



European Medicines Agency  
*Pre-authorisation Evaluation of Medicines for Human Use*

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## **COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS**

### **PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF dimethyl sulfoxide for the treatment of severe closed traumatic brain injury**

On 3 March 2005, orphan designation (EU/3/05/263) was granted by the European Commission to AOP Orphan Pharmaceuticals AG, Austria, for dimethyl sulfoxide for the treatment of severe closed traumatic brain injury.

#### **What is severe closed traumatic brain injury?**

Closed traumatic brain injury occurs when following a trauma there are not fractures in the skull, and thus the brain or structures within the skull are not exposed to the environment. Closed traumatic brain injury can be minor, moderate or severe according to the symptoms present following the trauma. Symptoms include impairment of speech, movement or vision; breathing problems; disturbed orientation with regard to time, place or person and in the most severe cases loss of consciousness. The symptoms are often related to the fact that the injury caused a bleeding (hemorrhage) or a swelling of the brain tissue (oedema), which can increase the pressure within the skull, thus modifying the normal brain functions. People with severe traumatic brain injuries undergo repeated examinations to assure that the condition does not worsen. A so-called computed tomography (abbreviation: CT scan) is the test used most often to evaluate head injuries. This technique is a special diagnostic procedure that uses special x-ray equipment associated to computer elaboration in order to obtain internal cross-sectional pictures of the body. It is useful for identifying the localisation and extent of the injuries to the brain. Severe closed traumatic brain injuries are chronically debilitating and life-threatening.

#### **What are the methods of treatment available?**

Various therapeutic methods (e.g. medicinal products and surgery), aimed at reducing the increased pressure in the skull were used in the Community for the treatment of severe closed traumatic brain injury at the time of submission of the application for orphan drug designation. Several products were authorised for the condition in some countries in the Community at the time of submission of the application for orphan drug designation.

Dimethylsulfoxide (DMSO) for treatment of severe closed traumatic brain injury might be of potential significant benefit as a new treatment option of severe closed traumatic brain injury. This benefit will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

#### **What is the estimated number of patients affected by the condition\*?**

According to the information provided by the sponsor, severe, closed traumatic brain injury was considered to affect about 92,000 persons in the European Union.

**How is this medicinal product expected to act?**

Dimethylsulfoxide is supposed to reduce the pressure in the skull by preventing brain oedema following injury and by allowing a better blood flow and thus a better oxygen delivery to the brain cells. Dimethylsulfoxid blocks the functioning of some structures present in the brain cells (and throughout the body) called sodium channels that control the uptake of the fluids in the body.

**What is the stage of development of this medicinal product?**

The effects of dimethylsulfoxid were evaluated in experimental models and in two small clinical studies.

Dimethylsulfoxide had not been marketed anywhere worldwide for treatment of severe closed traumatic brain injury, at the time of submission. Orphan designation of dimethyl sulfoxide had been granted in the United States for treatment of increased intracranial pressure in patients with severe, closed-head injury, also known as traumatic brain coma, for whom no other effective treatment is available.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 13 January 2005 a positive opinion recommending the grant of the above-mentioned designation.

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Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for 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 will be necessary before this product can be granted a marketing authorisation.

**For more information:**

Sponsor's contact details:

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\*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 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

Patients' associations contact points:

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

| <b>Language</b> | <b>Active Ingredient</b> | <b>Indication</b>                                                 |
|-----------------|--------------------------|-------------------------------------------------------------------|
| English         | Dimethyl sulfoxide       | Treatment of severe closed traumatic brain injury                 |
| Czech           | Dimethylsulfoxidu        | Léčba těžkého mozkového traumatu                                  |
| Danish          | Dimethylsulfoxid         | Behandling af svært, lukket hjernetraume                          |
| Dutch           | Dimethylsulfoxide        | Behandeling van ernstig niet-penetrerend traumatisch hersenletsel |
| Estonian        | Dimetüülsulfoksiid       | Raske kinnise traumaatilise ajukahjustuse ravi.                   |
| Finnish         | dimetyylisulfoksidi      | Vakavan suljetun aivovamman hoito                                 |
| French          | Diméthylsulfoxyde        | Traitement des traumatismes crâniens fermés graves                |
| German          | Dimethylsulfoxyd         | Behandlung von schwerem geschlossenem Schädel-Hirn Trauma         |
| Greek           | Διμεθυλικό σουλφοξειδίο  | Θεραπεία των σοβαρών κλειστών εγκεφαλικών τραυμάτων               |
| Hungarian       | Dimetil szulfoxid        | Súlyos, traumás koponyaüri sérülés kezelése                       |
| Italian         | Dimetilsolfossido        | Trattamento del trauma cranio-encefalico chiuso grave             |
| Latvian         | Dimetilsulfoksīda        | Smagas slēgtas galvas smadzeņu traumas ārstēšana                  |
| Lithuanian      | Dimetilsulfoksidas       | Stipraus uždaro trauminio galvos smegenų pažeidimo gydymas        |
| Polish          | Dimetylu sulfotlenek     | Leczenie ciężkich, zamkniętych, pourazowych uszkodzeń mózgu       |
| Portuguese      | Dimetilssulfóxido        | Tratamento do traumatismo craniano grave fechado                  |
| Slovak          | Dimetylsulfoxid          | Liečba ťažkého uzavretého traumatického poškodenia mozgu          |
| Slovenian       | Dimetilsulfoksid         | Zdravljenje hudih zaprtih možganskih poškodb                      |
| Spanish         | Dimetilsulfóxido         | Tratamiento del traumatismo craneoencefálico grave no penetrante  |
| Swedish         | Dimetylsulfoxid          | Behandling av alvarlig stängd traumatisk hjärnskada               |
| Norwegian       | Dimetylsulfoksid         | Behandling av alvorlig lukket traumatisk hjerneskade              |
| Icelandic       | Tvímetýlsúlfoxíð         | í Meðferð á alvarlegum lokuðum heilaáverka                        |