

31 March 2016  
EMA/COMP/75479/2016  
Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

### Tolfenamic acid for the treatment of behavioural variant frontotemporal dementia

On 17 February 2016, orphan designation (EU/3/16/1614) was granted by the European Commission to RV Developpement, France, for tolfenamic acid 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 (side) lobes.

Behavioural variant frontotemporal dementia is a debilitating disease that is 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 2.2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 113,000 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).

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\*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).

## **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 supported in their day-to-day activities by caregivers with help from experts such as psychologists, physiotherapists and speech therapists.

## **How is this medicine expected to work?**

Brain cells of patients with behavioural variant frontotemporal dementia 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 behavioural variant frontotemporal dementia.

## **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 behavioural variant frontotemporal dementia had been started.

At the time of submission, tolfenamic acid was not authorised anywhere in the EU for behavioural variant frontotemporal dementia 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<sup>1</sup>, Norwegian and Icelandic**

Language	Active ingredient	Indication
English	Tolfenamic acid	Treatment of behavioural variant frontotemporal dementia
Bulgarian	Толфенамова киселина	Лечение на поведенчески вариант на фронтотемпорална деменция
Croatian	Tolfenamička kiselina	Liječenje bihevioralnog oblika frontotemporalne demencije
Czech	Kyselina tolfenamová	Léčba behaviorální varianty fronto-temporální demencie
Danish	Tolfenamsyre	Behandling af frontotemporal demens varianten karakteriseret af adfærdsforstyrrelser
Dutch	Tolfenaminezuur	Behandeling van gedragsvariant frontotemporale dementie.
Estonian	Tolfenaamhape	Frontotemporaalse dementsuse käitumusliku variandi ravi
Finnish	Tolfenaamihappo	Frontotemporaalisen, käytöshäiriöpainotteisen dementian hoito
French	Acide tolénamique	Traitemennt du variant de la démence fronto-temporale comportementale
German	Tolfenaminsäure	Behandlung der Fronto-temporalen Demenz vom Verhaltenstyp
Greek	Τολφαιναμικό οξύ	Θεραπεία της μετωποκροταφικής ανοίας με συμπεριφορικές διαταραχές
Hungarian	Tolfenaminsav	Frontotemporális demencia viselkedészavaros változatának kezelése
Italian	Acido tolfenamico	Trattamento della variante comportamentale della demenza frontotemporale
Latvian	Tolfenamīnskābe	Frontotemporālās demencijas uzvedības traucējumu varianta ārstēšanai
Lithuanian	Tolfenamo rūgštis	Frontotemporalinės demencijos elgsenos tipo gydymas
Maltese	Tolfenamic acid	Kura tad-dimenzja varjanti frontotemporali tal-imġieba
Polish	Kwas tolfenamowy	Lecznie wariantu behawioralnego otępienia czołowo-skroniowego
Portuguese	Ácido tolfenâmico	Tratamento da variante comportamental da demência frontotemporal
Romanian	Acid tolfenamic	Tratamentul variantei comportamentale a demenței frontotemporale
Slovak	Kyselina tolfenamová	Liečba behaviorálneho variantu frontotemporálnej demencie
Slovenian	Tolfenaminska kislina	Zdravljenje vedenjske variante frontotemporalne demence
Spanish	Ácido tolfenámico	Tratamiento de la variante frontal de la demencia frontotemporal
Swedish	Tolfenamic syra	Behandling av frontotemporal demens beteendevariant
Norwegian	Tolfenamsyre	Behandling av frontotemporal demens med atferdsvariant
Icelandic	Tolfenamik sýra	Meðferð hegðunar frávika frontotemporal vitglapa

<sup>1</sup> At the time of designation