



European Medicines Agency  
Pre-authorisation Evaluation of Medicines for Human Use

**Document Date:** London, 12 December 2007  
Doc.Ref.: EMEA/COMP/465553/2006

## **COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS**

### **PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF forodesine hydrochloride for the treatment of cutaneous T cell lymphoma**

On 29 January 2007, orphan designation (EU/3/06/428) was granted by the European Commission to Napp Pharmaceuticals Research Limited, United Kingdom, for forodesine hydrochloride for the treatment of cutaneous T cell lymphoma.

The name of the sponsor changed to Mundipharma Research Limited in 2007.

#### **What is cutaneous T cell lymphoma?**

Cutaneous T cell lymphoma is a type of cancer of the lymphatic system. The lymphatic system is part of the body's immune system and helps fighting infections. It is a complex system made up of organs such as the bone marrow, the thymus (a gland behind the breast bone), the spleen (an organ in the abdomen, near the stomach), and the lymph nodes (or lymph glands, located throughout the body), which are connected by a network of tiny lymphatic vessels; in addition, there are isolated lymphatic cells in most tissues of the body, including the skin. One of the main cells that make up the lymphatic tissue is the lymphocyte, which belongs to the group of white blood cells. There are two main types of lymphocytes: B-lymphocytes (B cells) and T-lymphocytes (T cells). Cutaneous T-cell lymphoma is characterised by uncontrolled growth of the T-lymphocytes, mainly affecting the skin. This condition most often occurs in people aged between 40 and 60. Although in many cases the condition is chronic and survival for more than 10-20 years is common, cutaneous T-cell lymphoma can be a serious and life-threatening condition.

#### **What are the methods of treatment available?**

Current treatment for cutaneous T-cell lymphoma can be divided into local treatments and systemic (given to the whole body) treatments. Local treatments include medicines applied to the skin, therapies using light of a particular wavelength (ultraviolet light) and x-rays. Systemic treatments included medicines such as glucocorticoids (a group of medicines that are similar to cortisone), cytotoxic agents (medicines that kill cells), interferon-alfa (a compound that can help the immune system to fight against the cancer cells) and photopheresis (blood is temporarily removed from the body and exposed to ultraviolet light, after being treated with a sensitizing compound). Several products were authorised for the treatment of cutaneous T cell lymphoma within the Community at the time of submission of the application for orphan drug designation. Forodesine might be of potential significant benefit for the treatment of cutaneous T-cell lymphoma because it is expected to act in a different way than other available medicines. This assumption will have to be confirmed at the time of marketing authorisation. This will be necessary to maintain the orphan status of forodesine.

7 Westferry Circus, Canary Wharf, London, E14 4HB, UK  
Tel. (44-20) 74 18 84 00 Fax (44-20) 75 23 70 40

E-mail: [orphandrugs@emea.europa.eu](mailto:orphandrugs@emea.europa.eu) <http://www.emea.europa.eu>

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

According to the information provided by the sponsor, cutaneous T cell lymphoma was considered to affect about 66,000 persons in the European Union.

**How is this medicinal product expected to act?**

Forodesine hydrochloride is a substance acting specifically on an enzyme called purine nucleoside phosphorylase (PNP). Enzymes are proteins produced by the cells of the body; they speed up the conversion of certain substances into other substances. Forodesine is an inhibitor of PNP. Reducing the activity of this enzyme may cause the accumulation of a substance, called dGTP, which is toxic to these cells if present in high concentrations. Human lymphocytes, particularly malignant T- and B-cells may be susceptible to forodesine, because they have a relatively high activity of another enzyme, dCK, which actually generates dGTP, and a low activity of an opposing enzyme (5' nucleotidase), which instead would prevent dGTP accumulation. Since cutaneous T cell lymphoma is caused by the uncontrolled growth of the malignant T-cells lymphocytes, forodesine might help in slowing down or stopping this uncontrolled cell growth.

**What is the stage of development of this medicinal product?**

The effects of forodesine are being evaluated in preliminary clinical studies in humans; one study has been completed and one is ongoing.

