30 March 2015
EMA/COMP/43938/2015
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

N-(3-(4-(3-(diisobutylamino)propyl)piperazin-1-yl)propyl)-1H-benzo[d]imidazol-2-amine disulphate salt for the treatment of progressive supranuclear palsy

On 12 February 2015, orphan designation (EU/3/15/1446) was granted by the European Commission to AlzProtect S.A.S., France, for N-(3-(4-(3-(diisobutylamino)propyl)piperazin-1-yl)propyl)-1H-benzo[d]imidazol-2-amine disulphate salt (also known as AZP2006) for the treatment of progressive supranuclear palsy.

What is progressive supranuclear palsy?

Progressive supranuclear palsy, which is also known as Steele-Richardson-Olszewski syndrome, is a rare disease that involves the gradual deterioration of brain cells. Symptoms include loss of balance with unexplained falls, stiffness, difficulty moving the eyes, particularly up and down, personality changes and dementia (loss of intellectual function). The disease usually starts in people aged over 60 years and gradually gets worse over a number of years.

Patients with progressive supranuclear palsy have abnormal tangles of a protein called 'tau' in their brain, which are thought to cause the gradual deterioration of brain tissue seen in these patients.

Progressive supranuclear palsy is a debilitating and life-threatening disease that leads to parkinsonism, paralysis and premature death.

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

At the time of designation, progressive supranuclear palsy affected approximately 1.4 in 10,000 people in the European Union (EU). This was equivalent to a total of around 72,000 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 512,900,000 (Eurostat 2015).

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What treatments are available?

At the time of designation, no satisfactory methods were authorised in the EU for the treatment of progressive supranuclear palsy. Because of their tendency to fall, patients were often offered walking aids, as well as special glasses to help them to look down. Physiotherapy was used to keep the joints flexible. For patients unable to swallow, a feeding tube leading through the tummy to the stomach was used. Medicines developed to treat Parkinson's disease were also used in some patients, but their effect was usually limited, and did not last long.

How is this medicine expected to work?

In patients with progressive supranuclear palsy, the tau protein has extra phosphate groups attached at multiple points (a process called phosphorylation); the changes to the protein cause it to fold wrongly and become tangled. The medicine is expected to work by blocking phosphorylation of tau proteins which will prevent them from folding incorrectly. In addition, it is expected that the medicine will stimulate certain cellular mechanisms (called macroautophagy) that help to clear and destroy misfolded proteins. This is expected to reduce the deterioration of brain tissue thereby improving the symptoms of the disease.

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 progressive supranuclear palsy were ongoing.

