14 October 2013
EMA/COMP/521235/2006 Rev.3
Committee for Orphan Medicinal Products

Public summary of opinion on orphan designation

Complement factor H for the treatment of atypical Haemolytic Uraemic Syndrome (aHUS) associated with an inherited abnormality of the complement system

First publication	18 July 2007
Rev.1: sponsor's name change	29 July 2008
Rev.2: withdrawal from the Community Register	18 June 2012
Rev.3: administrative update	14 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.

Please note that this product was withdrawn from the Community Register of designated orphan medicinal products in June 2012 on request of this sponsor.

On 26 January 2007, orphan designation (EU/3/06/425) was granted by the European Commission to Laboratoire français du Fractionnement et des Biotechnologies (LFB), France, for complement factor H for the treatment of atypical Haemolytic Uraemic Syndrome (aHUS) associated with an inherited abnormality of the complement system.

The sponsor's name changed to Laboratoire français du Fractionnement et des Biotechnologies (LFB) S.A. in April 2008.

What is atypical Haemolytic Uraemic Syndrome associated with an inherited abnormality of the complement system?

Haemolytic Uraemic Syndrome (HUS) is a disorder marked by kidney failure, haemolysis (destruction of red blood), thrombocytopoenia (platelet deficiency), coagulation defects, and variable nervous system symptoms. This disorder is most common in children, and typically occurs after a gastrointestinal infection, often one caused by a specific subtype of the bacterium *E.coli*. It has also

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

been associated with other gastrointestinal infections, including those caused by Shigella and Salmonella bacteria.

Its less frequent form, atypical HUS (a-HUS), has been associated with other conditions, such as some non-enteric infections or diseases of the immune system, and in some instances with inherited abnormalities of the complement system. It is the latter condition which is the subject of the orphan drug designation. The complement system is a group of proteins in the blood, which help the immune system (antibodies and immune cells) in fighting infections.

Atypical HUS associated with an inherited abnormality of the complement system can occur in both children and adults. Multiple members of one family may be affected. Due to an inherited (genetic) defect, the production of complement proteins is disrupted, resulting in a- HUS. A-Hus can be chronic, or recur at intervals (relapsing form).

The condition is life-threatening and chronically debilitating, in particular due to kidney failure and a high likelihood of kidney transplant rejection.

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

At the time of designation, atypical Haemolytic Uraemic Syndrome associated with an inherited abnormality of the complement system affected less than 0.1 in 10,000 people in the European Union (EU). This was equivalent to a total of around 5,000 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?

No satisfactory methods exist that were authorised at the time of application.

The current treatment is supportive. Transfusions of packed red cells and platelets are given as needed. Kidney dialysis may be indicated.

Plasmapheresis, also called plasma exchange (or passage of the blood plasma through a filter) may be performed, although its role is not completely clear. In plasmapheresis, the blood plasma (the portion that does not contain cells, but does contain antibodies) is removed and replaced with fresh (donated) plasma.

How is this medicine expected to work?

Complement factor H is a major regulator of the complement system. It is normally produced in the liver, and is present in the blood. In genetic abnormalities of the complement system, supplementation of purified complement factor H is thought to alleviate the disease, by restoring a normal capacity to regulate complement activity.

What is the stage of development of this medicine?

The evaluation of the effects of complement factor H in experimental models is on-going.

At the time of submission of the application for orphan designation, no clinical trials in patients with a-HUS associated with an inherited abnormality of the complement system were initiated.

*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 27), Norway, Iceland and Liechtenstein.
At the time of designation, this represented a population of 500,300,000 (Eurostat 2007).

Complement factor H was not authorised anywhere worldwide for a-HUS associated with an inherited abnormality of the complement system or designated as orphan medicinal product elsewhere for this condition, at the time of submission.

