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EMA/COMP/125750/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Chimeric 2'-O-(2-methoxyethyl) modified oligonucleotide targeted to huntingtin RNA for the treatment of Huntington's disease

On 19 March 2015, orphan designation (EU/3/15/1453) was granted by the European Commission to Isis USA Ltd, United Kingdom, for chimeric 2'-O-(2-methoxyethyl) modified oligonucleotide targeted to huntingtin RNA for the treatment of Huntington's disease.

What is Huntington's disease?

Huntington's disease is a hereditary disease that causes brain cells to die. This leads to symptoms such as involuntary jerky movements, behavioural problems and dementia (loss of intellectual function). The disease is usually first noticed between 35 and 45 years of age, and gets worse over time.

Huntington's disease is caused by defects in the gene responsible for the production of a protein called huntingtin. The gene abnormalities result in an abnormal form of the protein being produced, which causes damage to the cells in specific areas of the brain.

Huntington's disease is a debilitating and life-threatening condition because it causes severe behavioural and mental problems, a progressive loss of the ability to move and potentially life-threatening complications.

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

At the time of designation, Huntington's disease affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 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 treatments authorised in the EU for Huntington's disease were aimed at relieving the symptoms of the disease. In some Member States, haloperidol, pimozide, tetrabenazine

*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 512,900,000 (Eurostat 2015).

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and tiapride were authorised for the abnormal involuntary movements that occur in Huntington's disease. In addition, benzodiazepines were used for anxiety, and antidepressants and lithium to treat depression and mood swings.

The sponsor has provided sufficient information to show that this medicine might be of significant benefit for patients with Huntington's disease because it works in a different way to existing treatments, targeting the production of the abnormal protein responsible for symptoms, which may lead to improvements in several aspects of the condition. Early studies in experimental models showed that it may slow the progression of the disease. 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', a very short piece of synthetic RNA (a type of genetic material), which has been designed to attach specifically to genetic material in the cell responsible for the production of the huntingtin protein in Huntington's disease. This prevents the abnormal protein from being produced, which is expected to reduce damage to brain cells and hence improve symptoms and slow the progression of the disease.

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, no clinical trials with the medicine in patients with Huntington's disease had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for Huntington's disease or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 12 February 2015 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 2'-O-(2-methoxyethyl) modified oligonucleotide targeted to huntingtin RNA	Treatment of Huntington's disease
Bulgarian	Химерен 2'-O-(2-метоксиетил) модифициран олигонуклеотид, насочен срещу РНК на хънтингтин	Лечение на болест на Хънтингтон
Croatian	Kimerični 2'-O-(2-metoksietil)-modificirani oligonukleotid usmjeren na RNK za huntingtin	Liječenje Huntingtonove bolesti
Czech	Chimerický modifikovaný oligonukleotid 2'-O-(2-methoxyethyl) cílený na RNA huntingtinu	Léčba Huntingtonovy nemoci
Danish	Kimerisk 2'-O-(2-methoxyethyl) modificeret oligonukleotid målrettet mod huntingtin-RNA	Behandling af Huntington's sygdom
Dutch	Chimerische 2'-O-(2-methoxyethyl) gemodificeerd oligonucleotide gericht op huntingtine-RNA	Behandeling van de ziekte van Huntington
Estonian	Huntingtiini RNA-le suunatud kimäärne 2'-O-(2-metoksüetüül) modifitseeritud oligonukleotiid	Huntington'i tõve ravi
Finnish	Kimeerinen 2'-O-(2-metoksietyyli) huntingtin-RNA:han kohdistettu modifioitu oligonukleotidi	Huntingtonin taudin hoito
French	Oligonucléotide chimérique 2'-O-(2-méthoxyéthyl) modifié dirigé contre l'ARN de la huntingtine	Traitement de la maladie d'Huntington
German	Chimäres 2'-O-(2-methoxyethyl) modifiziertes Oligonukleotid gegen Huntingtin-RNA	Behandlung der Huntington Erkrankung
Greek	Χιμαιρικό 2'-O-(2-μεθοξυαιθυλο) τροποποιημένου ολιγονουκλεοτίδιο που στοχεύει το RNA της χαντιγκτίνης	Θεραπεία της νόσου Huntington
Hungarian	Chimerikus 2'-O-(2-metoxietil) Huntingtin RNS-re célzott módosított oligonukleotid	Huntington kór kezelése
Italian	Oligonucleotide chimerico modificato con 2'-O-(2-metossietile) diretto contro l'RNA dell'huntingtina	Trattamento della malattia di Huntington
Latvian	Himērisks 2'-O-(2-metoksietil) pārveidots oligonukleotīds, kas iedarbojas uz hantingtīna RNS	Hantingtona slimības ārstēšanai
Lithuanian	Chimerinis 2'-O-(2-metoksietil) modifikuotas oligonukleotidas, skirtas huntingtino RNR	Huntington'o ligos gydymas
Maltese	Oligonukleotide kimeriku immodifikat b' 2'-O-(2-methoxyethyl) immirat għal RNA ta' huntingtin	Kura tal-marda ta' Huntington

[1] At the time of designation

Language	Active ingredient	Indication
Polish	Chimeryczny oligonukleotyd zawierający modyfikacje 2'-O-(2-metoksyetylowe) skierowany przeciw RNA huntingtyny	Leczenie pląsawicy Huntingtona
Portuguese	Oligonucleotídeo quimérico de 2'-O-(2-metoxietilo) modificado específico para o ARN da huntingtina	Tratamento da doença de Huntington
Romanian	Oligonucleotid chimeric 2'-O-(2-metoxietil) modificat cu, direcţionat împotriva ARN-ului huntingtinei	Tratamentul bolii Huntington
Slovak	Autológne bunky pochádzajúce zo stromálnej vaskulárnej frakcie tukového tkaniva	Liečba Huntingtonovej choroby
Slovenian	Himerni 2'-O-(2-metoksietil) modificiran oligonukleotid usmerjen na huntingtinovo RNK	Zdravljenje Huntingtonove bolezni
Spanish	Oligonucleótido quimérico 2'-O-(2-metoxietil) modificado dirigido al ARN de la huntingtina	Tratamiento de la enfermedad de Huntington
Swedish	Chimerisk 2'-O-(2-metoxietyl)-modifierad oligonukleotid riktad mot huntingtin-RNA	Behandling av Huntingtons sjukdom
Norwegian	Kimerisk 2'-O-(2-metoksyetyl) modifisert oligonukleotid målrettet til huntingtin-RNA	Behandling av Huntingtons sykdom.
Icelandic	Kímeríska 2'-O-(2-metoxýetýl) breytt oligónúkleótíð við huntingtin-ríbósakjarnasýru	Meðferð við Huntingtons sjúkdómi