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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Arsenic trioxide for the treatment of acute promyelocytic leukaemia

First publication	15 October 2004
Rev.1: transfer of sponsorship	22 February 2007
Rev.2: transfer of sponsorship	3 July 2007
Rev.3: withdrawal from the Community Register	25 June 2012
Rev.2: administrative update	14 October 2013
Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in March 2012 at the end of the period of market exclusivity.

On 18 October 2000, orphan designation (EU/3/00/008) was granted by the European Commission to Voisin Consulting SARL, France, for arsenic trioxide for the treatment of acute promyelocytic leukaemia.

The sponsorship was transferred to Cell Therapeutics (UK) Ltd in 2001 and subsequently to Cephalon UK Limited, United Kingdom, in April 2006 and finally to Cephalon Europe, France, in June 2007.

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

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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 0.8 in 10,000 people in the European Union (EU). This was equivalent to a total of not more than 30,000 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?

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 leukemia 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. 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?

It is not completely understood how arsenic trioxide works in the human body. The sponsor claims that arsenic trioxide breaks down the fundamental genetic material (DNA) of the cancer cells and thereby induces cell death.

What is the stage of development of this medicine?

The effects of arsenic trioxide have not been evaluated in experimental models.

Clinical trials in patients with acute promyelocytic leukaemia were ongoing at the time of submission of the application for orphan designation.

Arsenic trioxide was not marketed or designated as orphan medicinal product elsewhere, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 13 September 2000 recommending the granting of this designation.

*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.
At the time of designation, this represented a population of 375,500,000 (Eurostat 2000).

Update: Arsenic trioxide (Trisenox) has been authorised in the EU since 5 March 2002 for induction of remission and consolidation in adult patients with relapsed/refractory acute promyelocytic leukaemia (APL), characterised by the presence of the t(15;17) translocation and/or the presence of the Pro-Myelocytic Leukaemia/Retinoic-Acid-Receptor-alpha (PML/RAR-alpha) gene. Previous treatment should have included a retinoid and chemotherapy. The response rate of other acute myelogenous leukaemia subtypes to TRISENOX has not been examined.

More information on Trisenox can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports

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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

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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[1], Norwegian and Icelandic

Language	Active ingredient	Indication
English	Arsenic trioxide	Treatment of acute promyelocytic leukaemia
Bulgarian	Арсенов триоксид	Лечение на остра промиелоцитна левкемия
Czech	Trioxid arsenitý	Léčba akutní promyelocytární leukemie
Danish	Arsenik trioxid	Behandling af akut promyelocytleukæmi
Dutch	Arseentrioxide	Behandeling van acute promyelocytaire leukemie
Estonian	Arseentrioksiid	Ägeda promüelotsütaarse leukeemia ravi
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
Hungarian	Arsenum trioxydatum	Akut promyelocitás leukémia kezelése
Italian	Triossido di arsenico	Trattamento della leucemia promielocitica acuta
Latvian	Arsēna trioksīds	Akūta promielocitāra leikoze
Lithuanian	Arseno trioksidas	Ūmios promielocitinės leukemijos gydymas
Maltese	Arsenic trioxide	Kura tal-lewkimja promjeloċitika akuta
Polish	Arsenu tritlenek	Leczenie ostrej białaczki promielocytowej
Portuguese	Trióxido de arsénico	Tratamento da Leucemia Promielocítica Aguda
Romanian	Trioxid de arsen	Tratamentul leucemiei promielocitare acute
Slovak	Oxid arzenitý	Liečba akútnej promyelocytárnej leukémie
Slovenian	Arzenov trioksid	Zdravljenje akutne promielocitne levkemije
Spanish	Trióxido de arsénico	Tratamiento de la leucemia promielocítica aguda
Swedish	Arseniktrioxid	Behandling av akut promyeloisk leukemi

[1] At the time of transfer of sponsorship