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

Document Date: London, 9 February 2006
Doc.Ref.: EMEA/COMP/355971/2005

COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF 1,2-bis(methylsulphonyl)-1-(2-chloroethyl)-2-[(methylamino)carbonyl]hydrazine for the treatment acute myeloid leukaemia

On 14 December 2005, orphan designation (EU/3/05/332) was granted by the European Commission to Vion (UK) Limited, United Kingdom, for 1,2-bis(methylsulphonyl)-1-(2-chloroethyl)-2-[(methylamino)carbonyl]hydrazine for the treatment of acute myeloid leukaemia.

What is acute myeloid leukaemia?

Acute myeloid 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 myeloid leukaemia blasts that are developing into a type of white blood cells called granulocytes 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 where they take the place of the other types of normal blood cells. When leukaemia develops quickly with many blasts it is called acute. Acute myeloid leukaemia is life-threatening.

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 age, the symptoms, and the general health of the patient. The primary treatment of acute myeloid leukaemia is chemotherapy (using drugs to kill cancer cells). Several products were authorised for the condition in the Community at the time of submission of the application for orphan drug designation.
1,2-bis(methylsulphonyl)-1-(2-chloroethyl)-2-[(methylamino)carbonyl]hydrazine could be of potential significant benefit for the treatment of acute myeloid leukaemia because it might improve the long-term outcome of the patients. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status.

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

According to the information provided by the sponsor, acute myeloid leukaemia was considered to affect about 32,000 persons in the European Union.

How is this medicinal product expected to act?

1,2-bis(methylsulphonyl)-1-(2-chloroethyl)-2-[(methylamino)carbonyl]hydrazine is an alkylating agent. These agents interfere with the fundamental genetic material of the cells (DNA or RNA). They block tumour cell growth by forming cross-bridges in the DNA chains (DNA strands), which makes

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 70 40
E-mail: orphandrugs@emea.eu.int www.emea.eu.int

the strands unable to uncoil and separate. This prevents DNA replication (making new copies) and thus the tumour cells can no longer divide.

What is the stage of development of this medicinal product?
The effects of 1,2-bis(methylsulphonyl)-1-(2-chloroethyl)-2-[(methylamino)carbonyl]hydrazine were evaluated in experimental models.

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

1,2-bis(methylsulphonyl)-1-(2-chloroethyl)-2-[(methylamino)carbonyl]hydrazine was not authorised anywhere worldwide for treatment of acute myeloid leukaemia, at the time of submission. Orphan designation of 1,2-bis(methylsulphonyl)-1-(2-chloroethyl)-2-[(methylamino)carbonyl]hydrazine was granted in the United States for treatment of acute myeloid leukaemia.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 24 October 2005 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:
Sponsor's contact details:
Vion (UK) Limited
% i3 Research
Sygnus Court
22-32 Market Street
Maidenhead SL6 8AD
United Kingdom
Telephone: +44 16 28 40 84 08
Telefax: +44 16 28 40 84 01
E-mail: vionuk@vionpharm.co.uk

*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 (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

Patients' associations contact points:

Leukaemia Care
2 Shrubbery Avenue
Worcester
WR1 1QH
United Kingdom
0800 169 6680 (freephone for UK residents)
Telephone: +44 19 05 33 00 03 / + 44 84 57 67 32 03
Telefax: +44 19 05 33 00 90
E-mail: enquiries@leukaemiaCARE.org.uk

Leukaemia Research Fund
43 Great Ormond Street
London
WC1N 3JJ
United Kingdom
Telephone: +44 20 74 05 01 01
Telefax : +44 20 74 05
E-mail: info@lrf.org.uk

Associazione Italiana contro le Leucemie-linfomi e mieloma ONLUS
Via Ravenna 34
00161 Roma
Italy
Telephone: +39 06 44 03 763
Telefax: +39 06 44 04 226
E-mail: ail@ail.it

Translations of the active ingredient and indication in all EU languages and Norwegian and Icelandic

