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Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in March 2009 on request of the Sponsor.

Committee for Orphan Medicinal Products

Public summary of positive opinion for orphan designation of Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptide, sequence 169-177, of proteinase 3) for the treatment of acute myeloid leukaemia

On 21 December 2004, orphan designation (EU/3/04/253) was granted by the European Commission to Accelsiors CRO & Consultancy Services GmbH, Germany, for Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptide, sequence 169-177, of proteinase 3) 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 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. When leukaemia develops quickly with many blasts it is called acute. Acute myeloid leukaemia is life-threatening.

What is the estimated number of patients affected by the condition?
At the time of designation, acute myeloid leukaemia affected approximately 0.7 in 10,000 people in the European Union (EU)[*]. This is equivalent to a total of around 32,000 people, and is below the threshold for orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and 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 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. Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptide, sequence 169-177, of

[*]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 (EU 25), Norway, Iceland and Liechtenstein. This represents a population of 459,700,000 (Eurostat 2004).

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proteinase 3) could be of potential significant benefit for the treatment of acute myeloid leukaemia because it may act in a different way and it might improve the long-term outcome of the patients. The 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?
Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptide, sequence 169-177, of proteinase 3) is a peptide, which is a part of a protein. It is similar to a part of a protein, present on the surface of certain cells, such as cancer cells. It is expected to work as a vaccine, thus upon administration of this peptide, the body's defense system (immune system) will recognize this peptide as a foreign body and react against this peptide. Since part of this foreign body is similar to parts of the protein on the cancer cells, it is expected that the immune system will not only recognize the vaccine as foreign, but also the cancer cells. The body's immune system could then kill these cancer cells.

What is the stage of development of this medicine?
The effects of Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptide, sequence 169-177, of proteinase 3) 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.

Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptide, sequence 169-177, of proteinase 3) was not marketed anywhere worldwide for the treatment of acute myeloid leukaemia or 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 11 November 2004 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;
- either the rarity of the condition (affecting not more than 5 in 10,000 people in the Community) 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.

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

Language	Active Ingredient	Indication
English	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptide, sequence 169-177, of proteinase 3)	Treatment of acute myeloid leukaemia
Czech	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptid, sekvence 169-177, proteinázy 3)	Léčba akutní myeloidní leukémie
Danish	Val-Leu-Gln-Glu-Leul Asn-Val-Thr-Val (Pr1 nanopeptid, sekvens 169-177, af proteinase 3) eukæmiassocieret PR1-antigen	Behandling af akut myeloid leukæmi
Dutch	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptide, sequentie 169-177, van proteinase 3)	Behandeling van acute myeloïde leukemie
Estonian	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Proteinaas 3 PR1 nanopeptiid, järjestusega 169-177)	Akuutse müeloidse leukeemia ravi
Finnish	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (proteinaasi 3 Pr1 nanopeptidi, 169-177 sekvenssi)	Akuutin myelooisen leukaemian hoito
French	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (nanopeptide Pr1, séquence 169-177 de la protéinase 3)	Traitement de la leucémie myéloïde aiguë
German	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 Nanopeptid, Sequenz 169-177, der Proteinase 3)	Behandlung der akuten myeloischen Leukämie
Greek	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 νοναπεπτίδιο, αλληλουχίας 169-177 της πρωτεϊνάσης 3)	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptid, proteináz3 169-177 szekvenciája)	Akut myeloid leukaemia kezelése
Italian	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptide, sequenza 169-177, di proteinasi 3)	Trattamento della leucemia mieloide acuta
Latvian	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (proteināzes 3 Pr1 nanopeptīds, virkne 169-177)	Akūtas mieloleikozes ārstēšana
Lithuanian	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptidas, proteinazės 3 seka 169-177)	Ūminės mieloleukozės gydymas
Polish	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (nanopeptyd w sekwencji 169-177 proteinazy 3)	Leczenie ostrej białaczki szpikowej
Portuguese	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptido, sequência 169-177, da proteinase 3)	Tratamento da leucemia mielóide aguda

Slovak	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptid, sekvencia 169-177, proteinázy 3)	Liečba akútnej myeloidnej leukémie
Slovenian	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptid, sekvenca 169-177 proteinaze 3)	Zdravljenje akutne mieloične levkemije
Spanish	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (nanopéptido Pr1, secuencia 169-177, de la proteinasa 3)	Tratamiento de la leucemia mieloide aguda
Swedish	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptid, sekvens 169-177, av proteinas 3)	Behandling av akut myeloisk leukemi
Norwegian	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptid, sekvens 169-177 av proteinase 3)	Behandling av akutt myelogen leukemi
Icelandic	Val-Leu-Gln-Glu-Leu-Asn-Val-Thr-Val (Pr1 nanopeptíð, röð 169-177, af próteinasa 3)	Til meðferðar við bráðu kyrningahvítblæði