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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 myeloid leukaemia

On 20 December 2007, orphan designation (EU/3/07/516) 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 myeloid leukaemia.

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

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”, which 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 should develop 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; they also accumulate in the bone marrow where they take the place of the other types of normal blood cells, causing anaemia, easy bruising, and frequent infections. Myeloid leukaemia can be acute, when it develops quickly with many blasts. 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 2 in 10,000 people in the European Union (EU). This was equivalent to a total of around 100,000 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).

*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 500,300,000 (Eurostat 2007).

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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. Satisfactory argumentation has been submitted by the sponsor to justify the assumption that recombinant human histone H1.3 and recombinant human N-bis-met-histone H1.3 might be of potential significant benefit for the treatment of acute myeloid leukaemia because of its mechanism of action which is different from existing treatments. This 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?

Histones including histone H1.3 are naturally occurring proteins of the human body where they predominantly occur in the nucleus of cells. Recombinant N-bis-met-histone H1.3 is an artificial molecule (a prodrug) which is transformed in the body to histone H1.3. Tumour cells differ from healthy cells as their outer membrane bear receptors (proteins that bind specific molecules) which bind histone H1.3 and N-bis-met-histone H1.3. These histones and the receptors form large aggregates in the membrane, leading to membrane ruptures and the ultimate death of the cancer cells.

What is the stage of development of this medicine?

The effects of recombinant human histone H1.3 and recombinant human N-bis-met-histone H1.3 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.

Recombinant human histone H1.3 and recombinant human N-bis-met-histone H1.3 was not authorised anywhere worldwide for the treatment of acute myeloid leukaemia, at the time of submission.

Orphan designation of amonafide l-malate was granted in the United States for the treatment of acute myeloid leukaemia.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 8 November 2007 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 myeloid leukaemia
Bulgarian	Рекомбинантен човешки гистон H1.3 и рекомбинантен човешки H-бис-мет-гистон H1.3	Лечение на остра миелоидна левкемия
Czech	Rekombinantní lidský histon H1.3 a rekombinantní lidský N-bis-met-histon H1.3	Léčba akutní myeloidní leukémie
Danish	Rekombinant humant histon H1.3 og rekombinant humant N-bis-met-histon H1.3	Behandling af akut myeloid leukæmi
Dutch	Recombinant humaan histon H1.3 en recombinant humaan N-bis-met-histon H1.3	Behandeling van acute myeloïde leukemie
Estonian	Rekombinantne inimese histoon H1.3 ja rekombinantne inimese N-bis-met-histoon H1.3	Akuutse müeloidse leukeemia ravi
Finnish	Rekombinantti ihmis-histoni H1.3 ja rekombinantti ihmis-n-bis-met-histoni H1.3	Akuutin myelooisen leukemian hoito
French	Histone humaine recombinante H1.3 et N-bis-met-histone humaine recombinante H1.3	Traitement de la leucémie aiguë myéloïde
German	Rekombinantes humanes Histon H1.3 und rekombinantes humanes N-bis-met-Histon H1.	Behandlung der akuten myeloischen Leukämie
Greek	ανασυνδυασμένη ανθρώπινη ιστόνη H1.3 και ανασυνδυασμένη ανθρώπινη N-bis-met-ιστόνη H1.3	Θεραπεία της οξείας μυελοειδούς λευχαιμίας
Hungarian	Rekombináns humán hiszton H1.3 és rekombináns human N-bis-met-hiszton H1.3	Akut myeloid leukaemia kezelése
Italian	Istone umano ricombinante H1.3 e N-bis-met-istone umano ricombinante H1.3	Trattamento della leucemia mieloide acuta
Latvian	Rekombinēts cilvēka histons H1.3 un rekombinēts cilvēka N-bis-met-histons H1.3	Akūtas mieloleikozes ārstēšana
Lithuanian	Rekombinantinis žmogaus histonas H1.3 ir rekombinantinis žmogaus N-bis-met-histonas H1.3	Ūmios mieloleukozės gydymas

[1] At the time of designation

Language	Active Ingredient	Indication
Maltese	Istone uman rikombinanti tat-tip H1.3 u N-bis-met-istone uman rikombinanti tat-tip H1.3	Kura tal-lewkimja mjelojda akuta
Polish	Ludzki histon rekombinowany H1.3 oraz ludzki N-bis-met-histon rekombinowany H1.3	Leczenie ostrej białaczki szpikowej
Portuguese	Histona recombinante humana H1.3 e N-bis-met-Histona recombinante humana H1.3 tipo	Tratamento da leucemia mielóide aguda
Romanian	Histonă H1.3 umană recombinantă şi N-bis-met-histonă H1.3 umană recombinantă	Tratamentul leucemiei mieloide acute
Slovak	Rekombinantný ľudský histón H1.3 a rekombinantný ľudský N-bis-met-histón H1.3	Liečba akútnej myeloickej leukémie
Slovenian	Ljudski rekombinantni histon H1.3 in ljudski rekombinantni N-bis-met-histon H1.3	Zdravljenje akutne mieloične levkemije
Spanish	Histona recombinante humana H1.3 y N-bis-met-Histona recombinante humana H1.3	Tratamiento de la leucemia mieloide aguda
Swedish	Rekombinant humant histon H1.3 och rekombinant humant N-bis-met-histon H1.3	Behandling av akut myeloisk leukemi
Norwegian	Rekombinant humant Histon H1.3 og rekombinant humant N-bis-met-histon H1.3	Behandling av akutt myelogen leukemi
Icelandic	Raðbrigða manna histón H1.3 og raðbrigða manna N-bis-met-histón H1.3	Meðferð við bráðu kyrningahvítblæði