Language	Active Ingredient	Indication
English	1,2-bis(methylsulphonyl)-1-(2-chloroethyl)-2-[(methylamino)carbonyl]hydrazine	Treatment of acute myeloid leukaemia
Czech	1,2-bis(metylsulfonyl)-1-(2-chlóretyl)-2-[(metylamino)karbonyl]hydrazin	Léčba akutní myeloidní leukémie
Danish	1,2-bis(methylsulphonyl)-1-(2-chlorethyl)-2-[(methylamino)carbonyl]hydrazin	Behandling af akut myeloid leukæmi
Dutch	1,2-bis(methylsulfonyl)-1-(2-chloorethyl)-2-[(methylamino)carbonyl]hydrazine	Behandeling van acute myeloïde leukemie
Estonian	1,2-bis(metüülsulfonüül)-1-(2-kloroetüül)-2-[(metüülamino)karbonüül]hüdrasiin	Akuutse müeloidse leukeemia ravi
Finnish	1,2-bis(metyylisulfonyyli)-1-(2-kloorietyyli)-2-[(metyyliamino)karbonyyli]hydratsiini	Akuutin myelooisen leukemian hoito
French	1,2-bis(méthylsulfonyl)-1-(2-chloroéthyle)-2-[(méthylamino)carbonyle]hydrazine	Traitement de la leucémie aiguë myéloïde
German	1,2-Bis(methylsulphonyl)-1-(2-chlorethyl)-2-[(methylamino)carbonyl]hydrazin	Behandlung der akuten myeloischen Leukämie
Greek	1,2-δις(μεθυλοσουλφονυλο)-1-(2-χλωροαιθυλο)-2-[(μεθυλαμινο)καρβινυλο]υδραζίνη	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	1,2-bisz(metilszulfonil)-1-(2-klór-etil)-2-[(metilamino)karbonil]hidrazin	Akut myeloid leukaemia kezelése
Italian	1,2-bis(metilsulfonil)-1-(2-cloroetil)-2-[(metilammino)carbonil]idrazina	Trattamento della leucemia mieloide acuta
Latvian	1,2-bis(metilsulfonīl)-1-(2-hloretīl)-2-[(metilamino)karbonil]hidrazīns	Akūtas mieloleikozes ārstēšana
Lithuanian	1,2-bis(metilsulfonil)-1-(2-chloretil)-2-[(metilamino)karbonil]hidrazinas	Ūmios mieloleukozės gydymas
Polish	1,2-bis(metylosulfonylo)-1-(2-chloroetylo)-2-[(metyloamino)karbonylo]hydrazyna	Leczenie ostrej białaczki szpikowej
Portuguese	1,2-bis(metilsulfonil)-1-(2-cloroetil)-2-[(metilamino)carbonil]hidrazina	Tratamento da leucemia mielóide aguda
Slovak	1,2-bis(metylsulfonyl)-1-(2-chloroetyl)-	Liečba akútnej myeloickej leukémie

	2-[(metylamíno)karbonyl]hydrazín	
Slovenian	1,2-bis(metilsulfonil)-1-(2-hloroetil)-2-[(metilamino)karbonil]hidrazin	Zdravljenje akutne mieloične levkemije
Spanish	1,2-bis(metilsulfonil)-1-(2-cloroetil)-2-[(metilamino)carbonil]hidracina	Tratamiento de la leucemia mieloide aguda
Swedish	1,2-bis(metylsulfonyl)-1-(2-kloretyl)-2-[(metylamin)karbonyl]hydrazin	Behandling av akut myeloisk leukemi
Norwegian	1,2-bis(metylsulfonyl)-1-(2-kloretyl)-2-[(metylamino)karbonyl]hydrazin	Behandling av akutt myelogen leukemi
Icelandic	1,2-bis(metýlsúlfónýl)-1-(2-klóróetýl)-2-[(metýlamínó)karbónýl]hýdrazín	Meðferð við bráðu kyrningahvítblæði