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EMA/COMP/75475/2016
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Tolfenamic acid for the treatment of progressive supranuclear palsy

On 17 February 2016, orphan designation (EU/3/16/1613) was granted by the European Commission to RV Developpement, France, for tolfenamic acid 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 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 build-up and tangles of a protein called tau in their brain, which is thought to cause the deterioration of brain tissue 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 0.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 31,000 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, 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

*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 513,700,000 (Eurostat 2016).

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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?

Brain cells of patients with progressive supranuclear palsy produce excessive tau protein. In addition, the protein has extra phosphate groups attached to it which cause it to fold wrongly and become tangled. Tolfenamic acid interferes with Sp1, a factor that is essential for controlling the amount of tau protein that a cell makes and the processes that add phosphate groups to the protein. This combined effect is expected to reduce the production of tau protein and the development of tangles, and thereby prevent cell damage and symptoms of progressive supranuclear palsy.

What is the stage of development of this medicine?

The effects of tolfenamic acid have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with tolfenamic acid in patients with progressive supranuclear palsy had been started.

At the time of submission, tolfenamic acid was not authorised anywhere in the EU for progressive supranuclear palsy or designated as an orphan medicinal product elsewhere for this condition.

Tolfenamic acid has been authorised in Europe for many years as a non-steroidal anti-inflammatory medicine (NSAID) for the treatment of pain and inflammation.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 21 January 2016 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:

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 languages[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Tolfenamic acid	Treatment of progressive supranuclear palsy
Bulgarian	Толфенамова киселина	Лечение на прогресивна супрануклеарна парализа
Croatian	Tolfenamička kiselina	Liječenje progresivne supranuklearne paralize
Czech	Kyselina tolefenamová	Léčba progresivní supranukleární paralýzy
Danish	Tolfenamsyre	Behandling af progressiv, supranukleær parese
Dutch	Tolfenaminezuur	Behandeling van progressieve supranucleaire paralyse
Estonian	Tolfenaamhape	Progressiivse supranukleaarse halvatuse ravi
Finnish	Tolfenaamihappo	Progressiivisen supranukleaarisen halvauksen hoito
French	Acide tolfénamique	Traitement de la paralysie supranucléaire progressive
German	Tolfenaminsäure	Behandlung der progressiven supranukleären Lähmung
Greek	Τολφαιναμικό οξύ	Θεραπεία προϊούσας υπερπυρηνικής παράλυσης
Hungarian	Tolfenaminsav	Progresszív supranuclearis bénulás kezelése
Italian	Acido tolfenamico	Trattamento della paralisi sopranucleare progressiva
Latvian	Tolfenamīnskābe	Progresējošās supranukleārās triekas ārstēšana
Lithuanian	Tolfenamo rūgštis	Progresuojančio supranuklearinio paralyžiaus gydymas
Maltese	Tolfenamic acid	Kura ta' paraliżi supranukleari progressiva
Polish	Kwas tolfenamowy	Leczenie postępującego porażenia nadjądrowego
Portuguese	Ácido tolfenâmico	Tratamento da paralisia supranuclear progressiva
Romanian	Acid tolfenamic	Tratamentul paraliziei supra-nucleare progresive
Slovak	Kyselina tolfenamová	Liečba progresívnej supranukleárnej paralýzy
Slovenian	Tolfenaminska kislina	Zdravljenje progresivne supranuklearne paralize
Spanish	Ácido tolfenámico	Tratamiento de parálisis supranuclear progresiva
Swedish	Tolfenamic syra	Behandling av progressiv supranukleär pares
Norwegian	Tolfenamsyre	Behandling av progressiv supranukleær parese
Icelandic	Tolfenamik sýra	Meðferð við ágengri ofankjarnalömun

[1] At the time of designation