



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

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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in December 2003 on request of the sponsor.

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of arsenic trioxide for the treatment of acute promyelocytic leukaemia

On 17 January 2001, orphan designation (EU/3/00/017) was granted by the European Commission to Pharmacie Centrale des Hôpitaux de Paris, France, for arsenic trioxide for the treatment of acute promyelocytic leukaemia.

The sponsor subsequently changed name to AGEPS-EPHP Agence Générale des Équipements et Produits de Santé.

What is acute promyelocytic leukaemia?

Acute promyelocytic leukaemia is a disease in which cancer cells are found in the blood and the bone marrow. The bone marrow is the spongy tissue inside the large bones in the body. Normally, the bone marrow makes cells called “blasts” that mature into several different types of blood cells that have specific functions in the body. These include red cells, white cells and platelets. Red blood cells carry oxygen and other materials to all tissues of the body. White blood cells fight infection. Platelets make the blood clot. When leukaemia develops, the bone marrow produces large numbers of abnormal blood cells. There are several types of leukaemias. In acute promyelocytic leukaemia blasts that are developing into white blood cells, called myeloid cells, are affected. The blasts do not mature and become too many. These blast cells are then found in the blood and also accumulate in the bone marrow. When the promyelocytic leukaemia develops quickly with many blasts it is defined as acute. Acute promyelocytic leukaemia is life-threatening.

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

At the time of designation acute promyelocytic leukaemia affected not more than 0.1 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 3,800 people.

What treatments are available?

Treatment for leukaemia is complex and depends on a number of factors including the type of leukaemia, the extent of the disease and whether the leukaemia has been treated before. It also depends on the patient's age, symptoms, and general health. Treatment of acute promyelocytic leukaemia is chemotherapy (using drugs to kill cancer cells) and vitamin A-derived drug that helps the myeloid stem cells to mature into normal white blood cells.

Arsenic trioxide could be of potential significant benefit for the treatment of acute promyelocytic leukaemia because it may work in patients that cannot be treated with existing methods. This

*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. This represents a population of 377,000,000 (Eurostat 2001).

assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

How is this medicine expected to work?

It is not completely understood how arsenic trioxide works in the human body. According to the sponsor, arsenic trioxide induces cell death in cancer cells by interfering with various functions including synthesis of DNA, signalling within the cell and several modifications (such as phosphorylation and other enzymatic activities) necessary for proteins to work normally.

What is the stage of development of this medicine?

The effects of arsenic trioxide were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with acute promyelocytic leukaemia were ongoing.

Arsenic trioxide was not authorised anywhere worldwide for the treatment of acute myelocytic leukaemia, nor 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 on 21 November 2000 a positive opinion recommending the grant 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:

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Translations of the active ingredient and indication in all EU languages

LANGUAGE	Active Ingredient	Indication
English	Arsenic trioxide	treatment of acute promyelocytic leukaemia
Danish	Arsenik trioxid	Behandling af akut promyelocyt leukæmi
Dutch	Arseentrioxide	Behandeling van acute promyelocyttaire leukemie
Finnish	Arseenitrioksidi	Akuutin promyelosyyttisen leukemian hoito
French	Trioxyde d'arsenic	Traitement de la leucémie aiguë promyélocytaire
German	Arsentrioxid	Behandlung der akuten Promyelozytenleukämie
Greek	Τριοξείδιο αρσενικού	Θεραπεία της οξείας προμυελοκυτταρικής λευχαιμίας
Italian	triossido di arsenico	Trattamento della leucemia promielocitica acuta
Portuguese	Trióxido de arsénico	Tratamento da Leucemia Promielocítica Aguda
Spanish	Trióxido de arsénico	Tratamiento de la leucemia promielocítica aguda
Swedish	Arseniktrioxid	Behandling av akut promyeloisk leukemi