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Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Dimethyl fumarate for the treatment of bullous pemphigoid

On 14 July 2016, orphan designation (EU/3/16/1698) was granted by the European Commission to Immungenetics AG, Germany, for dimethyl fumarate for the treatment of bullous pemphigoid.

What is bullous pemphigoid?

Bullous pemphigoid is an autoimmune skin disease mainly seen in elderly people that is characterised by the development of widespread, extremely itchy blisters affecting the skin, and sometimes the inside of the mouth. 'Autoimmune' means that the disease is caused by the immune system attacking the body's own cells.

In bullous pemphigoid, the immune system produces antibodies that attack proteins in the skin that act as a 'glue' attaching the cells of the epidermis (the outer layer of the skin) to the dermis (lower layer of the skin). As a result skin layers separate from each other and inflammation develops, causing blisters that can turn into sores or crusts, and can become infected. In some cases these blisters can cover large areas of the skin.

Bullous pemphigoid is a long-term debilitating disease because of the long-term blistering, itching and skin damage which can lead to infection. Suppression of the immune system by the medicines needed to treat the condition can be life-threatening.

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

At the time of designation, bullous pemphigoid affected approximately 2.6 in 10,000 people in the European Union (EU). This was equivalent to a total of around 134,000 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).

[*]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 28), Norway, Iceland and Liechtenstein. This represents a population of 513,700,000 (Eurostat 2016).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

What treatments are available?

At the time of designation patients with bullous pemphigoid were treated with medicines to reduce inflammation, in particular corticosteroids. The corticosteroid prednisolone was authorised in some EU countries for the treatment of bullous pemphigoid. Patients were also given medicines to suppress the immune system, such as azathioprine, to allow lower doses of corticosteroids to be used.

The sponsor has provided sufficient information to show that dimethyl fumarate might be of significant benefit for patients with bullous pemphigoid. This is because early studies suggest that it can be used in patients whose condition does not respond to corticosteroids, or in whom corticosteroids cannot be used. 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?

Dimethyl fumarate is thought to work by activating a protein called 'Nrf2' that regulates certain 'antioxidant' genes involved in protecting cells from damage. Dimethyl fumarate has been shown to reduce inflammation and modulate the activity of the immune system. In patients with bullous pemphigoid, it is expected to reduce the inflammation in the layers under the skin, reducing blistering and helping to control the symptoms of the disease.

What is the stage of development of this medicine?

The effects of dimethyl fumarate have been evaluated in experimental models.

At the time of submission of the application for orphan designation, no clinical trials with dimethyl fumarate in patients with bullous pemphigoid had been started.

At the time of submission, dimethyl fumarate was authorised in the EU for the treatment of psoriasis and as the medicine Tecfidera for the treatment of multiple sclerosis. It was not authorised anywhere in the EU for bullous pemphigoid or designated as an orphan medicinal product elsewhere for this condition.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 16 June 2016 recommending the granting of this designation.

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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:

Contact details of the current sponsor for this orphan designation can be found on EMA website, on the medicine's rare disease designations page.

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	Dimethyl fumarate	Treatment of bullous pemphigoid
Bulgarian	Диметилфумарат	Лечение на булозен пемфигоид
Croatian	Dimetil fumarate	Liječenje buloznog pemfigoida
Czech	Dimethyl-fumarát	Léčba bulózního pemfigoidu
Danish	Dimethylfumarat	Behandling af bulløs pemfigoid
Dutch	Dimethylfumaraat	Behandeling van parapemphigus
Estonian	Dimetüülfumaraat	Põiendpemfigoidi ravi
Finnish	Dimetyylifumaraatti	Rakkulaisen pemfigoidin hoito
French	Fumarate de diméthyle	Traitement de la pemphigoïde bulleuse
German	Dimethylfumarat	Behandlung von bullösem Pemphigoid
Greek	φουμαρικό διμεθύλιο	Θεραπεία της πομφολυγώδους πεμφιγοειδούς
Hungarian	Dimetil-fumarát	Bullózus pemfigoid kezelése
Italian	Dimetilfumarato	Trattamento del pemfigoide bolloso
Latvian	Dimetilfumerāts	Bullozā pemfigoīda ārstēšana
Lithuanian	Dimetilfumaratas	Pūslinio pemfigoido gydymas
Maltese	Dimethyl fumarate	Kura tal-pemfigojde bl-infafet
Polish	Fumaran dimetylu	Leczenie pęcherzowego pemfigoidu
Portuguese	Fumarato de dimetilo	Tratamento do penfigóide bolhoso
Romanian	Dimetil fumarat	Tratamentul pemfigoidului bulos
Slovak	Dimetylfumarát	Liečba bulózneho pemfigoidu
Slovenian	Dimetil fumarat	Zdravljenje buloznega pemfigoida
Spanish	Dimetilfumarato	Tratamiento de penfigoide ampolloso
Swedish	Dimetylfumarat	Behandling av bullös pemfigoid
Norwegian	Dimetylfumarat	Behandling av bulløs pemfigoid
Icelandic	Dímetýl fúmarat	Meðferð á blöðrumyndandi pemfigus

[1] At the time of designation