yl)ethyl]amino}ethyl)-N-[(3-fluoropyridin-2-yl)methyl]-1,3-oxazol-4-karboxamid trihydrochlorid	Léčení beta thalasémie intermedia a major
Danish	2-(2-{[2-(1H-benzimidazol-2-yl)ethyl]amino}ethyl)-N-[(3-fluoropyridin-2-yl)methyl]-1,3-oxazol-4-carboxamidtrihydrochlorid	Behandling af beta-thalassæmia intermedia og major
Dutch	2-(2-{[2-(1H-benzimidazool-2-yl)ethyl]amino}ethyl)-N-[(3-fluoropyridine-2-yl)methyl]-1,3-oxazool-4-carboxamide trihydrochloride	Behandeling van bètathalassemie intermedia en major
Estonian	2-(2-{[2-(1H-bensimidasool-2-üül)etüül]amino}etüül)-N-[(3-fluoropüridiin-2-üül)metüül]-1,3-oksasool-4-karboksamiidtrivesinikkloriid	Keskmise ja raske beetatalasseemia ravi
Finnish	2-(2-{[2-(1H-bentsimidatsoli-2-yyli)etyyli]amino}etyyli)-N-[(3-fluoropyridiini-2-yyli)metyyli]-1,3-oksatsoli-4-karboksamiditrihydrokloridi	Beetatalasseemia intermedia-ja major-tyypin hoito
French	2-(2-{[2-(1H-benzimidazole-2-yl)éthyle]amino}éthyle)-N-[(3-fluoropyridine-2-yl)méthyle]-1,3-oxazole-4-carboxamide trihydrochloride	Traitement de la bêta-thalassémie intermédiaire et majeure
German	2-(2-{[2-(1H-Benzimidazol-2-yl)ethyl]amino}ethyl)-N-[(3-fluoropyridin-2-yl)methyl]-1,3-oxazol-4-carboxamid-Trihydrochlorid	Behandlung der Beta-Thalassämie (Intermediäre und Major-Form)

<sup>1</sup> At the time of designation

Language	Active ingredient	Indication
Greek	Τρι-υδροχλωριούχο 2-(2-{[2-(1H-βενζιμιδαζολ-2-υλ)αιθυλ]αμινο}αιθυλ)-N-[(3-φθοροπυριδιν-2-υλ)μεθυλ]-1,3-αξαζολο-4-καρβοξαμίδιο	Θεραπεία της β-μεσογειακής αναιμίας, ενδιάμεσης και μείζονος
Hungarian	2-(2-{[2-(1H-benzimidazol-2-il)etil]amino}etil)-N-[(3-fluoropiridin-2-il)metil]-1,3-oxazol-4-karboxamid-trihidroklorid	Béta-talasszémia intermedia és major kezelése
Italian	2-(2-{[2-(1H-benzimidazolo-2-yl)etil]ammino}etil)-N-[(3-fluoropiridina-2-yl)metil]-1,3-ossazolo-4-carbossammide triidroccloruro	Trattamento della beta-talassemia intermedia e major
Latvian	2-(2-{[2-(1H-benzimidazol-2-il)etil]amino}etil)-N-[(3-fluorpiridīn-2-il)metil]-1,3-oksazol-4-karboksamīda trihidrohlorīds	Vidēji izteiktas un izteiktas bēta talasēmijas ārstēšana
Lithuanian	2-(2-{[2-(1H-benzimidazol-2-il)etil]amino}etil)-N-[(3-fluoropiridin-2-il)metil]-1,3-oksazol-4-karboksiamido trihidrochloridas	Vidutinio sunkumo ir sunkios β-talasemijos gydymas
Maltese	2-(2-{[2-(1H-benzimidazol-2-yl)ethyl]amino}ethyl)-N-[(3-fluoropyridin-2-yl)methyl]-1,3-oxazole-4-carboxamide trihydrochloride	Kura tal-beta talassemija intermedja u maġġuri
Polish	Trichlorowodorek 2-(2-{[2-(1H-benzimidazol-2-ylo)etylo]amino}etylo)-N-[(3-fluoropirydyn-2-ylo)metylo]-1,3-oksazolo-4-karboksyamidu	Leczenie talasemii beta-intermedia i major
Portuguese	Tricloridrato de 2-(2-{[2-(1H-benzimidazol-2-il)etil]amino}etil)-N-[(3-fluoropiridin-2-il)metil]-1,3-oxazol-4-carboxamida	Tratamento da beta talassémia intermédia e major
Romanian	Triclorhidrat de 2-(2-{[2-(1H-benzimidazol-2-il)etil]amino}etil)-N-[(3-fluoropiridin-2-il)metil]-1,3-oxazol-4-carboxamidă	Tratamentul beta talasemiei intermediare și majore
Slovak	2-(2-{[2-(1H-benzimidazol-2-yl)etyl]amino}etyl)-N-[(3-fluoropyridín-2-yl)metyl]-1,3-oxazol-4-karboxamid trihydrochlorid	Liečba stredne závažnej a závažnej beta talasémie
Slovenian	2-(2-{[2-(1H-benzimidazol-2-il)etil]amino}etil)-N-[(3-fluoropiridin-2-il)metil]-1,3-oksazol-4-karboksamid trihidroklorid	Zdravljenje srednje in velike talasemije beta
Spanish	2-(2-{[2-(1H-bencimidazol-2-il)etil]amino}etil)-N-[(3-fluoropiridina-2-il)metil]-1,3-oxazol-4-carboxamida triclorhidrato	Tratamiento de la beta talasemia intermedia y mayor
Swedish	2-(2-{[2-(1H-bensimidazol-2-yl)etyl]amino}etyl)-N-[(3-fluoripyridin-2-yl)metyl]-1,3-oxazol-4-karboxylsyra-amid-trihydroklorid	Behandling av beta-thalassaemia intermedia och major
Norwegian	2-(2-{[2-(1H-benzimidazol-2-yl)etyl]amino}etyl)-N-[(3-fluorpyridin-2-yl)metyl]-1,3-oksazol-4-karboksamidtrihydroklorid	Behandling av beta-thalassemia intermedia og beta-thalassemia major

Language	Active ingredient	Indication
Icelandic	2-(2-{[2-(1H-bensímídasól-2-ýl)etýll]amínó}etýll)-N-[(3-flúorópýrídín-2-ýl)metýl]-1,3-oxasól-4-karboxamíð trívetrnisklóríð	Meðferð á langvinnu járnofhleðslu sem krefst klómeðferðar