12 September 2013
EMA/COMP/432735/2013
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(1R,3R,4R,5S)-3-O-[2-O-benzoyl-3-O-(sodium(2S)-3-cyclohexyl-propanoate-2-yl)-β-D-galactopyranosyl]-4-O-(α-L-fucopyranosyl)-5-orothylamido-cyclohexane-1-carboxylic acid ethyl-2-amidyl-ethyloxy-2-acetyl-(8-amino-1,3,6-naphthalene-tris sodium sulfonate) amide for the treatment of sickle cell disease

On 5 August 2013, orphan designation (EU/3/13/1184) was granted by the European Commission to Pfizer Limited, United Kingdom, for (1R,3R,4R,5S)-3-O-[2-O-benzoyl-3-O-(sodium(2S)-3-cyclohexyl-propanoate-2-yl)-β-D-galactopyranosyl]-4-O-(α-L-fucopyranosyl)-5-orothylamido-cyclohexane-1-carboxylic acid ethyl-2-amidyl-ethyloxy-2-acetyl-(8-amino-1,3,6-naphthalene-tris sodium sulfonate) amide for the treatment of sickle cell disease.

What is sickle cell disease?

Sickle cell disease is a genetic disease in which the red blood cells become rigid and sticky, and change from being disc-shaped to being crescent-shaped (like a sickle). The change in shape is caused by the presence of an abnormal form of haemoglobin, the protein in red blood cells that carries oxygen around the body. In patients with sickle cell disease, the abnormal red blood cells attach to the walls of blood vessels and block them, restricting the flow of oxygen-rich blood to the internal organs such as the heart, lungs and spleen. Because the abnormal red blood cells have a shorter life span, they release haemoglobin into the blood circulation rather than carrying it to the internal organs where it is needed. As a result, the disease causes severe pain and damage to these organs as well as repeated infections and anaemia (low red blood cell counts).

Sickle cell disease is a severe disease that is long lasting and may be life threatening because of damage to the heart and the lungs, anaemia and infections.

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

At the time of designation, sickle cell disease affected approximately 1.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 76,000 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 only medicine authorised in the EU to treat sickle cell disease was hydroxycarbamide. The main treatment for sickle cell disease was blood transfusion. This was usually combined with 'iron chelators' (medicines used to reduce the high iron levels in the body caused by repeated blood transfusions), which are necessary in patients with long-term anaemias such as sickle cell disease. In some cases, haematopoietic (blood) stem cell transplantation was used (a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow) to allow the patient to produce red blood cells containing normal haemoglobin.

The sponsor has provided sufficient information to show that medicine might be of significant benefit for patients with sickle cell disease because early studies show that it might reduce the duration of 'vaso-occlusive crises' (painful episodes caused by sickle-shaped red blood cells obstructing blood vessels and restricting blood flow to an organ) in patients already treated with currently authorised medicines. 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 expected to work by blocking proteins called selectins that are present on the surface of the cells lining the blood vessels. Selectins are thought to be involved in the attachment of sickle cells and inflammatory cells to the blood vessels, leading to the blockage of the blood flow and pain in patients with sickle cell disease. By blocking selectins, the medicine is expected to prevent the deposit of sickle and inflammatory cells in blood vessels, thereby allowing a better blood flow and improving the symptoms of the disease.

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 sickle cell disease were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for sickle cell disease. Orphan designation of the medicine had been granted in the United States for the treatment of vaso-occlusive crisis in patients with sickle cell disease.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 11 July 2013 recommending the granting of this designation.

[*]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 27), Norway, Iceland and Liechtenstein. This represents a population of 509,000,000 (Eurostat 2013).