In accordance with Regulation (EC) No 141/2000 of 16 December 1999, the COMP adopted a positive opinion on 6 December 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

Sponsor's contact details:
Laboratoire français du Fractionnement et des Biotechnologies (LFB) S.A.
3 avenue des Tropiques
BP80097
91943 Courtaboeuf Cedex
France
Telephone: +33 1 69 82 70 10
Telefax: +33 1 69 07 19 03
E-mail: communication@lfb.fr

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	Complement factor H	Treatment of atypical Haemolytic Uraemic Syndrome (aHUS) associated with an inherited abnormality of the complement system
Bulgarian	Фактор H на комплемента	Лечение на атипичен хемолитичен уремичен синдром (аХУС) свързан с вродена аномалия на системата на комплемента
Czech	Komplementový faktor H	Léčba atypického hemolyticko-uremického syndromu (aHUS) spojeného s vrozenou abnormalitou v komplementovém systému
Danish	Komplementfaktor H	Behandling af atypisk hæmolytisk uræmisk syndrom (aHUS), der er forbundet med en nedarvet abnormalitet af komplementsystemet
Dutch	Complementfactor H	Behandeling van het atypisch hemolytisch-uremisch syndroom (aHUS) geassocieerd met erfelijke aandoening van het complementsysteem
Estonian	Komplemendi faktor H	Päriliku komplemendisüsteemi puudulikkusega seotud atüüpilise hemolüütilis-ureemilise sündroomi (aHUS) ravi
Finnish	Komplementin faktori H	Komplementtijärjestelmän perinnölliseen poikkeavuuteen liittyvän epätyypillisen hemolyyttis-ureemisen oireyhtymän (aHUS) hoito
French	Facteur H du Complément	Traitement du Syndrome Hémolytique Urémique atypique (SHUa) associé à une anomalie héréditaire du système du complément
German	Komplementfaktor-H	Behandlung des atypischen Hämolytisch-Urämischen Syndroms (aHUS), das in Zusammenhang mit einer erblichen Anomalie des Komplementsystems auftritt
Greek	Παράγων συμπληρώματος Η	Θεραπεία του Άτυπου Αιμολυτικού Ουραιμικού Σύνδρόμου (aHUS) που συνδέεται με κληρονομική ανωμαλία του συστήματος του συμπληρώματος
Hungarian	Komplement H faktor	Örökletes komplementrendszer abnormalitással összefüggő atípusos haemolyticus uraemiás szindróma
Italian	Fattore H del complemento	Trattamento della sindrome uremico-emolitica (SUE) atipica associata ad un'anomalia ereditaria del sistema del complemento

[1] At the time of designation

Language	Active ingredient	Indication
Latvian	Komplementa faktors H	Ar iedzimtu komplementa sistēmas anomāliju saistīta atipiska hemolītiska urēmiskā sindroma (aHUS) ārstēšana
Lithuanian	Komplemento faktorius H	Netipinio hemolizinio - ureminio sindromo (nHUS), susijusio su paveldimu komplemento sistemos pakitimu, gydymas
Polish	Czynnik H dopełniacza	Leczenie atypowego hemolitycznego zespołu mocznicowego (aHUS) w przebiegu dziedzicznej nieprawidłowości układu dopełniacza
Portuguese	Factor H do Complemento	Tratamento do Síndrome Hemolítico Urémico atípico (SHUa) associado a uma anomalia hereditária do sistema de complemento
Romanian	Factor H al complementului	Tratamentul sindromului hemolitic-uremic atipic asociat cu o anomalie ereditară a sistemului complementului
Slovak	Faktor komplementu H	Liečba atypického hemolyticko-uremického syndrómu (aHUS) spojeného s hereditárnou abnormalitou komplementového systému
Slovenian	Faktor H komplementa	Zdravljenje atipičnega hemolitičnega uremičnega sindroma (aHUS), povezanega z dedno nepravilnostjo komplementa
Spanish	Factor H del complemento	Tratamiento del síndrome urémico hemolítico atípico asociado a una anomalía hereditaria del sistema del complemento
Swedish	Komplementfaktor H	Behandling av atypiskt hemolytiskt uremiskt syndrom (aHUS) kopplat till en ärftlig felaktighet i komplementsystemet
Norwegian	Komplementfaktor H	Behandling av atypisk hemolytisk uremisk syndrom (atypisk HUS) forbundet med arvelig anomali i komplementsystemet
Icelandic	Magnaþáttur H	Meðferð við ódæmigerðu blóðlýsu-þvageitrunarheilkenni (aHUS) tengdu arfgengum afbrigðileika komplementkerfisins