



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

Document Date: London, 22 February 2007
Doc.Ref.: EMEA/COMP/1384/03 Rev.1

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in March 2006 on request of the sponsor.

COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF nolatrexed for the treatment of hepatocellular carcinoma

On 2 October 2003, orphan designation (EU/3/03/165) was granted by the European Commission to Scirex Ltd, United Kingdom, for nolatrexed for the treatment of hepatocellular carcinoma.

What is hepatocellular carcinoma?

Tumours that begin in the liver are known as liver tumours. Liver tumours which have the potential to grow rapidly and infiltrate healthy tissues are called hepatocellular carcinomas. Hepatocellular carcinoma is a life-threatening condition.

What are the methods of treatment available?

No medicinal products for the treatment of the condition had been authorised in the European Union at the time of submission of the application for orphan drug designation.

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

According to the information provided by the sponsor, hepatocellular carcinoma was considered to affect about 37,500 persons in the European Union.

How is this medicinal product expected to act?

Nolatrexed is a compound that inhibits the activity of a protein called thymidylate synthase. This protein is basic in the synthesis of DNA. DNA is the basic building block of all living things, including the instructions to make more cells. It has been demonstrated that thymidylate synthase is present in tumour cells in significantly higher quantities than in non-cancerous tissues. By slowing down or blocking the activity of this protein, nolatrexed may help to slow down or stop the growth of these tumour cells.

What is the stage of development of this medicinal product?

The effects of nolatrexed were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with hepatocellular carcinoma were completed. Additional confirmatory studies in patients with this condition were ongoing.

The medicinal product was not marketed anywhere worldwide for hepatocellular carcinoma at the time of submission. Orphan designation of nolatrexed was granted in the United States of America for treatment of hepatocellular carcinoma.

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According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 30 July 2003 a positive opinion recommending the grant of the above-mentioned designation.

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:

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*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 385,000,000 (Eurostat 2002) and may differ from the true number of patients affected by the condition. This estimate is based on available information and calculations presented by the sponsor at the time of the application.

Translations of the active ingredient and indication in all EU languages

Language	Active Ingredient	Indication
English	Nolatrexed	Treatment of hepatocellular carcinoma
Danish	Nolatrexed	Behandling af hepatocellulært carcinom
Dutch	Nolatrexed	Behandeling van hepatocellulair carcinoom
Finnish	Nolatreksedi	Hepatosellulaarisen karsinooman hoito
French	Nolatrexed	Traitement du carcinome hépatocellulaire
German	Nolatrexed	Behandlung des Leberzellkarzinoms
Greek	Nolatrexed	Θεραπεία του ηπατοκυτταρικού καρκινώματος
Italian	Nolatrexed	Trattamento del carcinoma epatocellulare
Portuguese	Nolatrexed	Tratamento do carcinoma hepatocelular
Spanish	Nolatrexed	Tratamiento del carcinoma hepatocelular
Swedish	Nolatrexed	Behandling av hepatocellulärt karcinom