20 June 2011
EMA/COMP/122781/2005 Rev.4
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

(E)-(1S,4S,10S,21R)-7-[(Z)-ethylidene]-4,21-diisopropyl-2-oxa-12,13-dithia-5,8,20,23- tetraazabicyclo[8.7.6]tricos-16-ene-3,6,9,19,22-pentone for the for the treatment of cutaneous T cell lymphoma

On 27 May 2005, orphan designation (EU/3/05/279) was granted by the European Commission to The Matthews Consultancy Ltd, United Kingdom, for (E)-(1S,4S,10S,21R)-7-[(Z)-ethylidene]-4,21-diisopropyl-2-oxa-12,13-dithia-5,8,20,23-tetraazabicyclo[8.7.6]tricos-16-ene-3,6,9,19,22-pentone (depsipeptide) for the treatment of cutaneous T cell lymphoma.

The sponsorship was transferred to Gloucester Pharmaceuticals Limited, United Kingdom, in October 2008 and to Celgene Europe Limited, United Kingdom, in September 2010.

What is the treatment of 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. There are two main types of cells, which make up the lymphatic tissue. These cells are called lymphocytes and belong to the group of white blood cells. The two types are called B lymphocytes (B cells) and T lymphocytes (T cells). Most lymphocytes start growing in the bone marrow. The T cells go from the bone marrow to the thymus where they continue to mature. Cutaneous T-cell lymphoma is a cancer of the T-lymphocytes which mainly affects the skin and most often occurs in people aged between 40 and 60. It is caused by the uncontrolled growth of the T-cells. Cutaneous T-cell lymphoma is a serious and life-threatening.

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

At the time of designation, cutaneous T-cell lymphoma affected not more than 1 in 10,000 people in the European Union (EU)*. This is equivalent to a total of 46,000 people, and is below the threshold for

*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 25), Norway, Iceland and Liechtenstein. This represents a population of 459,700,000 (Eurostat 2004).

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orphan designation, which is 5 people in 10,000. This is based on the information provided by the sponsor and knowledge of the Committee for Orphan Medicinal Products (COMP).

What treatments are available?

Current treatment for cutaneous T-cell lymphoma can be divided into local and systemic 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 glucocorticosteroids (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 (white blood cells are modified by exposure to ultraviolet light). 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. Depsipeptide 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.

How is this medicine expected to work?

Enzymes are proteins produced by the cells of the body that speed up the conversion of certain substances into other substances. Depsipeptide appears to inhibit or reduce the activity of an enzyme, called histone deacetylase, which is important for cells growth as it provides the cell with basic components of the genetic material (DNA). As these proteins are no more available to form new genetic material, this might lead to the arrest of cell growth. Since cutaneous T-cell lymphoma is caused by the uncontrolled growth of the T-cells, depsipeptide might help in slowing down or stopping this uncontrolled cell growth.

What is the stage of development of this medicine?

The effects of depsipeptide were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with cutaneous T cell lymphoma were ongoing.

Depsipeptide was not authorised anywhere worldwide for the treatment of cutaneous T-cell lymphoma, at the time of submission. Orphan designation of depsipeptide was granted in the United States for the treatment of cutaneous T cell lymphoma.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 7 April 2005 recommending the granting of this designation.

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	(E)-(1S,4S,10S,21R)-7-[(Z)-ethylidene]-4,21-diisopropyl-2-oxa-12,13-dithia-5,8,20,23-tetraazabicyclo[8.7.6]tricos-16-ene-3,6,9,19,22-pentone	Treatment of cutaneous T-cell lymphoma
Bulgarian	(E)-(1S,4S,10S,21R)-7-[(Z)-етилиден]-4,21-диизопропил-2-окса-12,13-дитиа-5,8,20,23-тетраазабицикло[8.7.6] трикос-16-ен-3,6,9,19,22-пентон	Лечение на кожен Т-клетъчен лимфом
Czech	(E)-(1S,4S,10S,21R)-7-[(Z)-etylidén]-4,21-diizopropyl-2-oxo-12,13-ditio-5,8,20,23-tetraazabicyklo[8.7.6]tricos-16-én-3,6,9,19,22-pentone	Léčba kožního T-lymfomu
Danish	(E)-(1S,4S,10S,21R)-7-[(Z)-ethyliden]-4,21-diisopropyl-2-oxa-12,13-dithia-5,8,20,23-tetraazabicyclo[8.7.6]tricos-16-en-3,6,9,19,22-penton	Behandling af kutant T-celle-lymfom
Dutch	(E)-(1S,4S,10S,21R)-7-[(Z)-ethylideen]-4,21-diisopropyl-2-oxa-12,13-dithia-5,8,20,23-tetraazabicyclo[8.7.6]tricos-16-een-3,6,9,19,22-pentone	Behandeling van cutaan T-cel-lymfoom
Estonian	(E)-(1S,4S,10S,21R)-7-[(Z)-etülideen]-4,21-diisopropüül-2-oksa-12,13-ditia-5,8,20,23-tetraasabitsüklo[8.7.6]trikos-16-een-3,6,9,19,22-pentoon	Kutaanse T-rakulise lümfoomi ravi
Finnish	(E)-(1S,4S,10S,21R)-7-[(Z)-etyylideeni]-4,21-di-isopropyyli-2-oksa-12,13-ditia-5,8,20,23- tetra-atsabisyklo[8.7.6]trikos-16-eeni-3,6,9,19,22-pentoni	Ihon T-solulymfooman hoito
French	(E)-(1S,4S,10S,21R)-7-[(Z)-éthylidène]-4,21-diisopropyl-2-oxa-12,13-dithia-5,8,20,23-tétraazabicyclo[8.7.6]tricos-16-ène-3,6,9,19,22-pentone	Traitement des lymphomes cutanés à cellules T
German	(E)-(1S,4S,10S,21R)-7-[(Z)-ethyliden]-4,21-diisopropyl-2-oxa-12,13-dithia-5,8,20,23-tetraazabicyclo[8.7.6]tricos-16-en-3,6,9,19,22-penton	Behandlung von kutanem T-Zell-Lymphom
Greek	(E)-(1S,4S,10S,21R)-7-[(Z)-αιθυλιδενο]-4,21-διισοπροπυλ-2-οξα-12,13-διθεια-5,8,20,23-τετρααζαδικυκλο[8.7.6]τρικοσ-16-ενε-3,6,9,19,22-πεντόνη	Θεραπεία του δερματικού λεμφώματος Τα κυττάρων

