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Public summary of opinion on orphan designation

5,7-Dichloro-2-((ethylamino)methyl)-8-hydroxy-3-methylquinazolin-4(3H)-one mesilate for the treatment of multiple system atrophy

On 16 December 2019, orphan designation EU/3/19/2228 was granted by the European Commission to Alterity Therapeutics UK Limited, United Kingdom, for 5,7-dichloro-2-((ethylamino)methyl)-8-hydroxy-3-methylquinazolin-4(3H)-one mesilate (also known as PBT434) for the treatment of multiple system atrophy.

What is multiple system atrophy?

Multiple system atrophy is a disease of the nervous system, where nerve cells in certain areas of the brain and spinal cord gradually deteriorate, causing loss of voluntary and involuntary muscle function. This leads to symptoms such as loss of bladder control as well as shaking, rigidity and loss of muscle coordination, light-headedness due to excessive drop in blood pressure when standing up, and difficulties with speech and breathing. Some of these features are similar to those of Parkinson's disease, which makes it hard to distinguish between the two in the early stages.

Multiple system atrophy is a long-term debilitating and life-threatening disease because of the gradual loss of muscle function and its effects on muscles used for breathing.

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

At the time of designation, multiple system atrophy affected approximately 0.34 in 10,000 people in the European Union (EU). This was equivalent to a total of around 18,000 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, there were no satisfactory methods authorised in the EU for the treatment of multiple system atrophy. Treatments used for relieving symptoms of the disease included

*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 518,400,000 (Eurostat 2019).

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vasopressin for managing hypotension (low blood pressure), anticholinergic medicines to treat bladder problems and levodopa for Parkinson-type symptoms.

How is this medicine expected to work?

In patients with multiple system atrophy, the amount of iron in nerve cells in certain parts of the brain is increased and this can damage the cells. The abnormal amount of iron also leads to the aggregation of a substance called alpha-synuclein which can damage cells. This medicine is intended to work by reducing iron levels in nerve cells preventing the formation of deposits. This in turn is expected to reduce aggregation of alpha-synuclein, slow down cell damage and improve 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 multiple system atrophy had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for the treatment of multiple system atrophy. Orphan designation had been granted in the United States for multiple system atrophy.

In accordance with Regulation (EC) No 141/2000, the COMP adopted a positive opinion on 7 November 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	5,7-dichloro-2-((ethylamino)methyl)-8-hydroxy-3-methylquinazolin-4(3H)-one mesilate	Treatment of multiple system atrophy
Bulgarian	5,7-дихлоро-2-((етиламино)метил)-8-хидрокси-3-метилквиназолин-4(3H)-он мезилат	Лечение на мултисистемна атрофия
Croatian	5,7-dikloro-2-((etilamino)metil)-8-hidroksi-3-methilkinazolin-4(3H)-on mesilat	Liječenje multisistemne atrofije
Czech	5,7-dichloro-2-((ethylamino)methyl)-8-hydroxy-3-methylchinazolin-4(3H)-on mesylát	Léčba multisystémové atrofie
Danish	5,7-dichloro-2-((ethylamino)methyl)-8-hydroxy-3-methylquinazolin-4(3H)-on mesilat	Behandling af multipel systematrofi
Dutch	5,7-dichloro-2-((ethylamino)methyl)-8-hydroxy-3-methylquinazolin-4(3H)-on mesilaat	Behandeling van multisysteematrofie
Estonian	5,7-dikloro-2-((etüülamino)metüül)-8-hüdroksü-3-metüülkinasoliin-4(3H)-oon mesülaat	Multisüsteemse atroofia ravi
Finnish	5,7-dikloori-2-((etyyliamiini)metyyli)-8-hydroksi-3-metyylikinatsolin-4(3H)-oni mesilaatti	Monijärjestelmäsurkastuman hoito.
French	5,7-dichloro-2-((ethylamino)methyl)-8-hydroxy-3-methylquinazolin-4(3H)-one mesilate	Traitement de l'atrophie multisystématisée.
German	5,7-dichloro-2-((ethylamino)methyl)-8-hydroxy-3-methylquinazolin-4(3H)-one mesilate	Behandlung einer Multisystematrophie
Greek	5,7-διχλωρο-2-((αιθυλαμινο)μεθυλ)-8-υδροξυ-3-μεθυλκιναζολιν-4(3H)-όνη μεσυλική	Θεραπεία ατροφίας πολλαπλών συστημάτων
Hungarian	5,7-dikloro-2-((etilamino)metil)-8-hidroxi-3-metilquinazolin-4(3H)-one mezilát	Multi-szisztémás atrófia kezelése
Italian	5,7-dicloro-2-((etilamino)metil)-8-idrossi-3-metilquinazolin-4(3H)-one mesilato	Trattamento dell'atrofia multisistemica
Latvian	5,7-dihloro-2-((etilamino)metil)-8-hidroksi-3-metilkvinazolīn-4(3H)-ona mesilāts	Multisistēmas atrofijas ārstēšana
Lithuanian	5,7-dichloro-2-((etilamino)metil)-8-hidroksi-3-metilkvinazolin-4(3H)-ono mesilatas	Daugiasisteminės atrofijos gydymas
Maltese	5,7-dikloro-2-((etilammino)metil)-8-idrossi-3-metilkinażolina-4(3H)-meżilat wieħed	Kura tal-atrofija ta' sistemi multipli
Polish	Mesylat 5,7-dichloro-2-((etylamino)metylo)-8-hydroksy-3-metylkwinazolino-4(3H)-onu	Tratamento da atrofia multisistémica

[1] At the time of designation

Language	Active ingredient	Indication
Portuguese	Mesilato de 5,7-di-cloro-2-((etilamino)metil)-8-hidroxi-3-metilquinazolin-4(3H)-ona	Tratamento da atrofia de múltiplos sistemas
Romanian	Mesilat de 5,7-dicloro-2-((etilamino)metil)-8-hidroxi-3-metilchinazolin-4(3H)-onă	Tratamentul atrofiei sistemice multiple
Slovak	5,7-dichloro-2-((etylamino)metyl)-8-hydroxy-3-metylchinazolín-4(3H)-ón mesilát	Liečba multisystémovej atrofie.
Slovenian	5,7-dikloro-2-((etilamino)metil)-8-hidroksi 3-metilkvinazolin-4(3H)-ena mezilat	Zdravljenje multiple sistemske atrofije
Spanish	5,7-dicloro-2-((etilamino)metil)-8-hidroiy-3-metilquinazolin-4(3H)-uno mesilate	Tratamiento de la atrofia multisistémica
Swedish	5,7-dikloro-2-((etylamino)metyl)-8-hydroxy-3-metylquinazolin-4(3H)-on mesilat	Behandling av multipel systematrofi
Norwegian	5,7-dikloro-2-((etylamino)metyl)-8-hydroksy-3-metylkinazolin-4(3H)-on mesilat	Behandling ved multippel systematrofi (MSA)
Icelandic	5,7-dichloro-2-((ethylamino)methyl)-8-hydroxy-3-methylquinazolin-4(3H)-one mesílat	Meðferð á fjölkerfarýrnun