19 February 2015
EMA/COMP/722694/2014
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

1-(2-isopropoxyethyl)-2-thioxo-1,2,3,5-tetrahydro-pyrrolo[3,2-d] pyrimidin-4-one for the treatment of multiple system atrophy

On 16 December 2014, orphan designation (EU/3/14/1404) was granted by the European Commission to Astra Zeneca AB, Sweden, for 1-(2-isopropoxyethyl)-2-thioxo-1,2,3,5-tetrahydro-pyrrolo[3,2-d] pyrimidin-4-one for the treatment of multiple system atrophy.

What is multiple system atrophy?

Multiple system atrophy is a progressive disease of the nervous system, where nerve cells in the certain areas of the brain and spinal cord gradually deteriorate, causing loss of voluntary and involuntary muscle function. This leads to symptoms such as impotence in men and loss of bladder control as well as shaking, rigidity and/or loss of muscle coordination, light-headedness due to orthostatic hypotension (excessive drop in blood pressure) and difficulties with speech, breathing and gait (the way a person walks). Some of these features are similar to those seen in Parkinson's disease, which makes these disorders difficult to be distinguished in the early stages of the disease.

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 0.3 in 10,000 people in the European Union (EU). This was equivalent to a total of around 15,000 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 511,100,000 (Eurostat 2014).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

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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. Different treatments were used to relieve the symptoms of the disease, such as beta blockers and vasopressin for the treatment of hypotension (low blood pressure) and anticholinergic medicines to treat bladder problems. Parkinson medicines such as levodopa are not effective in treating the Parkinson-type symptoms of multiple system atrophy.

How is this medicine expected to work?

The cause of the damage to nerves cells in multiple system atrophy is unclear but there is evidence that toxic molecules containing oxygen called 'reactive nitrogen species' (NOS) could be involved.

This medicine is expected to work by blocking the action of an enzyme called myeloperoxidase, which generates NOS in the nervous system. By reducing NOS the medicine is expected to improve the symptoms of multiple system atrophy.

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 multiple system atrophy were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for multiple system atrophy 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 13 November 2014 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:

AstraZeneca AB
SE-151 85 Södertälje
Sweden
Tel. +46 8 553 260 00
Fax +46 8 553 290 00
E-mail: orphandrugs@astrazeneca.com

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	1-(2-isopropoxyethyl)-2-thioxo-1,2,3,5-tetrahydro-pyrrolo[3,2-d]pyrimidin-4-one	Treatment of multiple system atrophy
Bulgarian	1-(2-изопропоксиетил)-2-тиоксо-1,2,3,5-тетрахидро-пироло[3,2-d]пиримидин-4-он	Лечение на мултисистемна атрофия
Croatian	1-(2-izopropoksietil)-2-tiokso-1,2,3,5-tetrahidro-pirolo[3,2-d] pirimidin-4-on	Liječenje multisistemne atrofije
Czech	1-(2-isopropoxyethyl)-2-thioxo-1,2,3,5-tetrahydro-pyrolo[3,2-d]pyrimidin-4-on	Léčba multisystémové atrofie
Danish	1-(2-isopropoxyethyl)-2-thioxo-1,2,3,5-tetrahydro-pyrrolo[3,2-d]-pyrimidin-4-one	Behandling af multipel systematrofi
Dutch	1-(2-isopropoxyethyl)-2-thioxo-1,2,3,5-tetrahydropyrrolo[3,2-d]-pyrimidine-4-on	Behandeling van multisysteematrofie
Estonian	1-(2-isopropoksüetüül)-2-tiokso-1,2,3,5-tetrahüdro-pürrolo[3,2-d]pürimidiin-4-oon	Multisüsteemse atroofia ravi
Finnish	1-(2-isopropoksietyyli)-2-tiokso-1,2,3,5-tetrahydro-pyrrolo[3,2-d]-pyrimidiini-4-oni	Monijärjestelmäsurkastuman hoito.
French	1-(2-isopropoxyéthyl)-2-thioxo-1,2,3,5-tétrahydro-pyrrolo[3,2-d]pyrimidin-4-one	Traitement de l'atrophie multisystématisée.
German	1-(2-Isopropoxyethyl)-2-thioxo-1,2,3,5-tetrahydropyrrolo[3,2-d]pyrimidin-4-one	Behandlung einer Multisystematrophie
Greek	1-(2-ισοπροποξυαιθυλ)-2-θειοξο-1,2,3,5-τετραϋδρο-πυρρολο[3,2-d]πυριμιδιν-4-όνη	Θεραπεία ατροφίας πολλαπλών συστημάτων
Hungarian	1-(2-izopropoxietil)-2-tioxo-1,2,3,5-tetrahidro-pirrolo[3,2-d]pirimidin-4-on	Multi-szisztémás atrófia kezelése
Italian	1-(2-isopropossietanolo)-2-tiosso-1,2,3,5-tetraidropirrolo[3,2-d]pirimidina-4-1	Trattamento dell'atrofia multisistemica
Latvian	1-(2-izopropoksietil)-2-tiokso-1,2,3,5-tetrahidro-pirolo[3,2-d]pirimidīn-4-ons	Multisistēmas atrofijas ārstēšana
Lithuanian	1-(2-izopropoksietil)-2-tiokso-1,2,3,5-tetrahidro-pirolo[3,2-d]pirimidin-4-onas	Daugiasisteminės atrofijos gydymas
Maltese	1-(2-isopropoxyethyl)-2-thioxo-1,2,3,5-tetrahydro-pyrrolo[3,2-d]pyrimidin-4-one	Kura tal-atrofija ta' sistemi multipli
Polish	1-(2-izopropoksyetylo)-2-tiokso-1,2,3,5-tetrahydro-pirolo[3,2-d]pirymidyn-4-on	Tratamento da atrofia multisistémica
Portuguese	1-(2-isopropoxi-etil)-2-tioxo-1,2,3,5-tetrahidropirrolo[3,2-d]pirimidin-4-ona	Tratamento da atrofia de múltiplos sistemas
Romanian	1-(2-Isopropoxietil)-2-tioxo-1,2,3,5-tetrahidropirol[3,2-d]pirimidin-4-onă	Tratamentul atrofiei sistemice multiple
Slovak	1-(2-izopropoxyetyl)-2-tioxo-1,2,3,5-tetrahydro-pyrolo[3,2-d]pyrimidín-4-ón	Liečba multisystémovej atrofie.

[1] At the time of designation

Language	Active ingredient	Indication
Slovenian	1-(2-izopropoksietil)-2-tiokso-1,2,3,5-tetrahidro-pirolo[3,2-d]pirimidin-4-on	Zdravljenje multiple sistemske atrofije
Spanish	1-(2-isopropoxietil)-2-tioxo-1,2,3,5-tetrahidropirrolo[3,2-d]pirimidin-4-ona	Tratamiento de la atrofia multisistémica
Swedish	1-(2-isopropoxietyl)-2-tioxo-1,2,3,5-tetrahydropyrrol[3,2-d]pyrimidin-4-on	Behandling av multipel systematrofi
Norwegian	1-(2-isopropoksyetyl)-2-tiokso-1,2,3,5-tetrahydro-pyrrolo[3,2-d]pyrimidin-4-on	Behandling ved multippel systematrofi (MSA)
Icelandic	1-(2-ísóprópoxýetýl)-2-tíoxó-1,2,3,5-tetrahýdró-pýrróló[3,2-d]pýrimídín-4-ón	Meðferð á fjölkerfarýrnun