4 October 2013
EMA/COMP/132163/2006 Rev.2
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Methoxsalen for the treatment of Graft-versus-Host disease

First publication	24 April 2009
Rev.1: sponsor's change of address	9 November 2011
Rev.2: transfer of sponsorship	4 October 2013

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 2006, orphan designation (EU/3/06/374) was granted by the European Commission to Johnson & Johnson Medical Ltd, United Kingdom, for methoxsalen for the treatment of Graft-versus-Host disease.

The sponsorship was transferred to Therakos (UK) Limited, United Kingdom, in September 2013.

What is Graft-versus-Host disease?

Graft-versus-host disease (GvHD) is a complication of bone marrow transplant. The bone marrow is the spongy tissue inside the large bones in the body that makes blood cells and platelets (components that help the blood to clot). Bone marrow transplants are used for diseases such as leukaemia or multiple myeloma (cancer of the white blood cells).

In GvHD, the cells in the transplanted bone marrow react against the patients' organs, such as the stomach, gut, skin and liver, leading to organ damage. GvHD may happen in the short term, or later after transplantation, in which case a wider range of organs can be involved. GvHD is a serious, life-threatening disease.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7040
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

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

At the time of designation, Graft-versus-Host disease affected less than 1 in 10,000 people in the European Union (EU). This was equivalent to a total of fewer than 47,000 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?

The methods of treatment authorised for GvHD in the Community, at the time of submission of the application for orphan designation, included of anti-T cell immunoglobulins (proteins called antibodies that block the effect of T cells of the immune system) and ciclosporin (an immunosuppressant). In addition, systemic corticosteroids (synthetic steroid hormones administered so that they can affect the body as a whole) are usually administered at high doses. Other therapies include various immunosuppressants (drugs that inhibit the immune response). Satisfactory argumentation has been submitted by the sponsor to justify the assumption that the medicinal product might be of potential significant benefit for the treatment of GvHD, particularly in terms of improved efficacy and limiting drug toxicity (steroid sparing effect).

How is this medicine expected to work?

Methoxsalen is pharmacologically active only when exposed to ultraviolet light and it has been proposed for use in conjunction with a method called extracorporeal photopheresis (ECP) for treatment of GvHD. Briefly, the ECP procedure involves chemical treatment of graft cells (cells that will be inserted to the body) with a drug that is activated by light (e.g. methoxsalen), exposing this mix to ultraviolet light and returned to the patient. Methoxsalen is thought to bind to the genetic material (DNA helix) of graft-reactive cells and block their division and growth. The exact mechanisms by which ECP and methoxsalen can lead to improvement in GvHD have not been fully clarified. ECP may be involved in enhancing the apoptotic process (a form of programmed cell death) which might destroy graft-reactive T cells. Another possibility is that the photoactivated methoxsalen might trigger the induction of specific T cells able to suppress the immune response against the host tissues.

What is the stage of development of this medicine?

The effects of methoxsalen were evaluated in experimental models.

At the time of submission of the application for orphan designation, clinical trials in patients with GvHD were ongoing.

Methoxsalen was not authorised anywhere worldwide for Graft versus Host Disease, at the time of submission. Orphan designation of methoxsalen was granted in the United States for Graft-versus-Host disease.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 5 April 2006 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 25), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 468,900,000 (Eurostat 2006).

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:

Therakos (UK) Limited
West Forest Gate
Wellington Road
Wokingham
Berkshire RG40 2AT
United Kingdom
Tel.: +44 118 315 0805
http://www.therakos.co.uk/home/contact-us

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	Methoxsalen	Treatment of Graft-versus-Host disease
Bulgarian	Метоксален	Лечение на реакция на присадката срещу приемателя
Croatian	Metoksalen	Liječenje reakcije presatka protiv primatelja
Czech	Methoxsalenu	Léčba reakce štěpu proti hostiteli
Danish	Methoxsalen	Behandling af graft versus host reaktion
Dutch	Methoxsaleen	Behandeling van graft versus host ziekte
Estonian	Metoksaleen	*Graft versus host* haiguse ravi
Finnish	Metoksaleenia	Käänteishyljintäreaktion hoito
French	Méthoxsalène	Traitement de la réaction du greffon contre l'hôte
German	Methoxsalen	Behandlung der Graft-versus-Host-Reaktion
Greek	Μεθοξαλένη	Θεραπεία της αντίδρασης του μοσχεύματος
Hungarian	Methoxsalen	Graft-versus-host betegség kezelése
Italian	Metossalene	Trattamento della reazione del trapianto contro l'ospite
Latvian	Metoksalēns	Saimnieka-transplantāta slimības ārstēšana
Lithuanian	Metoksalenas	Transplantato atmetimo ligos gydymas
Maltese	Methoxsalen	Kura tal-marda tat-tessut għat-trapjant kontra dak li jirċievih
Polish	Metoksalen	Leczenie choroby przeszczep przeciw gospodarzowi
Portuguese	Metoxsaleno	Tratamento da reacção do enxerto contra o hospedeiro
Romanian	Metoxalen	Tratamentul reacţiei grefei contra gazdei
Slovak	Metoxsalen	Liečba reakcie štepu proti hostiteľovi
Slovenian	Metoksalen	Zdravljenje bolezni presadka proti gostitelju
Spanish	Metoxaleno	Tratamiento de la enfermedad de injerto contra huésped
Swedish	Metoxalen	Behandling av graft-värd host reaktion
Norwegian	Metoksalen	Behandling av graft-versus-host -reaksjon
Icelandic	Metoxsalen	Til meðferðar á hýsilsótt

[1] At the time of transfer of sponsorship