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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:

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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	(1R,3R,4R,5S)-3-O-[2-O-benzoyl-3-O-(sodium(2S)-3-cyclohexyl-propanoate-2-yl)-β-D-galactopyranosyl]-4-O-(α-L-fucopyranosyl)-5-orothylamido-cyclohexane-1-carboxylic acid ethyl-2-amidyl-ethyloxy-2-acetyl-(8-amino-1,3,6-naphthalene-tris sodium sulfonate) amide	Treatment of sickle cell disease
Bulgarian	(1R,3R,4R,5S)-3-O-[2-O-бензоил-3-O-(натрий(2S)-3-циклохексил-пропаноат-2-ил)-β-D-галактопиранозил]-4-O-(α-L-фукопиранозил)-5-оротиламидо-циклохексан-1-карбонова киселина (етил-2-амидил-етилокси-2-ацетил-(8-амино-1,3,6-нафтален-трис натриев сулфонат) амид	Лечение на сърповидно-клетъчна анемия
Croatian	Etil-2-amidil-etiloksi-2-acetil-(8-amino-1,3,6-naftalen-tris natrijev sulfonat) amid (1R,3R,4R,5S)-3-O-[2-O-benzoil-3-O-(natrijev(2S)-3-cikloheksil-propanoat-2-il)-β-D-galaktopiranozil]-4-O-(α-L-fukopiranozil)-5-orotilamido-cikloheksan-1-karboksilatne kiseline	Liječenje bolesti srpastih stanica
Czech	(ethyl-2-amidyl-ethyloxy-2-acetyl-(8-amino-1,3,6-naphthalene-tris natrium sulfonat) amid (1R,3R,4R,5S)-3-O-[2-O-benzoyl-3-O-(natrium(2S)-3-cyclohexyl-propanoat-2-yl)-β-D-galactopyranosyl]-4-O-(α-L-fucopyranosyl)-5-orothylamido-cyclohexan-1-kyseliny karboxylové	Léčba srpkovité anémie
Danish	(1R,3R,4R,5S)-3-O-[2-O-benzoyl-3-O-(natrium(2S)-3-cyclohexyl-propanoat-2-yl)-β-D-galactopyranosyl]-4-O-(α-L-fucopyranosyl)-5-orothylamido-cyclohexan-1-carboxylsyre (ethyl-2-amidyl-ethyloxy-2-acetyl-(8-amino-1,3,6-naphthalen-tris natriumsulfonat) amid	Behandling af seglcellesygdom
Dutch	1R,3R,4R,5S)-3-O-[2-O-benzoyl-3-O-(sodium(2S)-3-cyclohexyl-propanoaat-2-yl)-β-D-galactopyranosyl]-4-O-(α-L-fucopyranosyl)-5-orothylamido-cyclohexaan-1-carboxylic zuur (ethyl-2-amidyl-ethyloxy-2-acetyl-(8-amino-1,3,6-naphthaleen-tri sodium sulfonaat) amide	Behandeling van sikkelcelaandoening
Estonian	(1R,3R,4R,5S)-3-O-[2-O-bensoüül-3-O-(naatrium(2S)-3-tsükloheksüül-propanoaat-2-üül)-β-D-galaktopüranosüül]-4-O-(α-L-fukopüranosüül)-5-orotüülamido-tsükloheksaan-1-karboksüülhappe (etüül-2-amidüül-etüüloksü-2-atsetüül-(8-amino-1,3,6-naftaleen-tris naatriumsulfonaat) amiid	Sirprakulise aneemia ravi

