



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Methoxsalen for the treatment of Graft-versus-Host disease

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.

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.

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 is equivalent to a total of fewer than 46,000 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

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



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.

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

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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 languages¹, Norwegian and Icelandic

Language	Active Ingredient	Indication
English	Methoxsalen	Treatment of Graft-versus-Host disease
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	<i>Graft versus host</i> 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
Polish	Metoksalen	Leczenie choroby przeszczep przeciw gospodarzowi
Portuguese	Metoxsaleno	Tratamento da reacção do enxerto contra o hospedeiro
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 designation