4 June 2014
EMA/COMP/1317/2003 Rev.3
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Cladribine (subcutaneous use) for the treatment of indolent non-Hodgkin's lymphoma

First publication	8 July 2003
Rev.1: information about Marketing Authorisation	29 November 2005
Rev.2: sponsor's change of address	31 March 2011
Rev.3: withdrawal from the Community Register	4 June 2014
Disclaimer Please note that revisions to the Public Summary of Opinion are purely administrative updates. Therefore, the scientific content of the document reflects the outcome of the Committee for Orphan Medicinal Products (COMP) at the time of designation and is not updated after first publication.	

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in April 2014 at the end of the period of market exclusivity.

On 18 September 2001, orphan designation EU/3/01/055 was granted by the European Commission to Lipomed GmbH, Germany, for cladribine (subcutaneous use) for the treatment of indolent non-Hodgkin's lymphoma.

What is indolent non-Hodgkin's lymphoma?

Non-Hodgkin's lymphomas are a type of cancer of the lymphatic system. The lymphatic system is part of the immune system: the body's natural defence against infection and disease. It is a complex system made up of organs such as bone marrow (the spongy tissue inside the large bones in the body), the thymus and the spleen, and a network of lymph nodes throughout the body that are connected by lymphatic vessels. Normally, the proliferation of lymphatic cells takes place in a controlled manner but, in non-Hodgkin's lymphoma, this process gets out of control and the cells continue to divide, developing into a tumour. Lymphoma cells generally grow in lymph nodes. Sometimes the lymphoma cells spread from the original site to affect other lymph nodes and they may occasionally enter the bloodstream which carries them to various organs making the cancer spread. There are about 20 different types of non-Hodgkin's lymphoma. Indolent or low-grade (slow-growing)

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non-Hodgkin's lymphoma including hairy cell leukaemia, chronic lymphocytic leukaemia, grade I and II follicular lymphoma and lymphoplasmacytic lymphoma is characterised by a very slow growth of the cancer. Indolent non-Hodgkin's lymphoma is a serious and life-threatening condition.

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

At the time of designation, indolent non-Hodgkin's lymphoma affected 2.4 to 3.65 in 10,000 people in the European Union (EU). This was equivalent to a total of between 90,000 and 137,000 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?

Currently the first treatment is chemotherapy (using drugs to kill cancer cells). Radiotherapy (using high-dose x-rays or other high-energy rays to kill cancer cells) can be useful to treat specific areas. Interferon alpha is a protein normally produced by the body during viral infections, such as flu, and is used for the treatment of certain types of non-Hodgkin's lymphoma. There are currently several medicinal products authorised in the Community for treatment of indolent non-Hodgkin's lymphoma. Cladribine is currently marketed within the European Union. It is generally given by slow infusion into a vein (either for two hours per day or continuously). Cladribine injected under the skin (subcutaneous use) could be of potential significant benefit for the treatment of indolent non-Hodgkin's lymphoma. It might be as active as cladribine given through a vein. Because it is injected under the skin, it may offer a convenient way of giving cladribine and a shorter duration of treatment. These assumptions 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?

Cladribine (subcutaneous use) is purine nucleoside analogue. The purine nucleosides are part of the fundamental genetic material of cells (DNA). Cladribine (subcutaneous use) inhibits the synthesis of DNA and the DNA repair mechanism by competing with the natural purine nucleosides and thus inhibits growth of tumour cells.

What is the stage of development of this medicine?

At the time of submission of the application for orphan designation, several clinical trials in patients with indolent non-Hodgkin's lymphoma were completed and some were ongoing.

Cladribine (subcutaneous use) was registered in Switzerland for indolent non-Hodgkin's lymphoma at the time of submission. Orphan designation of cladribine (subcutaneous use) had not been granted in any country worldwide for non-Hodgkin's lymphoma at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 18 July 2001 recommending the granting of this designation.

[*]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.
At the time of designation, this represented a population of 375,500,000 (Eurostat 2000).

Update: Cladribine (subcutaneous use) (Litak) has been authorised in the EU since 14 April 2004 for treatment of hairy cell leukaemia.

More information on Litak can be found in the European public assessment report (EPAR) on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European Public Assessment Reports

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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	Cladribine (subcutaneous use)	Treatment of indolent Non-Hodgkin's lymphoma
Danish	Cladribin (subkutan anvendelse)	Behandling af indolent Non-Hodgkins lymfom
Dutch	Cladribine (Subcutaan gebruik)	Behandeling van indolent Non-Hodgkin-lymfoom
Finnish	Kladribiini (Ihon alle)	Alhaisen asteen Non-Hodgkinin lymfooman hoito
French	Cladribine (Voie sous-cutanée)	Traitement des lymphomes non-Hodgkiniens indolents
German	Cladribin (subkutane Anwendung)	Behandlung von Non-Hodgkin Lymphomen von niedrigem Malignitätsgrad
Greek	Κλαδριβίνη (Υποδορια χρηση)	Θεραπεία χαμηλού βαθμού Non-Hodgkin's λεμφώματος
Italian	Cladribina (Uso sottocutaneo)	Trattamento del linfoma non Hodgkin indolente
Portuguese	Cladribina (via subcutânea)	Tratamento do linfoma não-Hodgkin indolente
Spanish	Cladribina (Vía subcutánea)	Tratamiento del linfoma no Hodgkin indolente
Swedish	Cladribin (Subkutan användning)	Behandling av indolent non-Hodgkins lymfom

[1] At the time of designation