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Public summary of opinion on orphan designation

Anti-neonatal Fc receptor human monoclonal antibody for the prevention of haemolytic disease of the foetus and newborn

On 17 October 2019, orphan designation EU/3/19/2209 was granted by the European Commission to Biopharma Excellence GmbH, Germany, for anti-neonatal Fc receptor human monoclonal antibody (also known as M281) for the prevention of haemolytic disease of the foetus and newborn.

What is haemolytic disease of the foetus and newborn?

Haemolytic disease of the foetus and newborn (HDFN) is a condition in which red blood cells in the foetus or a newborn baby break down rapidly. This can cause anaemia in the baby and a build-up of bilirubin, a breakdown product of blood. The condition may cause the baby to have a large liver, spleen or heart. The excess bilirubin may cause jaundice and it can enter the brain to cause kernicterus, which affects brain development.

HDFN commonly occurs because the baby's red blood cells have a protein (antigen) that is absent from the mother's red blood cells. A common antigen associated with HDFN is called Rhesus antigen D protein (RhD). The baby is said to have RhD positive blood. The mother's immune system (the body's defence) makes antibodies against RhD if the mother's and baby's blood have come into direct contact. The antibodies enter the baby's circulation and attack the baby's red blood cells. Other types of antigens present on red blood cells can trigger HDFN.

HDFN is a life-threatening and chronically debilitating condition due to the development of haemolytic anaemia, which often requires red blood cells transfusion. It can damage the baby's vital organs including the brain and, in the most severe form, can cause the baby's death inside the womb.

What is the estimated number of patients at risk of developing the condition?

At the time of designation, the number of patients at risk of HDFN was estimated to be approximately 3.6 people in 10,000 in the European Union (EU). This was equivalent to a total of around 190,000 people*, and is below the ceiling for orphan designation which is 5 people in 10,000. This is based on

*Disclaimer: For the purpose of the designation, the number of patients at risk of developing 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 information provided by the sponsor and the knowledge of the Committee for Orphan Medicinal Products (COMP).

What methods of prevention are available?

At the time of submission, pregnant women who were RhD negative typically received prophylaxis with Rh immunoglobulins if their foetus was confirmed to be RhD positive. This prevented certain types of disease (those associated with D-type antigens of Rh group). However, no prophylactic therapy was available to prevent HDFN associated with other types of antigens or if a pregnant woman had already developed HDFN-associated antibodies. For pregnancies at risk of HDFN, specialised prenatal care by maternal–foetal medicine doctors was recommended. Intrauterine transfusion was used when the pregnancy was more advanced and the foetus had anaemia.

The sponsor has provided sufficient information to show that the medicine might be of significant benefit for patients at risk of developing HDFN. Early laboratory data showed that the medicine can reduce transfer across the placenta of maternal antibodies and therefore prevent HDFN associated with different types of antigens. 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 is a monoclonal antibody (a type of protein) designed to block a receptor (target) called FcRn, which is involved in the circulation of antibodies. When given to the mother during pregnancy it is expected to reduce the level of antibodies in the mother's blood circulation and thereby the transfer of maternal antibodies across the placenta. This should lower the amount of antibodies transferred to the foetus, and therefore prevent or reduce the destruction of the baby's red blood cells.

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 HDFN were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for the prevention of HDFN 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 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	Anti-neonatal Fc receptor human monoclonal antibody	Prevention of haemolytic disease of the foetus and newborn
Bulgarian	Анти-неонатално Fc рецепторно човешко моноклонално антитяло	Предотвратяване на хемолитична болест на плода и новороденото
Croatian	Ljudsko monoklonsko protutijelo na neonatalni Fc receptor	Sprječavanje hemolitičke bolesti fetusa i novorođenčeta
Czech	Lidská monoklonální protilátka proti neonatálnímu Fc receptoru	Prevence hemolytického onemocnění plodu a novorozence
Danish	Anti-neonatal Fc-receptor humant monoklonalt antistof	Forebyggelse af hæmolytisk sygdom hos fostre og nyfødte
Dutch	Humaan monoklonaal antilichaam gericht tegen neonatale Fc-receptor	Preventie van hemolytische ziekte van de foetus en pasgeborene
Estonian	Nneonataalse Fc retseptori vastane inimese monokloonne antikeha	Loote ja vastsündinu hemolüütilise tõve ennetamine
Finnish	Humaani monoklonaalinen vasta-aine vastasyntyneen Fc-reseptorille	Sikiön ja vastasyntyneen hemolyyttisen taudin ehkäisy
French	Anticorps humains monoclonaux dirigés contre le récepteur Fc néonatalneonatal	Prévention de la maladie hémolytique du fœtus et du nouveau-né
German	Humaner monoklonaler Antikörper gegen den neonatalen Fc-Rezeptor	Vorbeugung der hämolytischen Krankheit bei Feten und Neugeborenen
Greek	Ανθρώπινο μονοκλωνικό αντίσωμα έναντι του νεογνικού Fc υποδοχέα	Πρόληψη της αιμολυτικής νόσου εμβρύου και νεογνού
Hungarian	Neonatális Fc-receptor elleni humán monoklonális antitest	A magzat és az újszülött hemolitikus betegségének megelőzése
Italian	Anticorpo monoclonale umano anti-recettore Fc neonatale	Prevenzione della malattia emolitica del feto e del neonato
Latvian	Cilvēka monoklonālā antiviela pret jaundzimušā Fc receptoru	Augļa un jaundzimušā hemolītiskās slimības profilakse
Lithuanian	Žmogaus monokloninis antikūnas prieš naujagimių Fc receptorių	Vaisiaus ir naujagimio hemolizinės ligos prevencija
Maltese	Antikorp monoklonali uman kontra r-riċettur Fc tat-tarbija tat-twelid	Prevenzjoni jew tnaqqis fis-severità tal-marda emolitika tal-fetu u tat-tarbija tat-twelid
Polish	Ludzkie przeciwciało monoklonalne przeciw noworodkowemu receptorowi Fc	Zapobieganie chorobie hemolitycznej płodu i noworodka
Portuguese	Anticorpo monoclonal humano anti-recetor Fc neonatal	Prevenção da doença hemolítica fetal e do recém-nascido
Romanian	Anticorp monoclonal uman anti-receptor Fc neonatal	Prevenirea bolii hemolitice a fătului și nou născutului

[1] At the time of designation

Language	Active ingredient	Indication
Slovak	Ľudská monoklonálna protilátka proti neonatálnemu Fc receptoru	Prevencia hemolytickej choroby plodu a novorodenca
Slovenian	Človeško monoklonsko protitelo proti neonatalnem receptorju Fc	Preprečevanje ali zmanjševanje jakosti hemolitične bolezni ploda in novorojenčka
Spanish	Anticuerpo monoclonal humano contra el receptor Fc neonatal	Prevención de la enfermedad hemolítica del feto y el recién nacido
Swedish	Monoklonal anti-neonatal Fc-receptor-humanantikropp	Förebyggande eller minskning av allvarlighetsgrad av hemolytisk sjukdom hos foster och nyfödda
Norwegian	Anti-neonatal Fc-reseptor, humant monoklonalt antistoff	Forebygging eller reduksjon av alvorlighetsgraden av hemolytisk sykdom hos foster og nyfødte
Icelandic	Einstofna mannamótefni gegn Fc viðtaka nýbura	Til að fyrirbyggja eða draga úr alvarleika rauðkornaleysandi sjúkdóms hjá fóstrum og nýburum