[1] At the time of designation

Language	Active ingredient	Indication
Finnish	(1R,3R,4R,5S)-3-O-[2-O-bentsoyyli-3-O-(natrium(2S)-3-sykloheksyyli-propanoaatti-2-yyli)-β-D-galaktopyranosyyli]-4-O-(α-L-fukopyranosyyli)-5-orotylamido-sykloheksaani-1-karboksyylihappo (etyyli-2-amidyyli-etyloksi-2-asetyyli-(8-amino-1,3,6-naftaleeni-trinatriumsulfonaatti) amidi	Sirppisolusyndrooman hoito
French	(1R,3R,4R,5S)-3-O-[2-O-benzoyle-3-O-(sodium(2S)-3-cyclohexyle-propanoate-2-yl)-β-D-galactopyranosyl]-4-O-(α-L-fucopyranosyl)-5-orothylamido-cyclohexane-1-acide carboxylique (éthyl-2-amidyl-éthyloxy-2-acétyl-(8-amino-1,3,6-naphthalène-tris sodium sulfonate) amide	Traitement de la drépanocytose
German	(1R,3R,4R,5S)-3-O-[2-O-Benzoyl-3-O-(Natrium(2S)-3-cyclohexyl-propanoat-2-yl)-β-D-galactopyranosyl]-4-O-(α-L-Fucopyranosyl)-5-Orothylamido-cyclohexan-1-carbonsäure (Ethyl-2-amidyl-ethyloxy-2-acetyl-(8-Amino-1,3,6-naphthalen-tris(Natriumsulfonat) amid	Behandlung der Sichelzellanämie
Greek	(1R,3R,4R,5S)-3-O-[2-O-βενζοϋλο-3-O-(νάτριο(2S)-3-κυκλοεξυλο-προπανοϊκό-2-υλο)-β-D-γαλακτοπυρανοσυλο]-4-O-(α-L-φουκοπυρανοσυλο)-5-οροθυλαμιδο-κυκλοεξανο-1-καρβοξυλικό οξύ αιθυλο-2-αμιδυλο-αιθυλοξυ-2-ακετυλο-(8-αμινο-1,3,6-ναφθαλινο-τρις σουλφονικό νάτριο) αμίδη	Θεραπεία της δρεπανοκυτταρικής αναιμίας
Hungarian	(1R,3R,4R,5S)-3-O-[2-O-benzoil-3-O-(nátrium(2S)-3-ciklohexil-propanoát-2-il)-β-D-galactopiranozil]-4-O-(α-L-fucopiranozil)-5-orothilamido-ciklohexán-1-karboxilsav etil-2-amidil-etiloxi-2-acetil-(8-amino-1,3,6-naftalén-trinátrium- szulfonát) amid	Sarlósejtes anaemia kezelése
Italian	(1R,3R,4R,5S)-3-O-[2-O-benzoil-3-O-(sodio(2S)-3-cicloesil-propanoato-2-il)-β-D-galattopiranosile]-4-O-(α-L-fucopiranosile)-5-orotilamido-cicloesano-1-acido carbossilico etil-2-amidil-etilossi-2-acetil-(8-ammino-1,3,6-tris-naftalene sodio solfonato) ammide	Trattamento dell'anemia falciforme
Latvian	(1R,3R,4R,5S)-3-O-[2-O-benzoil-3-O-(nātrija(2S)-3-cikloheksil-propionāt-2-il)-β-D-galaktopiranozil]-4-O-(α-L-fukopiranozil)-5-orotilamīd-cikloheksān-1-karboksilskābes etil-2-amidil-etiloksi-2-acetil-(8-amino naftalēn-nātrija-1,3,6 -trisulfonāt) amīds	Sirpjveida šūnu anēmijas ārstēšana
Lithuanian	(1R,3R,4R,5S)-3-O-[2-O-benzoil-3-O-(natrio(2S)-3-cikloheksil-propanoato-2-il)- β-D-galaktopiranozil]-4-O-(α-L-fukopiranozil)-5-orotilamido-cikloheksano-1-karboksilo rūgšties etil-2-amidil-etiloksi-2-acetil-(8-amino-1,3,6-naftaleno-tri natrio sulfonato) amidas	Siklemijos gydymas