At the time of submission, the medicine was not authorised anywhere in the EU for progressive supranuclear palsy 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 9 January 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	N-(3-(4-(3-(diisobutylamino)propyl)piperazin-1-yl)propyl)-1H-benzo[d]imidazol-2-amine disulphate salt	Treatment of progressive supranuclear palsy
Bulgarian	N-(3-(4-(3-(диизобутиламино)пропил)пиперазин-1-ил)пропил)-1H-бензо[д]имидазол-2-амин дисулфат сол	Лечение на прогресивна супрануклеарна парализа
Croatian	Disulfatna sol N-(3-(4-(3-(diisobutilamino)propil)piperazin-1-il)propil)-1H-benzo[d]imidazol-2-amina	Liječenje progresivne supranuklearne paralize
Czech	N-(3-(4-(3-(diisobutylamino)propyl)piperazin-1-yl)propyl)-1H-benzo[d]imidazol-2-amin disulphatová sůl	Léčba progresivní supranukleární paralýzy
Danish	N-(3-(4-(3-(diisobutylamino)propyl)piperazin-1-yl)propyl)-1H-benzo[d]imidazol-2-amin disulfat salt	Behandling af progressiv, supranukleær parese
Dutch	N-(3-(4-(3-(diisobutylamino)propyl)piperazine-1-yl) propyl)-1H-benzo[d]imidazool-2-amine zout disulphate	Behandeling van progressieve supranucleaire paralyse
Estonian	N-(3-(4-(3-(diisobutüülaminorühma)propüül)piperasiin-1-üül) propüül)-1-benso[d]imidasool-2-amiin disulfaatsool	Progressiivse supranukleaarse halvatuse ravi
Finnish	N-(3-(4-(3-(isobutyyliamino)propyyli)piperatsiini-1-yyli)propyyli)-1H-bentso[d]imidatsoli-2-amiini disulfaatin suola	Progressiivisen supranukleaarisen halvauksen hoito
French	Sel bisulfate N-(3-(4-(3-(diisobutylamino)propyl)pipérazin-1-yl)propyl)-1H-benzo[d]imidazol-2-amine	Traitement de la paralysie supranucléaire progressive
German	N-(3-(4-(3-(Diisobutylamino)propyl)piperazin-1-yl)propyl)-1H-benzo[d]imidazol-2-amin Disulfat Salz	Behandlung der progressiven supranukleären Lähmung
Greek	Διθειϊκό άλας N-(3-(4-(3-(διισοβουτυλαμινο)προπυλ)πιπεραζιν-1-υλ)προπυλ)-1H-βενζο[d]ιμιδαζολ-2-αμίνης	Θεραπεία προϊούσας υπερπυρηνικής παράλυσης
Hungarian	N-(3-(4-(3-(diizobutilamino)propil)piperazin-1-il)propil)-1H-benzo[d]imidazol-2-amin-só-diszulfát	Progresszív supranuclearis bénulás kezelése
Italian	N-(3-(4-(3-(diisobutylamino)propil)piperazin-1-il)propil)-1H-benzo[d]imidazol-2-ammina sale disolfato	Trattamento della paralisi sopranucleare progressiva
Latvian	N-(3-(4-(3-(diizobutilamino)propil)piperazīn-1-il)propil)-1H-benzo[d]imidazol-2-amīna disulfāta sāls	Progresējošās supranukleārās triekas ārstēšana
Lithuanian	N-(3-(4-(3-(diizobutilamino)propil)piperazin-1-il)propil)-1H-benzo[d]imidazol-2-amino disulfatas	Progresuojančio supranuklearinio paralyžiaus gydymas

[1] At the time of designation

Language	Active ingredient	Indication
Maltese	N-(3-(4-(3-(diisobutylamino)propyl)-piperazin-1-yl)propyl)-1H-benzo[d]imidazol-2-amine disulphate salt	Kura ta' paraliżi supranukleari progressiva
Polish	N-(3-(4-(3-(diizobutyloamino)propylo)piperazyn-1-yl)propylo)-1H-benzo[d]imidazol-2-aminy sól dwusiarczanowa	Leczenie postępującego porażenia nadjądrowego
Portuguese	N-(3-(4-(3-(isobutilamino)propil)piperazin-1-il)propil)-1H-benzo[d]imidazol-2-amina, sal de dissulfato	Tratamento da paralisia supranuclear progressiva
Romanian	Sare disulfat de N-(3-(4-(3-(diizobutilamino)propil)piperazin-1-il)propil)-1H-benzo[d]imidazol-2-amină	Tratamentul paraliziei supra-nucleare progresive
Slovak	N-(3-(4-(3-(diisobutylamino)propyl)piperazín-1-yl)propyl)-1H-benzo[d]imidazol-2-amin disulphate soľ	Liečba progresívnej supranukleárnej paralýzy
Slovenian	N-(3-(4-(3-(diizobutilamino)propil)piperazin-1-il)propil)-1H-benzo[d]imidazol-2-amin disulphate sol	Zdravljenje progresivne supranuklearne paralize
Spanish	N-(3-(4-(3-(diisobutilamino)propil)piperazin-1-il)propil)-1H-benzo[d]imidazol-2-amina sal disulfato	Tratamiento de parálisis supranuclear progresiva
Swedish	N-(3-(4-(3-(diisobutylamino)propyl)piperazin-1-yl)propyl)-1H-benso[d]imidazol-2-amin disulfat salt	Behandling av progressiv supranukleär pares
Norwegian	N-(3-(4-(3-(diisobutylamino)propyl)piperazin-1-yl)propyl)-1H-benzo[d]imidazol-2-amindisulfat salt	Behandling av progressiv supranukleær parese
Icelandic	N-(3-(4-(3-(díísóbútýlamínó)própýl)píperasín-1-ýl)própýl)-1H-bensó[d]ímídasól-2-amín dísúlfat salt	Meðferð við ágengri ofankjarnalömun