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 2-chloro-9-[2-deoxy-2-fluoro-ß-D-arabinofuranosyl]adenine for the treatment of acute lymphoblastic leukaemia

On 5 February 2002, orphan designation (EU/3/01/082) was granted by the European Commission to ILEX Services Limited, United Kingdom, for 2-chloro-9-[2-deoxy-2-fluoro-ß-D-arabinofuranosyl]adenine (clofarabine) for the treatment of acute lymphoblastic leukaemia (ALL).
The sponsorship was transferred to Bioenvision, United Kingdom, in December 2002 and subsequently to Genzyme Europe BV, The Netherlands, in May 2008.

## What is acute lymphoblastic leukaemia?

When leukaemia develops, the body produces large numbers of abnormal blood cells. There are several types of leukaemias. They are grouped by how quickly the disease develops and by the type of blood cell that is affected. This form of leukaemia is characterised by an abnormal proliferation of immature lymphocytes. It is the most common type of leukaemia in young children. This disease also affects adults, especially those aged 65 and older. Many people with acute leukaemia can be cured. However, despite the available treatments, acute lymphoblastic leukaemia remains a serious and life threatening condition in a subgroup of patients.

## What are the methods of treatment 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. Treatments that had been authorised at the time of submission of the application for orphan drug designation included different chemotherapeutic agents. Bone marrow transplantation is also available.
Satisfactory argumentation has been submitted by the sponsor to justify the assumption that clofarabine might be of potential significant benefit for the treatment of acute lymphoblastic leukaemia, particularly in terms of its potential activity in relapsed disease.

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

Based on the information provided by the sponsor and previous knowledge of the Committee, acute lymphoblastic leukaemia was considered to affect approximately 0.4 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 15,000 persons.

* Disclaimer: The number of patients affected by the condition is estimated and assessed for the purpose of the designation, for a European Community population of 377,000,000 (Eurostat 2001). This estimate is based on available information and calculations presented by the sponsor at the time of the application and may thus differ from the true number of patients affected by the condition.

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**How is this medicinal product expected to act?**
Clofarabine is an analogue of adenine which is part of the fundamental genetic material of cells (DNA and RNA). Clofarabine inhibits the synthesis of DNA and thus inhibits growth of tumour cells.

**What is the stage of development of this medicinal product?**
The effects of clofarabine have been evaluated in experimental models and clinical studies with clofarabine in adult patients with refractory acute lymphoblastic leukaemia were ongoing in the United States at the time of submission of the application for orphan designation.

Clofarabine had not been marketed or designated as orphan medicinal product elsewhere, 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 2001 a positive opinion recommending the grant of the above mentioned designation.

Update: 2-chloro-9-[2-deoxy-2-fluoro-ß-D-arabinofuranosyl]adenine (Evoltra) is authorised in the European Union as of 29 May 2006 for the treatment of acute lymphoblastic leukaemia (ALL) in paediatric patients who have relapsed or are refractory after receiving at least two prior regimens and where there is no other treatment option anticipated to result in a durable response.
Safety and efficacy have been assessed in studies of patients ≤ 21 years old at initial diagnosis.
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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 be affecting 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 have been 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.

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