9 January 2020
EMADOC-628903358-1520

Public summary of opinion on orphan designation

2-(3-(4-(1H-Indazol-5-ylamino)quinazolin-2-yl)phenoxy)-N-isopropylacetamide-methane sulfonic acid salt for the treatment of graft-versus-host disease

On 17 October 2019, orphan designation EU/3/19/2205 was granted by the European Commission to Quality Regulatory Clinical Ireland Limited, Ireland, for 2-(3-(4-(1H-indazol-5-ylamino)quinazolin-2-yl)phenoxy)-N-isopropylacetamide-methane sulfonic acid salt (also known as KD025) for the treatment of graft-versus-host disease.

What is graft-versus-host disease?

Graft-versus-host disease is a complication that can occur in patients who have had a transplant. In this disease, the transplanted cells recognise the patient's body as 'foreign' and attack the patient's organs, such as the stomach, gut, skin and liver, leading to organ damage. The disease may occur shortly after transplantation or later on, in which case more organs can be affected.

Graft-versus-host disease is a serious and life-threatening disease with a high mortality rate.

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

At the time of designation, graft-versus-host disease affected approximately 0.8 in 10,000 people in the European Union (EU). This was equivalent to a total of around 41,000 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, several medicines were authorised in the EU for the treatment of graft-versus-host disease, such as ciclosporin and corticosteroids. Treatment aimed to reduce the activity of transplanted cells involved in graft-versus-host disease, thereby reducing their ability to attack the patient's organs.

*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).

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The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients with graft-versus-host disease. Early data showed that patients' condition improved and they used less corticosteroids after treatment with the medicine. 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 an enzyme called Rho-associated protein kinase 2 (ROCK2) that plays a role in the inflammation that occurs in graft-versus-host disease and leads to organ damage. By blocking this enzyme, the medicine is expected to help reduce inflammation and thereby relieve 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 graft-versus-host disease were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of graft-versus-host disease. Orphan designation had been granted in the United States for chronic graft-versus-host disease.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 12 September 2019, 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.

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	2-(3-(4-(1H-indazol-5-ylamino)quinazolin-2-yl)phenoxy)-N-isopropylacetamide-methane sulfonic acid salt	Treatment of graft-versus-host disease
Bulgarian	Сол на 2-(3-(4-(1H-индазол-5-иламино)квиназолин-2-ил)фенокси)-N-изопропилацетамид-метан и сулфонова киселина	Лечение на болестта на присадката срещу приемателя
Croatian	2-(3-(4-(1H-indazol-5-ilamino)kinazolin-2-il)fenoksi)-N-izopropilacetamid-metanska sulfonska sol	Liječenje reakcije presatka protiv primatelja
Czech	2-(3-(4-(1H-indazol-5-ylamino)chinazolin-2-yl)fenoxy)-N-isopropylacetamid-methan sulfonát	Léčba reakce štěpu proti hostiteli
Danish	2-(3-(4-(1H-indazol-5-ylamino)quinazolin-2-yl)phenoxy)-N-isopropylacetamid-methan sulfonylsyre salt	Behandling af graft versus host reaktion
Dutch	2-(3-(4-(1H-indazol-5-ylamino)quinazolin-2-yl)phenoxy)-N-isopropylacetamide-methane sulfonic acide zout	Behandeling van graft versus host ziekte
Estonian	2-(3-(4-(1H-indasool-5-üülamino)kvinasoliin-2-üül)fenoksü)-N-isopropüülatseetamiid-metaan sulfoonhappe sool	Graft versus host haiguse ravi
Finnish	2-(3-(4-(1H-indatsol-5-yyliamino)kinatsolin-2-yyli)fenoksi)-N-isopropyyliasetamidi-metaani sulfonihappo suola	Käänteishyljintäreaktion hoito
French	Sel de 2-(3-(4-(1H-indazol-5-ylamino)quinazolin-2-yl)phenoxy)-N-isopropylacetamide-methane sulfonic acide	Traitement de la réaction du greffon contre l'hôte
German	2-(3-(4-(1H-indazol-5-ylamino)quinazolin-2-yl)phenoxy)-N-isopropylacetamide-methane Sulfonsäurensalz	Behandlung der Graft-versus-Host-Reaktion
Greek	2-(3-(4-(1H-ινδαζολ-5-υλαμινο)κιναζολιν-2-υλ)φαινοξυ)-N-ισοπροπυλακεταμιδο-μεθανιο σουλφονικό άλας	Θεραπεία της αντίδρασης του μοσχεύματος
Hungarian	2-(3-(4-(1H-indazol-5-ilamino)quinazolin-2-yl)phenoxy)-N-izopropylacetamid-metán szulfonsav só	Graft-versus-host betegség kezelése
Italian	2-(3-(4-(1H-indazol-5-ylamino)quinazolin-2-yl)fenossi)-N-isopropilacetamide-metano sale dell’ acido sulfonico	Trattamento della reazione del trapianto contro l’ospite
Latvian	2-(3-(4-(1H-indazol-5-ilamīn)hinazolīn-2-il)fenoksi)-N-izopropilacetamīda-metāna sulfoskābes sāls	Saimnieka-transplantāta slimības ārstēšana

