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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Chimeric locked nucleic acid-deoxynucleoside phosphorothioate-linked oligonucleotide directed against microRNA-451 for the treatment of polycythaemia vera

On 11 January 2012, orphan designation (EU/3/11/940) was granted by the European Commission to Miragen Therapeutics Europe Ltd, United Kingdom, for chimeric locked nucleic acid-deoxynucleoside phosphorothioate-linked oligonucleotide directed against microRNA-451 for the treatment of polycythaemia vera.

What is polycythaemia vera?

Polycythaemia vera is a disease in which the bone marrow (the spongy tissue inside the large bones where blood cells are produced) produces too many red blood cells. This makes the blood thicker and can result in reduced blood flow to the organs and occasionally the formation of blood clots. While some patients with polycythaemia vera do not have any symptoms, others may have itching, tiredness, headache, blurred vision and an enlarged liver and spleen. Patients who develop blood clots in the small blood vessels can also experience a wide range of symptoms including burning pains in the hands. Patients with blood clots in the arteries can have strokes.

Polycythaemia vera is a long-term debilitating and life-threatening condition because it may lead to the formation of blood clots and bleeding, and can result in leukaemia (cancer of the white blood cells) and myelofibrosis (a disease of the bone marrow).

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

At the time of designation, polycythaemia vera affected approximately 3 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 152,000 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).

[*]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 506,300,000 (Eurostat 2011).

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What treatments are available?

At the time of designation, hydroxycarbamide, pipobroman and busulfan were authorised in some Member States to reduce the number of red blood cells in patients with polycythaemia vera. In addition, phlebotomy (removal of some of the blood from the body) and long-term treatment with low-dose aspirin were recommended in some patients to reduce the risk of blood clot formation.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with polycythaemia vera because it works in a different way to existing treatments and early studies in experimental models show that it might improve the treatment of patients with this condition. 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 an 'anti-sense oligonucleotide' medicine. It is expected to work by blocking a molecule called 'microRNA-451'. MicroRNA-451 is found in high levels inside blood cells, where it is thought to regulate their production. By blocking microRNA-451, the abnormal production of red blood cells is expected to decrease, relieving the symptoms of polycythaemia vera.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, the evaluation of the effects of this medicine in experimental models was ongoing.

At the time of submission, no clinical trials with the medicine in patients with polycythaemia vera had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for polycythaemia vera. Orphan designation of the medicine had been granted in the United States of America for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 9 November 2011 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:

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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	Chimeric locked nucleic acid-deoxynucleoside phosphorothioate-linked oligonucleotide directed against microRNA-451	Treatment of polycythaemia vera
Bulgarian	Химерна олигонуклеотидна молекула с дезоксинуклеотиди със "заключена" конформация и фосфоротиоатен край, насочена срещу микроРНК-451	Лечение на полицитемия вера
Czech	Chimerický oligonukleotid tvořený deoxynukleosidthiofosfáty (tzv. uzamčená nukleová kyselina) cílený proti mikroRNA-451	Léčba polycythemia vera
Danish	Kimært LNA-DNA fosforothioate-koblet oligonukleotid rettet mod microRNA-451	Behandling af polycythæmia vera
Dutch	Chimerisch oligonucleotide gericht tegen microRNA-451 en bestaande uit vergrendeld nucleïnezuur en deoxynucleoside gekoppeld via fosforothioaat	Behandeling van polycythaemia vera
Estonian	microRNA-451 vastane kimeeriline lukustatud nukleiinhappe-desoksünukleosiidi fosforotioaadiga seotud oligonukleotiid	Polycythemia vera ravi.
Finnish	MikroRNA-451:tä vastaan suunnattu kimeerinen, lukittu nukleiinihappo-deoksinukleosidi-fosforotioaattiin kiinnittynyt oligonukleotidi	Polysytemia veran hoito
French	Oligonucléotide chimérique dirigé contre le microARN-451 et constitué d'acide nucléique bloqué et de désoxynucléoside liés par une liaison phosphorothioate	Traitement de la Polyglobulie de Vaquez
German	Gegen MicroRNA-451 gerichtetes, chimäres Locked Nucleic Acid (LNA)-Desoxynukleosid Phosphorothioat verknüpftes Oligonukleotid	Behandlung von Polycythemia vera
Greek	Χιμαιρικό ολιγονουκλεοτίδιο από κλειδωμένο νουκλεϊνικό οξύ-δεοξυνουκλεοσίδιο, με σύνδεση με φωσφοροθειικό, που κατευθύνεται έναντι του microRNA-451	Θεραπεία της αληθούς πολυκυτταραιμίας, ή ερυθραιμίας (Polycythaemia vera)
Hungarian	Kiméra jellegű zárt nukleinsav - deoxinukleozid foszforotioát-kapcsolt oligonukleotid mikro RNS-451 ellen	Polycythaemia vera kezelésére
Italian	Oligonucleotide chimerico costituito da acido nucleico bloccato e da deossinucleoside legati con legame fosforotioato, diretto contro microRNA-451	Terapia della policitemia vera

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Fosfortioāta saistīts slēgtas nukleīnskābes – dezoksinukleozīda himērisks oligonukleotīds, kas vērsts pret mikroRNS-451	Polycythemia vera ārstēšanai
Lithuanian	Chimerinis fosforotioato sujungtų uždarosios nukleorūgšties ir deoksinukleozido oligonukleotidas, nukreiptas prieš mikroRNR-451	Tikrosios policitemijos (Polycythemia vera) gydymas
Maltese	Oligonukleotide kimeriku dirett kontra microRNA-451 u magħmul minn aċidu nukleiku ibblokkat u deossinukleoside magħqudin b'phosphorothioate	Kura tal-poliċitemija vera
Polish	Chimeryczny oligonukleotyd LNA połączony wiązaniem deoksynukleotydowo-fosforotionianowym skierowany przeciwko mikroRNA-451	Leczenie czerwienicy prawdziwej
Portuguese	Oligonucleótido quimérico dirigido contra o microRNA-451 e constituído por ácido nucléico bloqueado e desoxinucleósidos ligados por uma ligação fosforotioato	Tratamento da policitemia vera
Romanian	Oligonucleotid chimeric îndreptat împotriva microARN-451 şi alcătuit din acid nucleic blocat şi din dezoxinucleozide, legate prin intermediul unor legături fosforotioat	Tratamentul policitemiei vera
Slovak	Chimerický oligonukleotid obsahujúci LNA (locked nucleic acid - uzamknutá nukleová kyselina)/deoxynukleozid s fosfotioátovými väzbami nasmerovaný proti mikroRNA-451	Liečba pravej polycytémie
Slovenian	Himerni zaklenjen oligonukleotid, povezan z nukleinsko kislino-deoksinukleozidnim fosforotioatom, usmerjen proti mikroRNA-451	Zdravljenje prave policitemije
Spanish	Oligonucleótido quimérico dirigido contra el microARN-451 que consiste de ácido nucléico bloqueado y desoxinucleósido con enlaces fosforotioato	Tratamiento de la policitemia vera
Swedish	Chimär låst nukleinsyre-deoxynukleosid fosforotioat oligonukleotid riktad mot mikroRNA-451	Behandling av polycytemia vera
Norwegian	Kimær LNA-DNAfosforotioat-koblet oligonukleotid rettet mot mikroRNA-451	Behandling av polycythemia vera
Icelandic	Blendings læstur kjarnsýru-deoxýnúkleósíðfosfórótíóat-tengdur ólígónúkleótíð gegn míkróRNA-451	Til meðferðar á polycythemia vera