Forodesine hydrochloride was not authorised anywhere worldwide for the treatment of cutaneous T cell lymphoma, at the time of submission of the request for orphan drug designation.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 6 December 2006 a positive opinion recommending the grant of the above-mentioned designation.

---

Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

**For more information:**

Sponsor's contact details:

Mundipharma Research Limited

Cambridge Science Park

Milton Road

Cambridge

Cambridgeshire CB4 0WG

United Kingdom

Telephone: +44 1223 424 900

Telefax: +44 1223 426 054

E-mail: [medicalinformationuk@napp.co.uk](mailto:medicalinformationuk@napp.co.uk)

---

\* Disclaimer: For the purpose of the designation, the number of patients affected by the condition is estimated and assessed based on data from the European Union (EU 25), Norway, Iceland and Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

Patients' associations contact points:

**Leukaemia Care**

2 Shrubbery Avenue

Worcester

WR1 1QH

United Kingdom

0800 169 6680 (freephone for UK residents)

Telephone: +44 19 05 33 00 03 / +44 84 57 67 32 03

Telefax: +44 19 05 33 00 90

E-mail: [enquiries@leukaemiaCARE.org.uk](mailto:enquiries@leukaemiaCARE.org.uk)

**DLH : Deutsche Leukämie- und Lymphom-Hilfe e.V.**

Thomas-Mann-Straße 40

53111 Bonn

Germany

Telephone: +49 22 83 90 440

Telefax: +49 22 83 90 44 22

E-mail: [info@leukaemie-hilfe.de](mailto:info@leukaemie-hilfe.de)

**Associazione Italiana contro le Leucemie-linfomi e mieloma ONLUS**

Via Ravenna 34

00161 Roma

Italy

Telephone: +39 06 44 03 763

Telefax: +39 06 44 04 226

E-mail: [ail@ail.it](mailto:ail@ail.it)

**Translations of the active ingredient and indication in all EU languages  
and Norwegian and Icelandic**

<b>Language</b>	<b>Active Ingredient</b>	<b>Indication</b>
English	Forodesine hydrochloride	Treatment of cutaneous T-cell lymphoma
Bulgarian	Фородезин хидрохлорид	Лечение на кожен Т-клетъчен лимфом
Czech	Forodesin hydrochlorid	Léčba kožního T-lymfomu
Danish	Forodesin hydroklorid	Behandling af kutant T-celle-lymfom
Dutch	Forodesinehydrochloride	Behandeling van cutaan T-cel-lymfoom
Estonian	Forodesiinihüdrokloriid	Kutaanse T-rakulise lümfoomi ravi
Finnish	Forodesiinihydrokloridi	Ihon T-solulymfooman hoito
French	Chlorhydrate de forodesine	Traitement des lymphomes cutanés à cellules T
German	Forodesinhydrochlorid	Behandlung von kutanem T-Zell- Lymphom
Greek	Υδροχλωρική Φοροδεσίνη	Θεραπεία του δερματικού λεμφώματος Τα κυττάρων
Hungarian	Forodezin -hidroklorid	T-sejtes cutan lymphoma kezelése
Italian	Forodesina cloridrato	Trattamento del linfoma cutaneo a cellule T
Latvian	Forodesīns hidrohlorīds	Ādas T-šūnu limfomas ārstēšana
Lithuanian	Forodesino hidrochloridas	Odos T ląstelių limfomos gydymas
Polish	Forodezyny chlorowodorek	Leczenie chłoniaka skórniego T-komórkowego
Portuguese	Cloridrato de forodesina	Tratamento do linfoma cutâneo de células T
Romanian	Clorhidrat de forodezină	Tratamentul limfomului cutanat cu celule T
Slovak	Forodezíniumchlorid	Liečba kutánneho T-bunkového lymfómu
Slovenian	Forodesin hidroklorid	Zdravljenje kožnega T-celičnega limfoma
Spanish	Forodesina clorhidrato	Tratamiento del linfoma cutáneo de células T
Swedish	Forodesinhydroklorid	Behandling av kutant T-cellslymfom
Norwegian	Forodesinhydroklorid	Behandling av kutant T-cellelymfom
Icelandic	Fóródesín hýdróklóríð	Meðferð T-eitilfrumukrabbameins í húð