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Public summary of opinion on orphan designation

2'-O-(2-methoxyethyl) antisense oligonucleotide targeting microtubule-associated protein tau pre-mRNA for the treatment of behavioural variant frontotemporal dementia

On 31 July 2018, orphan designation (EU/3/18/2041) was granted by the European Commission to Ionis USA Ltd, United Kingdom, for 2'-O-(2-methoxyethyl) antisense oligonucleotide targeting microtubule-associated protein tau pre-mRNA for the treatment of behavioural variant frontotemporal dementia.

What is behavioural variant frontotemporal dementia?

Behavioural variant frontotemporal dementia is a brain disorder in which patients gradually lose their ability to control or adjust their behaviour in different situations, leading to inappropriate behaviour. Language skills may also be affected, with the patient not being able to speak correctly, to pronounce words properly or to remember the right words.

The exact cause of the disease is unclear, but it is thought to be related to the abnormal build-up and tangling of a protein in the brain called tau, which leads to damage in different areas of the brain. The parts of the brain that are affected are the frontal and temporal lobes (front and sides of the brain).

Behavioural variant frontotemporal dementia is a debilitating disease that can be life threatening because of its damaging effects on the brain.

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

At the time of designation, behavioural variant frontotemporal dementia affected approximately 2.6 in 10,000 people in the European Union (EU). This was equivalent to a total of 135,000 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 28), Norway, Iceland and Liechtenstein. This represents a population of 517,400,000 (Eurostat 2018).

What treatments are available?

No satisfactory methods of treatment were authorised in the EU for behavioural variant frontotemporal dementia at the time of designation. Patients were managed with the help from experts such as psychologists, physiotherapists and speech therapists.

How is this medicine expected to work?

The medicine is an antisense oligonucleotide, a type of genetic material that interferes with the genetic material in cells and stops them from producing the tau protein.

By reducing levels of tau in the brain, the medicine is expected to reduce brain damage and help relieve patients' symptoms.

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, no clinical trials with the medicine in patients with behavioural variant frontotemporal dementia had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for behavioural variant frontotemporal dementia 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 21 June 2018 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, on the medicine's [rare disease designations page](#).

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 languages¹, Norwegian and Icelandic

Language	Active ingredient	Indication
English	2'-O-(2-methoxyethyl) antisense oligonucleotide targeting microtubule-associated protein tau pre-mRNA	Treatment of behavioural variant frontotemporal dementia
Bulgarian	2'-O-(2-метоксиетил) антисенс олигонуклеотид, насочен към пре-иРНК за синтеза на свързания с микротубулите протеин тау	Лечение на поведенчески вариант на фронто-темпорална деменция
Croatian	2'-O-(2-metoksietil) protusmjerni oligonukleotid usmjeren na pre-mRNA za mikrotubulima pridružen protein tau	Liječenje bihevioralnog oblika frontotemporalne demencije
Czech	2'-O-(2-methoxyethyl) antisense oligonukleotid zacílený na pre-mRNA tau proteinu asociovaného s mikrotubuly	Léčba behaviorální varianty fronto-temporální demencie
Danish	Præ-mRNA, kodende for mikrotubuli-associeret protein tau rettet mod 2'-O-(2-methoxyethyl) antisense-oligonukleotid	Behandling af frontotemporal demens varianten karakteriseret af adfærdsforstyrrelser
Dutch	2'-O-(2-methoxyethyl) antisense oligonucleotide gericht op het microtubulus-geassocieerd proteïne tau pre-mRNA	Behandeling van gedragsvariant frontotemporale demencie.
Estonian	Mikrotuubulitega seotud tau valgu eellas-mRNA vastu suunatud 2'-O-(2-metoksüetüül)-antisense oligonukleotiid	Frontotemporaalse dementsuse käitumusliku variandi ravi
Finnish	2'-O-(2-metoksietyyli) antisense-oligonukleotidi, jonka kohteena on mikrotubuluksiin liittyvän tau-proteiinin esi-mRNA	Frontotemporaalisen, käytöshäiriöpainotteisen dementian hoito
French	Oligonucléotide anti-sens 2'-O-(2-méthoxyéthyle) ciblant le pré-ARNm de la protéine tau associée aux microtubules	Traitement du variant de la démence fronto-temporale comportementale
German	2'-O-(2-Methoxyethyl)-Antisense-Oligonukleotid das auf gegen die pre-mRNA des mikrotubuli-assoziierten Proteins tau gerichtet ist	Behandlung der Fronto-temporalen Demenz vom Verhaltenstyp
Greek	2'-O-(2-μεθοξαιθυλ) αντινοηματικό ολιγονουκλεοτίδιο που στοχεύει το προ-mRNA της σχετιζόμενης με τα μικροσωληνάρια πρωτεΐνης ταυ	Θεραπεία της μετωποκροταφικής ανοίας με συμπεριφορικές διαταραχές
Hungarian	Mikrotubulus-asszociált tau-fehérje pre-mRNS-re célzott 2'-O-(2-metoxietil) antiszensz oligonukleotid	Frontotemporális demencia viselkedészavaros változatának kezelése
Italian	Oligonucleotide antisenso 2'-O-(2-metossietile) mirato al pre-mRNA della proteina tau associata ai microtubuli	Trattamento della variante comportamentale della demenza frontotemporale
Latvian	2'-O-(2-metoksietil) antisensa oligonukleotīds, kas vērsts pret mikrotubuļu asociētā proteīna tau pre-mRNS	Frontotemporālās demencijas uzvedības traucējumu varianta ārstēšanai