[1] At the time of transfer of sponsorship

Language	Active Ingredient	Indication
Hungarian	(E)-(1S,4S,10S,21R)-7-[(Z)-etilidén]-4,21-diizopropil-2-oxa-12,13-ditia-5,8,20,23-tetraazabiciklo[8.7.6]trikoz-16-én-3,6,9,19,22-penton	T-sejtes cutan lymphoma kezelése
Italian	(E)-(1S,4S,10S,21R)-7-[(Z)-etilidene]-4,21-diisopropil-2-ossa-12,13-ditia-5,8,20,23-tetraazabiciclo[8.7.6]tricos-16-ene-3,6,9,19,22-pentone	Trattamento del linfoma cutaneo a cellule T
Latvian	(E)-(1S,4S,10S,21R)-7-[(Z)-etilidēn]-4,21-diizopropil-2-oksa-12,13-ditia-5,8,20,23-tetraazabiciklo[8.7.6]trikoz-16-ēn-3,6,9,19,22-pentons	Ādas T-šūnu limfomas ārstēšana
Lithuanian	(E)-(1S,4S,10S,21R)-7-[(Z)-etilideno]-4,21-diizopropil-2-oksa-12,13-ditia-5,8,20,23-tetraazabiciklo[8.7.6]trikoz-16-en-3,6,9,19,22-pentonas	Odos T ląstelių limfomos gydymas
Maltese	(E)-(1S,4S,10S,21R)-7-[(Z)-ethylidene]-4,21-diisopropyl-2-oxa-12,13-dithia-5,8,20,23-tetraazabicyclo[8.7.6]tricos-16-ene-3,6,9,19,22-pentone	Kura tal-limfoma taċ-ċelluli tat-tip T tal-ġilda
Polish	*(E)*-(1S,4S,10S,21R)-7-[(Z)-etylideno]-4,21-diizopropylo-2-oksa-12,13-ditia-5,8,20,23-tetraazobicyklo[8.7.6]trikoz-16-eno-3,6,9,19,22-penton	Leczenie chłoniaka skórnego T-komórkowego
Portuguese	(E)-(1S,4S,10S,21R)-7-[(Z)-etilideno]-4,21-diisopropil-2-oxa-12,13-ditia-5,8,20,23-tetraazabiciclo[8.7.6]tricos-16-eno-3,6,9,19,22-pentona	Tratamento do linfoma cutâneo de células T
Romanian	(E)-(1S,4S,10S,21R)-7-[(Z)-etilidenă]-4,21-diisopropil-2-oxa-12,13-ditia-5,8,20,23-tetraazabiciclo[8.7.6]tricos-16-ene-3,6,9,19,22-pentonă	Tratamentul limfomului cutanat cu celule T
Slovak	(E)-(1S,4S,10S,21R)-7-[(Z)-etylidén]-4,21-diizopropyl-2-oxo-12,13-ditio-5,8,20,23-tetraazabicyklo[8.7.6]tricos-16-én-3,6,9,19,22-penton	Liečba kutánneho T-bunkového lymfómu
Slovenian	(E)-(1S,4S,10S,21R)-7-[(Z)-etiliden]-4,21-diizopropil-2-oksa-12,13-ditia-5,8,20,23-tetraazabiciklo[8.7.6]trikoz-16-en-3,6,9,19,22-penton	Zdravljenje kožnega T-celičnega limfoma
Spanish	(E)-(1S,4S,10S,21R)-7-[(Z)-etiliden]-4,21-diisopropil-2-oxa-12,13-ditia-5,8,20,23-tetraazabiciclo[8.7.6]tricos-16-eno-3,6,9,19,22-pentona	Tratamiento del linfoma cutáneo de células T

Language	Active Ingredient	Indication
Swedish	(E)-(1S,4S,10S,21R)-7-[(Z)-etyliden]-4,21-diisopropyl-2-oxa-12,13-ditia-5,8,20,23-tetraazabicyklo[8.7.6]tricos-16-ene-3,6,9,19,22-penton	Behandling av kutant T-cellslymfom
Norwegian	(E)-(1S,4S,10S,21R)-7-[(Z)-etyliden]-4,21-diisopropyl-2-oksa-12,13-ditia-5,8,20,23-tetraazabisyklo[8.7.6]trikos-16-en-3,6,9,19,22-penton	Behandling av kutant T-cellelymfom
Icelandic	(E)-(1S,4S,10S,21R)-7-[(Z)-etýlíden]-4,21-tvíísóprópýl-2-oxa-12,13-tvítía-5,8,20,23-tetraazatvísýkló[8.7.6]tríkós-16-ene-3,6,9,19,22-pentón	Meðferð T-eitilfrumukrabbameins í húð