

12 September 2013  
EMA/COMP/439251/2013  
Committee for Orphan Medicinal Products

## Public summary of opinion on orphan designation Cladribine for the treatment of mastocytosis

On 5 August 2013, orphan designation (EU/3/13/1182) was granted by the European Commission to Lipomed GmbH, Germany, for cladribine for the treatment of mastocytosis.

### What is mastocytosis?

Mastocytosis is a group of disorders in which there are too many mast cells, a type of white blood cell, in various organs in the body. These cells release large amounts of histamine and other chemicals into the blood, causing symptoms such as a skin rash, itchy skin and hot flushes.

In children, the disorder usually only affects the skin ('cutaneous mastocytosis') and causes a red and itchy rash, which may disappear on its own. In some patients, mainly adults, the disorder progresses into 'systemic mastocytosis', in which the mast cells become aggressive tumours that infiltrate organs, such as the intestine, the liver, the spleen and the bone marrow. This causes various symptoms such as palpitations and fainting, bone pain, tiredness, weight loss, diarrhoea, nausea (feeling sick), vomiting and stomach ache.

Mastocytosis is a condition that is debilitating in the long term and may be life threatening in those patients who develop the systemic form of the disorder.

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

At the time of designation, mastocytosis affected approximately 2.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 132,000 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?

At the time of designation, only treatments aimed at relieving the symptoms of mastocytosis were available. They included antihistamines to block the action of histamine produced by the mast cells.

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\*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. This represents a population of 509,000,000 (Eurostat 2013).

The sponsor has provided sufficient information to show that cladribine might be of significant benefit for patients with mastocytosis because it is expected to act on mast cells, while the currently authorised treatments only help to relieve symptoms. Good responses to treatment with cladribine have been seen in published studies, including a slowing down of disease progression. These assumptions 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?**

Cladribine is a known cytotoxic, a medicine that kills cells that are dividing, such as cancer cells. It belongs to the group of anticancer medicines called 'antimetabolites'. These medicines interfere with DNA production necessary for cell growth by taking the place of one of the substances (metabolites) used by the body in the production of the DNA. In mastocytosis, cladribine is expected to enter mast cells and work in the same way, interfering with DNA production, eventually killing the cell. This is expected to help reduce the number of mast cells, and thereby reduce the symptoms of mastocytosis.

Cladribine has been in use in anticancer medicines since the 1980s.

## **What is the stage of development of this medicine?**

At the time of submission of the application for orphan designation, no preclinical studies in experimental models had been performed. However, the sponsor provided results of clinical studies from the published literature.

At the time of submission, no clinical trials with cladribine in patients with mastocytosis had been started.

At the time of submission, cladribine was authorised in the EU for hairy cell leukaemia. At the time of submission, it was not authorised anywhere in the EU for mastocytosis 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 11 July 2013 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<sup>1</sup>, Norwegian and Icelandic**

Language	Active ingredient	Indication
English	Cladribine	Treatment of mastocytosis
Bulgarian	Кладрибин	Лечение на мастоцитоза
Croatian	Kladribin	Liječenje mastocitoze
Czech	Kladribin	Léčba mastocytózy
Danish	Cladribine	Behandling af mastocytose
Dutch	Cladribine	Behandeling van mastocytose
Estonian	Kladribiin	Mastotsüoosi ravi
Finnish	Kladribiini	Mastosytoosin hoito
French	Cladribine	Traitemennt de la mastocytose
German	Cladribin	Behandlung der Mastozytose
Greek	Κλαδριβίνη	Θεραπεία της μαστοκυττάρωσης
Hungarian	Kladribin	Mastocytosis kezelése
Italian	Cladribina	Trattamento della mastocitosi
Latvian	Kladribīns	Mastocitozes ārstēšana
Lithuanian	Kladribinas	Mastocitozés gydymas
Maltese	Cladribine	Kura tal-mastocitosi
Polish	Kladrybina	Leczenie mastocytózy
Portuguese	Cladribina	Tratamento da mastocitose
Romanian	Cladribină	Tratamentul mastocitozei
Slovak	Kladribín	Liečba mastocytózy
Slovenian	Kladribin	Zdravljenje dermatofibrosarkoma protuberans
Spanish	Cladribina	Tratamiento de la mastocitosis
Swedish	Kladribin	Bahandling av mastocytos
Norwegian	Kladribin	Behandling av mastocytose
Icelandic	Kladribin	Meðferð mastócytosis

<sup>1</sup> At the time of designation