



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## Public summary of opinion on orphan designation

Haematopoietic stem cells and blood progenitors umbilical cord-derived expanded with (1R, 4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexane-1,4-diamine dihydrobromide dihydrate for use in haematopoietic stem cell transplantation

On 22 April 2020, orphan designation EU/3/20/2271 was granted by the European Commission to CATS Consultants GmbH, Germany, for haematopoietic stem cells and blood progenitors umbilical cord-derived expanded with (1R, 4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexane-1,4-diamine dihydrobromide dihydrate (also known as ECT-001) for use in haematopoietic stem cell transplantation.

### What is haematopoietic stem cell transplantation?

Haematopoietic stem cell transplantation (HSCT) is a procedure where the patient's bone marrow is cleared of cells and replaced by cells from a donor to form new bone marrow that produces healthy blood cells. It can be used to treat serious diseases of the blood and immune system such as leukaemia.

HSCT can be a debilitating and life-threatening procedure due to graft-versus-host disease (when the transplanted cells regard the patient's body as 'foreign' and attack the patient's organs, leading to organ damage).

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

At the time of designation, approximately 0.7 in 10,000 people received HSCT every year in the European Union (EU). This was equivalent to a total of around 36,000 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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\*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, Iceland, Liechtenstein, Norway and the United Kingdom. This represents a population of 519,200,000 (Eurostat 2020).

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## **What treatments are available?**

At the time of designation, several medicines were authorised in the EU for patients undergoing HSCT. These included medicines that suppress the immune system, such as ciclosporin and corticosteroids, which were used for the treatment of graft-versus-host disease.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients undergoing haematopoietic stem cell transplantation. Early studies have shown that using this medicine for stem cell transplantation may lead to better outcomes than using other blood stem cells from donors.

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?**

This medicine is made of blood stem cells taken from the umbilical cord after it has been removed from a newborn baby. These cells, which have a low risk of causing graft-versus-host disease, are treated and grown in the laboratory to increase their numbers to useful levels. When given to patients undergoing haematopoietic stem cell transplantation, they are expected to lead to fewer cases of graft-versus-host disease and thereby improve patients' outcomes.

## **What is the stage of development of this medicine?**

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

At the time of submission of the application for orphan designation, clinical trials in patients with treatment in haematopoietic stem cell transplantation were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for use in haematopoietic stem cell transplantation. Orphan designation had been granted in the United States for the prevention of graft-versus-host disease.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 19 March 2020, 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   | Haematopoietic stem cells and blood progenitors umbilical cord-derived expanded with (1R, 4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexane-1,4-diamine dihydrobromide dihydrate                | Treatment in haematopoietic stem cell transplantation       |
| Bulgarian | Хематопоетични стволови клетки и кръвни прогенитори от пъпната връв, култивирани с (1R, 4R) -N1- (2-бензил-7- (2-метил-2H-тетразол-5-ил) -9H-пиримидо [4,5-b ] индол-4-ил) циклохексан-1,4-диамин дихидробромид дихидрат              | Лечение при трансплантация на хемопоетични стволови клетки  |
| Croatian  | Matične stanice hematopoetskih stanica i krvni potomci dobiveni iz pupčane vrpce prošireni s (1R, 4R) -NI- (2-benzil-7- (2-metil-2H-tetrazol-5-il) -9H-pirimido [4,5-b ] indol-4-il) cikloheksan-l, 4-diamin dihidrobromid dihidrat   | Liječenje u transplantaciji hematopoetskih matičnih stanica |
| Czech     | Hematopoetické kmenové buňky a progenitory derivované z pupečnickové krve expandované s (1R, 4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido [4,5-b]indol-4-yl)cyclohexan-1,4-diamin dihydrobromid dihydrátem              | Léčba transplantace hemopoetickými zárodečnými buňkami      |
| Danish    | Hæmatopoietiske stamceller og navlestrengsafledte hæmatopoietiske stamceller udvidet med (1R, 4R)-N1-(2-benzyl-7-(2-methyl-2H-tetrazol-5-yl)-9H-pyrimido[4,5-b]indol-4-yl)cyclohexan-1,4-diamindihydrobromiddihydrat                  | Behandling ved hæmatopoietisk stamcelletransplantation      |
| Dutch     | Hematopoietische stamcellen en bloedvoorlopers verkregen uit de navelstreng, geëxpandeerd met (1R, 4R) - N1- (2-benzyl-7- (2-methyl-2H-tetrazol-5-yl) -9H-pyrimido [4,5-b] indol-4-yl) cyclohexaan-1,4-diaminedihydrobromidedihydraat | Behandeling in haematopoïetische stemceltransplantatie      |

