

6 January 2017  
EMA/744548/2016  
Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation

### Arsenic trioxide for the treatment of graft-versus-host disease

On 12 December 2016, orphan designation (EU/3/16/1797) was granted by the European Commission to Medsenic, France, for arsenic trioxide for the treatment of graft-versus-host disease.

#### What is graft-versus-host disease?

Graft-versus-host disease is a complication that can affect patients who have had allogeneic haematopoietic (blood) stem-cell transplantation to treat diseases of the blood such as leukaemia (a cancer of the white blood cells). The procedure involves a patient receiving stem cells from a matched donor to help restore the bone marrow, which produces new blood cells.

Graft-versus-host disease occurs when transplanted cells recognise the patient's body as 'foreign' and attack the patient's organs, such as the stomach, gut, skin and liver, leading to organ damage. The disease may happen shortly after transplantation or later on, in which case a wider range of organs can be involved.

Graft-versus-host disease is a serious and life-threatening disease with a high mortality rate.

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

At the time of designation, graft-versus-host disease affected approximately 0.5 in 10,000 people in the European Union (EU). This was equivalent to a total of around 26,000 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, several medicines were authorised in the European Union (EU) for the treatment of graft-versus-host disease, such as ciclosporin and corticosteroids. Treatment aimed to reduce the activity of transplanted cells involved in graft-versus-host disease, thereby reducing their ability to attack the patient's organs.

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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).

The sponsor has provided sufficient information to show that arsenic trioxide might be of significant benefit for patients with graft-versus-host disease because laboratory studies suggest that it might improve the outcome of patients with this condition when used together with ciclosporin. This assumption will need to be confirmed at the time of marketing authorisation, in order to maintain the orphan status.

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

Arsenic trioxide is a chemical that has been used in medicines for many years and is currently authorised in the EU for the treatment of leukaemia. In graft-versus-host disease, arsenic trioxide is thought to work by increasing the production of reactive oxygen species (ROS, toxic molecules containing oxygen) to a level where ROS is toxic to the transplanted T cells and causes their death. Since transplanted T cells are involved in graft-versus-host disease, this is expected to improve the symptoms of the condition.

### **What is the stage of development of this medicine?**

The sponsor has provided laboratory data from the published literature to support the application for orphan designation.

At the time of submission of the application for orphan designation, no clinical trials with arsenic trioxide in patients with graft-versus-host disease had been started.

At the time of submission, arsenic trioxide was not authorised anywhere in the EU for graft-versus-host disease 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 4 November 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    | Arsenic trioxide      | Treatment of graft-versus-host disease                          |
| Bulgarian  | Арсенов триоксид      | Лечение на болестта на присадката срещу приемателя              |
| Croatian   | Arsenov trioksid      | Liječenje reakcije presatka protiv primatelja                   |
| Czech      | Trioxid arsenitý      | Léčba reakce štěpu proti hostiteli                              |
| Danish     | Arsenik trioxid       | Behandling af graft versus host reaktion                        |
| Dutch      | Arseentrioxide        | Behandeling van graft versus host ziekte                        |
| Estonian   | Arseentrioksiid       | Graft versus host haiguse ravi                                  |
| Finnish    | Arseenitrioksiidi     | Käänteishyljintäreaktion hoito                                  |
| French     | Trioxyde d'arsenic    | Traitement de la réaction du greffon contre l'hôte              |
| German     | Arsentrioxid          | Behandlung der Graft-versus-Host-Reaktion                       |
| Greek      | Τριοξείδιο αρσενικού  | Θεραπεία της αντίδρασης του μοσχεύματος                         |
| Hungarian  | Arsenum trioxydatum   | Graft-versus-host betegség kezelése                             |
| Italian    | Triossido di arsenico | Trattamento della reazione del trapianto contro l'ospite        |
| Latvian    | Arsēna trioksīds      | Saimnieka-transplantāta slimības ārstēšana                      |
| Lithuanian | Arseno trioksidas     | Transplantato atmetimo ligos gydymas                            |
| Maltese    | Arsenic trioxide      | Kura tal-marda tat-tessut għat-trapjant kontra dak li jirċievih |
| Polish     | Arsenu tritlenek      | Leczenie choroby przeszczep przeciw gospodarzowi                |
| Portuguese | Trióxido de arsénico  | Tratamento da reação do enxerto contra o hospedeiro             |
| Romanian   | Arsenic trioxide      | Tratamentul reacției grefei contra gazdei                       |
| Slovak     | Oxid arzenitý         | Liečba reakcie štepů proti hostiteľovi                          |
| Slovenian  | Arzenov trioksid      | Zdravljenje bolezni presadka proti gostitelju                   |
| Spanish    | Trióxido de arsénico  | Tratamiento de la enfermedad de injerto contra huésped          |
| Swedish    | Arseniktrioxid        | Behandling av graft-vård host reaktion                          |
| Norwegian  | Arsentrioksid         | Behandling av graft-versus-host -reaksjon                       |
| Icelandic  | Arsenik þríoxíð       | Til meðferðar á hýsilssótt                                      |

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