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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Recombinant human histone H1.3 and recombinant human N-bis-met-histone H1.3 for the treatment of acute lymphoblastic leukaemia

On 23 February 2011, orphan designation (EU/3/10/840) was granted by the European Commission to SymbioTec GmbH, Germany, for recombinant human histone H1.3 and recombinant human N-bis-met-histone H1.3 for the treatment of acute lymphoblastic leukaemia.

The sponsorship was transferred to Xenetic Biosciences Plc, United Kingdom, in October 2012.

What is acute lymphoblastic leukaemia?

Acute lymphoblastic leukaemia (ALL) is a cancer of the white blood cells called lymphocytes. In this disease, the lymphocytes multiply too quickly and live for too long, so there are too many of them circulating in the blood. These abnormal lymphocytes are not fully developed and do not work properly. Over a period of time, they replace the normal white blood cells, red blood cells and platelets in the bone marrow (the spongy tissue inside the large bones in the body).

ALL is the most common type of leukaemia in young children, but the disease also affects adults, especially those aged 65 years and older. Many people with ALL can be cured. However, despite the available treatments, ALL remains a serious and life-threatening disease in some patients.

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

At the time of designation, ALL affected approximately 1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 51,000 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 ALL is complex and depends on a number of factors including the extent of the disease, whether it has been treated before, and the patient's age, symptoms and general state of health. At

*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 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 507,700,000 (Eurostat 2011).

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the time of designation, the main treatment for ALL was chemotherapy (medicines to treat cancer) followed by or combined with radiotherapy (treatment with radiation). Haematopoietic (blood) stem cell transplantation was also used. This is a complex procedure where the patient receives stem cells from a matched donor to help restore the bone marrow.

The sponsor has provided sufficient information to show that recombinant human histone H1.3 and recombinant human N-bis-met-histone H1.3 might be of significant benefit for the treatment of ALL because it works in a different way to existing treatments and early studies show that it may improve the treatment of patients with ALL. 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?

Histones are proteins that are involved in 'coiling up' strands of DNA in cells into tightly packed chromosomes. Normally, they are only present within the nucleus of the cells, but cancer cells have been shown to also have histones on their surface. This medicine is made up of human histone H1.3, which is expected to attach to the histones on the surface of the cancer cells, forming large 'aggregates' (clumps) that cause the cell wall to break. This is expected to kill the cancer cells.

The medicine contains two types of histone H1.3, one that is identical to the human protein, and one (the 'N-bis-met' type) that is transformed in the body into the human protein. Both types of histone H1.3 in the medicine have been made using 'recombinant DNA technology': they are made by a bacterium that has received a gene that makes it able to produce them in large quantities.

What is the stage of development of this medicine?

The effects of the medicine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with recombinant human histone H1.3 and recombinant human N-bis-met-histone H1.3 in patients with ALL had been started.

At the time of submission, the medicine was not authorised anywhere in the EU for ALL or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 10 November 2010 recommending the granting of this designation.

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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

Sponsor's contact details:

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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	Recombinant human histone H1.3 and recombinant human N-bis-met-histone H1.3	Treatment of acute lymphoblastic leukaemia
Bulgarian	Рекомбинантен човешки гистон H1.3 и рекомбинантен човешки H-бис-мет-гистон H1.3	Лечение на остра лимфобластна левкемия
Czech	Rekombinantní lidský histon H1.3 a rekombinantní lidský N-bis-met-histon H1.3	Léčba akutní lymfoblastické leukémie
Danish	Rekombinant humant histon H1.3 og rekombinant humant N-bis-met-histon H1.3	Behandling af akut lymfoblastær leukæmi
Dutch	Recombinant humaan histon H1.3 en recombinant humaan N-bis-met-histon H1.3	Behandeling van acute lymfoblastaire leukemie
Estonian	Rekombinantne inimese histoon H1.3 ja rekombinantne inimese N-bis-met-histoon H1.3	Ägeda lümfoblastilise leukeemia ravi
Finnish	Rekombinantti ihmis-histoni H1.3 ja rekombinantti ihmis-n-bis-met-histoni H1.3	Akuutin lymfoblastileukemian hoito
French	Histone humaine recombinante H1.3 et N-bis-met-histone humaine recombinante H1.3	Traitement de la leucémie lymphoblastique aiguë
German	Rekombinantes humanes Histon H1.3 und rekombinantes humanes N-bis-met-Histon H1.	Behandlung der akuten lymphatischen Leukämie
Greek	ανασυνδυασμένη ανθρώπινη ιστόνη H1.3 και ανασυνδυασμένη ανθρώπινη N-bis-met-ιστόνη H1.3	Θεραπεία της οξείας λεμφοβλαστικής λευχαιμίας
Hungarian	Rekombináns humán hiszton H1.3 és rekombináns human N-bis-met-hiszton H1.3	Akut lymphoblastos leukaemia kezelése
Italian	Istone umano ricombinante H1.3 e N-bis-met-istone umano ricombinante H1.3	Trattamento della leucemia linfoblastica acuta
Latvian	Rekombinēts cilvēka histons H1.3 un rekombinēts cilvēka N-bis-met-histons H1.3	Akūtas limfoblastiskas leikozes ārstēšana
Lithuanian	Rekombinantinis žmogaus histonas H1.3 ir rekombinantinis žmogaus N-bis-met-histonas H1.3	Ūmios limfoblastinės leukemijos gydymas
Maltese	Istone uman rikombinanti tat-tip H1.3 u N-bis-met-istone uman rikombinanti tat-tip H1.3	Kura tal-lewkimja limfoblastika akuta
Polish	Ludzki histon rekombinowany H1.3 oraz ludzki N-bis-met-histon rekombinowany H1.3	Leczenie ostrej białaczki limfoblastycznej
Portuguese	Histona recombinante humana H1.3 e N-bis-met-Histona recombinante humana H1.3 tipo	Tratamento da leucémia linfoblástica aguda
Romanian	Histonă H1.3 umană recombinantă şi N-bis-met-histonă H1.3 umană recombinantă	Tratamentul leucemiei limfoblastice acute
Slovak	Rekombinantný ľudský histón H1.3 a rekombinantný ľudský N-bis-met-histón H1.3	Liečba akútnej lymfoblastickej leukémie

[1] At the time of designation

Slovenian	Ljudski rekombinantni histon H1.3 in ljudski rekombinantni N-bis-met-histon H1.3	Zdravljenje akutne limfoblastne levkemije
Spanish	Histona recombinante humana H1.3 y N-bis-met-Histona recombinante humana H1.3	Tratamiento de la leucemia linfoblástica aguda
Swedish	Rekombinant humant histon H1.3 och rekombinant humant N-bis-met-histon H1.3	Behandling av akut lymfatisk leukemi
Norwegian	Rekombinant humant Histon H1.3 og rekombinant humant N-bis-met-histon H1.3	Behandling av akutt lymfoblastisk leukemi
Icelandic	Raðbrigða manna histón H1.3 og raðbrigða manna N-bis-met-histón H1.3	Meðferð við bráðu eitilfrumuhvítblæði