Language	Active ingredient	Indication
Maltese	(1R,3R,4R,5S)-3-O-[2-O-benzoyl-3-O-(sodium(2S)-3-cyclohexyl-propanoate-2-yl)-β-D-galactopyranosyl]-4-O-(α-L-fucopyranosyl)-5-orothylamido-cyclohexane-1-carboxylic acid ethyl-2-amidyl-ethyloxy-2-acetyl-(8-amino-1,3,6-naphthalene-tris sodium sulfonate) amide	Kura tal-marda taċ-ċelluli sura ta' minġel
Polish	Amid etylo-2-amidyloetyloksy-2-acetylo-(8-amino-1,3,6-naftaleno-tris-sulfonianu sodu) kwasu (1R,3R,4R,5S)-3-O-[2-O-benzoilo-3-O-(sodu(2S)-3-cyklohesylopropioniano-2-yl β-D-galaktopiranozylo]-4-O-(α-L-fukopiranozylo)-5-orotyloamidocyklohekano-1-karboksylowego	Leczenie niedokrwistości sierpowatokrwinkowej
Portuguese	Etil-2-amidil-etiloxi-2-acetil-(sulfonato de 8-amino-1,3,6-tris-naftaleno sódico) amida de ácido (1R,3R,4R,5S)-3-O-[2-O-benzoílo-3-O-((2S)-3-ciclo-hexil-propanoato-2-il de sódio)-β-D- galactopiranosilo]-4-O-(α-L-fucopiranosilo)-5-orotilamido-ciclo-hexano-1-carboxílico	Tratmento do sindrome das células falciformes
Romanian	(1R,3R,4R,5S)-3-O-[2-O-benzoil-3-O-(sodiu(2S)-3-ciclohexil-propanoat-2-il)-β-D-galactopiranozil]-4-O-(α-L-fucopiranozil)-5-orotilamido-ciclohexan-1-acid carboxilic etil-2-amidil-etiloxi-2-acetil-(8-amino-1,3,6-naftalen-sulfonat de trisodiu) amidă	Tratamentul anemiei cu celule falciforme
Slovak	Etyl-2-amidyl-etyloxy-2-acetyl-(8-amino-1,3,6-naftalén-tris nátrium sulfonát) amid kyseliny (1R, 3R, 4R, 5S)-3-O-[2-O-benzoyl-3-cyclohexyl-propanoát-2-yl)-β-D-galaktopyranozyl]-4-O-(α-L-fukopyranozyl)-5-orotylamido-cyklohexán-1-karboxylovej	Liečba kosáčikovej anémie
Slovenian	Etil-2-amidil-etiloksi-2-acetil-(8-amino-1,3,6-naftalen-tris natrijev sulfonat) amid (1R,3R,4R,5S)-3-O-[2-O-benzoil-3-O-(natrijev(2S)-3-cikloheksil-propanoat-2-il)-β-D-galaktopiranozil]-4-O-(α-L-fukopiranozil)-5-orotilamido-cikloheksan-1-karboksilne kisline	Zdravljenje bolezni srpastih celic
Spanish	(1R,3R,4R,5S)-3-O-[2-O-benzoil-3-O-(sodio(2S)-3-ciclohexil-propanoato-2-il)-β-D-galactopiranosil]-4-O-(α-L-fucopiranosil)-5-orotilamido-ciclohexano-1-ácido carboxílico etil-2-amidil-etiloxi-2-acetil-(8-amino-1,3,6-naftaleno- tris sodiosulfonato) amida.	Tratamiento de la anemia drepanocítica
Swedish	(1R,3R,4R,5S)-3-O-[2-O-benzyl-3-O-(natrium(2S)-3-cyklohexyl-propanoat-2-yl)-β-D-galaktopyranosyl]-4-O-(α-L-fukopyranosyl)-5-orotylamido-cyklohexan-1-karboxylsyra etyl-2-amidyl-etyloxy-2-acetyl-(8-amino-1,3,6-naftalen-tris natriumsulfonat) amid	Behandling av sickle cell syndrom
Norwegian	(1R,3R,4R,5S)-3-O-[2-O-benzoyl-3-O-(natrium(2S)-3-sykloheksyl-propanoat-2-yl)-β-D-galaktopyranosyl]-4-O-(α-L-fukopyranosyl)-5-orotylamido-sykloheksan-1-karboksylsyre etyl-2-amidyl-etyloksy-2-acetyl-(8-amino-1,3,6-naftalen-tris natriumsulfonat) amid	Behandling av sigdcellesykdom

Language	Active ingredient	Indication
Icelandic	(1R,3R,4R,5S)-3-O-[2-O-benzóýl-3-O-(natríum(2S)-3-cýklóhexýl-própanóat-2-ýl)-β-D-galaktópýranósýl]-4-O-(α-L-fúkópýranósýl)-5-óróthýlamídó-cýklóhexan-1-carboxýlic sýra ethýl-2-amidýl-ethýloxý-2-acetýl-(8-amínó-1,3,6-naphthalen-tris natríum súlfónat) amíð	Meðferð sigðkornablóðleysis