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

| Language  | Active ingredient  | Indication   |
|-----------|--|--|
| Estonian  | Nabaväädist saadud vereloome tüvirakud ja vere eellasrakud, mis on paisutatud paljundatud (1R, 4R) -N1- (2-bensüül-7- (2-metüül-2H-tetrasool-5-üül) -9H-pürimido [4,5-b abil ] indool-4-üül) tsükloheksaan-1,4-diamiindihüdrobromiidihüdraadi abilt  | Kasutamiseks hematopoeetiliste tüvirakkude transplantatsiooni ravis. |
| Finnish   | Hematopoeettiset kantasolut ja napanuorasta peräisin olevat laajennetut verisolujen esisolut , (1R, 4R) -N1- (2-bentsyyli-7- (2-metyyli-2H-tetratsol-5-yyli) -9H-pyrimidi [4,5-b ] indol-4-yyli) sykloheksaani-1,4-diamiinidihydrobromididihydraatti | Hoito hematopoeettisen kantasolusiirron yhteydessä                   |
| French    | Cellules souches hématopoïétiques et progéniteurs du sang dérivés du cordon ombilical expansés avec (1R, 4R) -N1- (2-benzyl-7- (2-méthyl-2H-tétrazol-5-yl) -9H-pyrimido [4,5-b] indol-4-yl) cyclohexane-1,4-diamine dihydrobromure de dihydrate      | Traitement dans la greffe de moëlle osseuse                          |
| German    | Aus der Nabelschnur stammende hämatopoetische Stammzellen und Blutvorläufer, expandiert mit (1R, 4R) -N1- (2-Benzyl-7- (2-methyl-2H-tetrazol-5-yl) -9H-pyrimido [4,5-b] Indol-4-yl) cyclohexan-1,4-diamin-dihydrobromiddihydrat                      | Behandlung in hämatopoetischer Stammzelltransplantation              |
| Greek     | Αιμοποιητικά βλαστικά και προγονικά κύτταρα προερχόμενα από ομφάλιο λώρο πολλαπλασιασμένα με (1R, 4R)-N1-(2-βενζυλ-7-(2-μεθυλ-2H-τετραζολ-5υλ)-9H-πυριμιδο [4,5-b] ινδολ-4-υλ)κυκλοεξανο-1,4-διαμίνη διένυδρο διϋδροβρωμίδιο                         | θεραπεία σε μεταμόσχευση αρχέγονων αιμοποιητικών κυττάρων            |
| Hungarian | A hematopoietikus őssejtek és a vér progenitorainak köldökzsínorból származó származéka (1R, 4R) -N1- (2-benzil-7- (2-metil-2H-tetrazol-5-il) -9H-pirimido [4,5-b] indol-4-il) ciklohexán-1,4-diamin-dihydrobromid-dihidrát                          | Hematopoietikus őssejt-transzplantáció esetén alkalmazandó           |