[1] At the time of designation

Language	Active ingredient	Indication
Lithuanian	2-(3-(4-(1H-indazol-5-ilamino)kvinazolin-2-il)fenoksi)-N-izopropilacetamido-metano sulfoninės rūgšties druska	Transplantato atmetimo ligos gydymas
Maltese	2-(3-(4-(1H-indażol-5-ilammino)kwinażolin-2-yl)fenossi)-N-isopropilaċetamid-metan melħ tal-aċidu sulfoniku	Kura tal-marda tat-tessut għat-trapjant kontra dak li jirċievih
Polish	Sól kwasu 2-(3-(4-(1H-indazol-5-ylamino)kwinazolin-2-ylo)fenoksy)-N-izopropylacetamid-metano sulfonowego	Leczenie choroby przeszczep przeciw gospodarzowi
Portuguese	Sal do ácido sulfónico 2-(3-(4-(1*H*-indazol-5-il-amino)quinazolin-2-il)fenoxi)-*N*-isopropilacetamida-metano	Tratamento da reacção do enxerto contra o hospedeiro
Romanian	Sare a acidului 2-(3-(4-(1H-indazol-5-ilamino)chinazolin-2-il)fenoxi)-N-izopropilacetamidă-metan sulfonic	Tratamentul reacţiei grefei contra gazdei
Slovak	Soľ 2-(3-(4-(1H-indazol-5-ylamino)chinazolín-2-yl)fenoxy)-N-izopropylacetamid-metán sulfónovej kyseliny	Liečba reakcie štepu proti hostiteľovi
Slovenian	2-(3-(4-(1H-indazol-5-ilamino)kvinazolin-2-il)fenoksi)-N-izopropilacetamid-metansol sulfonske kisline	Zdravljenje bolezni presadka proti gostitelju
Spanish	Sal de N-isopropilacetamide-metane 2-(3-(4-(1H-indazol-5-ilamino)quinazolin-2-yl)fenoxi)	Tratamiento de la enfermedad de injerto contra huésped
Swedish	2-(3-(4-(1H-indazol-5-ylamino)quinazolin-2-yl)fenoxy)-N-isopropylacetamid-metan sulfonsyrasalt	Behandling av graft-värd host reaktion
Norwegian	2-(3-(4-(1H-indazol-5-ylamino)kinazolin-2-yl)fenoksy)-N-isopropylacetamid-metansulfonsyresalt	Behandling av graft-versus-host -reaksjon
Icelandic	Salt af 2-(3-(4-(1H-indazól-5-ylamino)quinazólín-2-yl)fenoxý)-N-ísopropýlacetamíð-metansúlfónsýru	Til meðferðar á hýsilssótt