5 March 2015
EMA/COMP/60984/2012 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Chlormethine for the treatment of cutaneous T-cell lymphoma

First publication	3 July 2012
Rev.1: transfer of sponsorship	26 June 2014
Rev.2: sponsor's change of address	5 March 2015

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.

On 22 May 2012, orphan designation (EU/3/12/963) was granted by the European Commission to TMC Pharma Services Ltd, United Kingdom, for chlormethine for the treatment of cutaneous T-cell lymphoma.

The sponsorship was transferred to Actelion Registration Limited, United Kingdom, in April 2014.

What is cutaneous T-cell lymphoma?

Cutaneous T-cell lymphoma (CTCL) is a cancer of the lymphatic system, a network of vessels that transport fluid from tissues through the lymph nodes and into the bloodstream. In CTCL there is uncontrolled growth of the T lymphocytes (T cells), a type of white blood cell found in the lymphatic system. The cancerous T cells appear in the skin, causing lesions (rashes, plaques and tumours) which can be itchy and painful.

CTCL usually happens in people aged between 40 and 60 years. In many cases, the disease is long lasting, with survival for more than 10 to 20 years being common. However, it can be a serious and life-threatening disease because it can develop into more aggressive forms of cancer. The condition may have a large impact on quality of life, particularly because the skin lesions can cause disfigurement.

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

At the time of designation, CTCL affected less than 2.6 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 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, several products were authorised for the treatment of CTCL within the EU. Treatments for CTCL can be divided into topical (applied to the skin) and systemic (affecting the whole body):

- topical treatments include topical corticosteroids, the topical anticancer medicine carmustine, ultraviolet light and X-rays;
- systemic treatments include cytotoxic medicines (medicines that kill cells that are dividing, such as cancer cells), interferon alfa (a medicine that helps the immune system to fight against the cancer cells) and photopheresis. Photopheresis is a technique in which blood is temporarily removed from the body to be treated with ultraviolet light. A substance is first added to the blood, that, when exposed to ultraviolet light, becomes activated and able to damage the T cells. When these damaged cells are re-introduced in the patient's blood, they trigger the immune system to attack and kill cancerous T cells in the body.

The sponsor has provided sufficient information to show that chlormethine might be of significant benefit for patients with CTCL because it works in a different way to existing treatments and, when used in the early stages of the disease, it may improve the treatment options for patients with this condition when compared with other topical treatments. 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?

Chlormethine is a well-known anticancer medicine that belongs to the group 'alkylating agents'. Alkylating agents kill cancer cells by attaching to their DNA while they are reproducing, that stops cell division. As a result, cancer cells cannot divide and this slows down the growth of tumours. For the treatment of CTCL, chlormethine is expected to be applied directly onto the skin in the form of a gel.

What is the stage of development of this medicine?

The effects of chlormethine have been evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials with chlormethine in patients with CTCL had finished.

At the time of submission, chlormethine was not authorised anywhere in the EU for CTCL. Orphan designation of chlormethine had been granted in the United States of America for CTCL.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 11 January 2012 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 (EU 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 509,000,000 (Eurostat 2012).

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	Chlormethine	Treatment of cutaneous T-cell lymphoma
Bulgarian	Хлорметин	Лечение на кожен Т-клетъчен лимфом
Croatian	Klormetin	Liječenje kožnog limfoma T-stanica
Czech	Chlormethin	Léčba kožního T-lymfomu
Danish	Chlormethin	Behandling af kutant T-celle-lymfom
Dutch	Chloormethine	Behandeling van cutaan T-cel-lymfoom
Estonian	Kloormetiin	Kutaanse T-rakulise lümfoomi ravi
Finnish	Kloorimetiini	Ihon T-solulymfooman hoito
French	Chlorméthine	Traitement des lymphomes cutanés à cellules T
German	Chlormethin	Behandlung von kutanem T-Zell- Lymphom
Greek	Χλωρομεθίνη	Θεραπεία του δερματικού λεμφώματος Τ-κυττάρων
Hungarian	Klórmetin	T-sejtes cutan lymphoma kezelése
Italian	Cloremina	Trattamento del linfoma cutaneo a cellule T
Latvian	Hlormetīns	Ādas T-šūnu limfomas ārstēšana
Lithuanian	Chlormetinas	Odos T ląstelių limfomos gydymas
Maltese	Chlormethine	Kura tal-limfoma taċ-ċelluli tat-tip T tal-ġilda
Polish	Chlormetyna	Leczenie chłoniaka skórnego T-komórkowego
Portuguese	Clorometina	Tratamento do linfoma cutâneo de células T
Romanian	Clormetină	Tratamentul limfomului cutanat cu celule T
Slovak	Chlórmetín	Liečba kutánneho T-bunkového lymfómu
Slovenian	Klormetin	Zdravljenje kožnega T-celičnega limfoma
Spanish	Clormetina	Tratamiento del linfoma cutáneo de células T
Swedish	Klormetin	Behandling av kutant T-cellslymfom
Norwegian	Klormetin	Behandling av kutant T-cellelymfom
Icelandic	Klórmetín	Meðferð T-eitilfrumukrabbameins í húð

[1] At the time of designation