



Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of

(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate for the treatment of moderate and severe closed traumatic brain injury

On 5 September 2008, orphan designation (EU/3/08/560) was granted by the European Commission to KeyNeurotek Pharmaceuticals AG, Germany, for (-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate for the treatment of moderate and severe closed traumatic brain injury.

What is moderate and severe closed traumatic brain injury?

Closed traumatic brain injury is brain damage caused by a head injury (such as a blow to the head in a traffic accident or a fall). 'Closed' means that the skull remains intact. The initial injury to the head and brain usually goes on to cause 'secondary' problems, most frequently due to bleeding or swelling of the brain tissue (oedema) increasing the pressure within the skull. Traumatic brain injury is classified as minor, moderate or severe according to the patient's symptoms: patients with moderate injury are lethargic (lacking in energy) or stuporous (unaware of their surroundings), and those with severe injury are comatose (unconscious). People with moderate or severe traumatic brain injury need to be admitted to hospital for observation and examination, in case the condition gets worse. Moderate and severe traumatic brain injury is chronically debilitating and life-threatening.

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

At the time of designation moderate and severe closed traumatic brain injury affected less than 4 in 10,000 people in the European Union (EU) *. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP). This is below the threshold for orphan designation which is 5 in 10,000. This is equivalent to a total of around 200,000 people.

What treatments are available?

Various treatments are available to reduce pressure in within the skull in patients with moderate or severe closed traumatic brain injury, including medicines and surgery.

Satisfactory argumentation has been submitted by the sponsor to justify the assumption that (-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate might be of potential significant benefit for the treatment of moderate and severe closed traumatic brain injury because it has a new mechanism of action. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain orphan status.

* Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 27), Norway, Iceland and Liechtenstein. This represents a population of 502,282,000 (Eurostat 2008).

How is this medicine expected to work?

This medicine is expected to attach to specific receptors in the brain called ‘cannabinoid receptors’. These receptors are involved in the sequence of events that occurs after the initial brain injury that can lead to secondary brain damage. Thus, by activating these “cannabinoid receptors”, this medicine is expected to reduce oedema and to decrease the pressure within the skull.

What is the stage of development of this medicine?

The effects of this medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with moderate and severe closed traumatic brain injury were ongoing.

The medicine was not authorised anywhere worldwide for the treatment of moderate or severe closed traumatic brain injury or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted a positive opinion on 11 June 2008 recommending the granting of the above-mentioned 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;
- and either the rarity of the condition (affecting not more than five in 10,000 people in the Community) or the 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 the 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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Patients’ association contact point: Not available

**Translations of the active ingredient and indication in all EU languages
and Norwegian and Icelandic**

Language	Active Ingredient	Indication
English	(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate	Treatment of moderate and severe closed traumatic brain injury
Bulgarian	(-)-(2R)-3-(2-хидроксиметилинданил-4-окси)-фенил-4,4,4-трифлуоробутан-1-сулфонат	Лечение на средно тежки и тежки и затворени травматични мозъчни наранявания
Czech	(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate	Léčba těžkého a středního uzavřeného mozkového traumatu
Danish	(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate	Behandling af moderat og svært, lukket hjernetraume
Dutch	(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate	Behandeling van matig en ernstig niet-penetrerend traumatisch hersenletsel
Estonian	(-)-(2R)-3-(2-hüdroksümetüüldanüül-4-oksü)-fenüül-4,4,4-trifluorobutaan-1-sulfonaat	Raske ja keskmise raskusastmega kinnise traumaatilise ajukahjustuse ravi.
Finnish	(-)-(2R)-3-(2-hydroksimetyylindanyyli-4-oksi)-fenyyli-4,4,4-trifluorobutaani-1-sulfonaatti	Kohtalaisen ja vaikean suljetun traumaattisen aivovaurion hoito
French	(-)-(2R)-3-(2-hydroxyméthylindanyl-4-oxy)-phényl-4,4,4-trifluorobutane-1-sulfonate	Traitement des traumatismes crâniens fermés graves et modérés
German	(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate	Behandlung des mittelschweren und schweren geschlossenen Schädel-Hirn-Traumas
Greek	(-)-(2R)-3-(2-υδροξυμεθυλινδανύλ -4-οξύ)-φαινύλ-4,4,4-τριφθοροβουτάνιο-1-σουλφονικό	Θεραπεία των μετρίων και σοβαρών κλειστών εγκεφαλικών τραυμάτων
Hungarian	(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate	Mérsékeltén súlyos és súlyos, traumás koponyaüri sérülés kezelése
Italian	(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate	Trattamento del trauma cranio-encefalico chiuso moderato e grave
Latvian	(-)-(2R)-3-(2-hidroksimetilindanil-4-oksi)-fenil-4,4,4-trifluorobutāna-1-sulfonāts	Smagas un viduvējas slēgtas galvas smadzeņu traumas ārstēšana
Lithuanian	(-)-(2R)-3-(2-hidroksimetilindanil-4-oksi)-fenil-4,4,4-trifluorobutano-1-sulfonatas	Stipraus ir vidutinio uždaro trauminio galvos smegenų pažeidimo gydymas
Maltese	(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate	Kura ta' feriti trawmatiċi magħluqa tal-moħħ moderati u severi
Polish	(-)-(2R)-3-(2-hydroksymetylindanyl-4-oksy)-feryl-4,4,4-trifluorobutan-1-sulfonian	Leczenie umiarkowanych i ciężkich, zamkniętych, pourazowych uszkodzeń mózgu
Portuguese	(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate	Tratamento do traumatismo craniano fechado moderado e grave
Romanian	(-)-(2R)-3-(2-hidroksimetilindanil-4-oxy)-fenil-4,4,4-trifluorobutan-1-sulfonat	Tratamentul leziunilor cerebrale traumatice închise, moderate și severe
Slovak	(-)-(2R)-3-(2-hydroxymetylindanyl-4-oxy)-feryl-4,4,4-trifluórbután-1-sulfonát	Liečba mierneho a ťažkého uzavretého traumatického poškodenia mozgu
Slovenian	(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate	Zdravljenje zmernih in hudih zaprtih možganskih poškodb
Spanish	(-)-(2R)-3-(2-hidroksimetilindanil-4-oxi)-fenil-4,4,4-trifluorobutano-1-sulfonato	Tratamiento del traumatismo craneoencefálico moderado y grave no penetrante

Swedish	(-)-(2R)-3-(2-hydroxymethylindanyl-4-oxy)-phenyl-4,4,4-trifluorobutane-1-sulfonate	Behandling av lindrig och alvarlig stängd traumatisk hjärnskada
Norwegian	(-)-(2R)-3-(2-hydroksymetylindanyl-4-oksy)-fenyl-4,4,4-trifluorobutan-1-sulfonat	Behandling av moderat og alvorlig lukket traumatisk hjerneskade
Icelandic	(-)-(2R)-3-(2-hýdroxýmethýlindanýl-4-oxý)-phenýl-4,4,4-tríflúoróbútan-1-súlfónat	Meðferð á meðalslæmum og alvarlegum lokuðum heilaáverka