¹ At the time of designation

Language	Active ingredient	Indication
Lithuanian	2'-O-(2-metoksietil) priešprasmis oligonukleotidas, nukreiptas mikrotubulėmis susieto baltymo tau prieš-mRNR	Frontotemporalinės demencijos elgsenos tipo gydymas
Maltese	2'-O-(2-metossietil) antisens oligonukleotid li jimmira l-proteina tau assoċjata ma' mikrotubula (<i>microtubule-associated protein tau</i>) ta' qabel l-mRNA	Kura tad-dimenszja varjanti frontotemporal tal-imġieba
Polish	2'-O-(2-metoksyetylo) antysensowny oligonukleotyd skierowany przeciw pre-mRNA białka tau związanego z mikrotubulami	Leczenie wariantu behawioralnego otępienia czołowo-skroniowego
Portuguese	Oligonucleótido anti-senSO 2'-O-(2-metoxietil) dirigido ao pré-mARN da proteína tau associada aos microtúbulos	Tratamento da variante comportamental da demência frontotemporal
Romanian	Oligonucleotid antisens 2'-O-(2-metoxietil) ce țintește pre-ARNm-ul proteinei tau asociate microtubulilor	Tratamentul variantei comportamentale a demenței frontotemporale
Slovak	2'-O-(2-metoxetyl)-antisense oligonukleotid zacielený na pre-mRNA tau proteínu asociovaného s mikrotubulmi	Liečba behaviorálneho variantu frontotemporálnej demencie
Slovenian	2'-O-(2-metoksietil) protismiselni oligonukleotid, ki cilja na pre-mRNA z mikrotubuli povezanega proteina tau	Zdravljenje vedenjske variante frontotemporalne demence
Spanish	Oligonucleótido antisentido 2'-O-(2-metoxietilo) dirigido al pre-ARNm de la proteína asociada a microtúbulos tau	Tratamiento de la variante frontal de la demencia frontotemporal
Swedish	2'-O-(2-metoksietyl) antisensoligonukleotid riktad mot mikrotubuliassocierat protein tau-pre-mRNA	Behandling av frontotemporal demens beteendevariant
Norwegian	2'-O-(2-metoksyetyl) antisense-oligonukleotid rettet mot mikrotubuliassosiert protein tau pre-mRNA	Behandling av frontotemporal demens med atferdsvariant
Icelandic	2'-O-(2-metoxýetyl) tjáningarhindri sem beinist gegn örpíplutengdu tau-próteini pre-mRNA	Meðferð hegðunar frávika frontotemporal vitglapa