| Language   | Active ingredient  | Indication   |
|------------|--|--|
| Italian    | Cellule staminali ematopoietiche e progenitori del sangue derivate dal cordone ombelicale espanse con (1R, 4R) - N1- (2-benzil-7- (2-metil-2H-tetrazol-5-il) -9H-pirimido [4,5-b ] indol-4-il) cicloesano-1,4-diammina diidrobromuro diidrato  | Trattamento nel trapianto di cellule staminali ematopoietiche            |
| Latvian    | No nabassaites iegūtas hematopoētiskās cilmes šūnas un asins progenitori, kas paplašināti ar (1R, 4R)-N1- (2-benzil-7-(2-metil-2H-tetrazol-5-il)-9H-pirimido [4,5-b] indol-4-il) cikloheksān-1,4-diamīna dihidrobromīda dihidrātu  | Ārstēšanai hematopoētisko cilmes šūnu transplantācijā                    |
| Lithuanian | (1R, 4R) -N1- (2-benzil-7- (2-metil-2H-tetrazol-5-il) -9H-pirimido [4,5-b ] indol-4-il) cikloheksan-1,4-diamino dihidrobromido dihidratas dihidratu  | Taikoma hematopoetinių kamieninių ląstelių transplantacijų gydyme        |
| Maltese    | Ċelloli staminali ematopojetiči u proġenituri tad-demm derivati mill-kurdun umbilicali mkabbra b'(1R, 4R)-N1-(2-benzil-7-(2-metil-2H-tetrazol-5-il)-9H-pirimido [4,5-b]indol-4-il)ċikloeżan-1,4-diammina diidrobromur diidrat  | Kura fi trapjant ta' ċelloli staminali ematopojetiči                     |
| Polish     | Hematopoetyczne komórki macierzyste i progenitory krwi pochodzące z pępowiny ekspandowane z dwuwodnym (1R, 4R) - N1- (2-benzylo-7- (2-metylo-2H-tetrazol-5-ilo) -9H-piryrido [4,5-b ] indol-4-ylo) cykloheksano-1,4-diamino dwuhydrobromkiem   | Leczenie w przebiegu przeszczepu hematopoetycznych komórek macierzystych |
| Portuguese | Células-estaminais hematopoiéticas e células progenitoras derivados do sangue do cordão umbilical expandidas com dihidrobrometo di-hidratado de (1R, 4R) - N1- (2-benzil-7- (2-metil-2H-tetrazol-5-il) -9H-pirimido [4,5-b ] di-hidrobrometo de indol-4-il) ciclo-hexano-1,4-diamina | Tratamento em transplantes de células estaminais hematopoiéticas         |
| Romanian   | Celule stem hematopoietice și progenitoare sangvine derivate din cordonul ombilical expandate cu (1R, 4R) -N1- (2-benzil-7- (2-metil-2H-tetrazol-5-il) -9H-pirimido [4,5-b ] indol-4-il) ciclohexan-1,4-diamina dihidrobromid dihidrat   | Tratament în transplantul de celule stem hematopoietice                  |

| Language  | Active ingredient  | Indication  |
|-----------|--|---|
| Slovak    | Hematopoetické kmeňové bunky a krvné progenitory derivované z pupočnej šnúry rozšírené o (1R, 4R) -N1- (2-benzyl-7- (2-metyl-2H-tetrazol-5-yl) -9H-pyrimido [4,5-b ] dihydrobromid dihydrobromid indol-4-yl) cyklohexán-1,4-diamín dihydrobromid dihydrát      | Liečba pri transplantácii hematopoietických kmeňových buniek  |
| Slovenian | Krvotvorne matične celice in progenitorske krvne celice popkovine, ekspandirane z z (1R, 4R) -N1- (2-benzil-7- (2-metil-2H-tetrazol-5-il) -9H-pirimido [4,5-b ] indol-4-il) cikloheksan-1,4-diamin dihidrobromid dihidratom                                    | Zdravljenje pritransplantaciji hematopoetskih matičnih celic  |
| Spanish   | Las células madre hematopoyéticas y los progenitores sanguíneos derivados del cordón umbilical se expandieron con (1R, 4R) -N1- (2-bencil-7- (2-metil-2H-tetrazol-5-il) -9H-pirimido [4,5-b ] diol-4-il) ciclohexano-1,4-diamina dihidrobromuro dihidrato      | Tratamiento en el trasplante de células madre hematopoyéticas |
| Swedish   | Hematopoietiska progenitor- och stamceller från navelsträng, expanderade med (1R, 4R) -N1- (2-bensyl-7- (2-metyl-2H-tetrazol-5-yl) -9H-pyrimido [4,5-b ] indol-4-yl) cyklohexan-1,4-diamin-dihydrobromid-dihydrat  | Behandling vid hematopoetisk stamcellstransplantation         |
| Norwegian | Hematopoietiske stamceller og forløperceller til blodblodforfedre avledet fra navlestreng-avledet ekspandertutvidet med (1R, 4R) -N1- (2-benzyl-7- (2-metyl-2H-tetrazol-5-yl) -9H-pyrimido [4,5-b ] indol-4-yl) scykloheksan-1,4-diamin-dihydrobromid-dihydrat | Behandling ved hematopoetisk stamcelletransplantasjon         |
| Icelandic | Blóðmyndandi stofnfrumur og blóðfrumuforverar úr naflastreng auknar með (1R, 4R) -N1- (2-bensýl-7- (2-metýl-2H-tetrazól-5-ýl) -9H-pýrimídó [4,5-b ] indól-4-ýl) cýklóhexan-1,4-díamín tvíhýdróbrómíð tvíhýdrat   | Meðferð við ígræðslu blóðmyndandi stofnfrumna                 |