



European Medicines Agency
Pre-authorisation Evaluation of Medicines for Human Use

Document Date: London, 29 July 2008
Doc.Ref.: EMEA/COMP/367733/2005 Rev.1

Please note that this product was withdrawn from the Community Register of designated Orphan Medicinal Products in March 2008 on request of the sponsor.

COMMITTEE FOR ORPHAN MEDICINAL PRODUCTS

PUBLIC SUMMARY OF POSITIVE OPINION FOR ORPHAN DESIGNATION OF

**human *Staphylococcus aureus* polyclonal immunoglobulin
and human *Staphylococcus epidermidis* polyclonal immunoglobulin
for the prevention of late onset sepsis in premature infants
of less than or equal to 32 weeks gestational age**

On 14 December 2005, orphan designation (EU/3/05/335) was granted by the European Commission to Omnicare Clinical Research, United Kingdom, for human *Staphylococcus aureus* polyclonal immunoglobulin and human *Staphylococcus epidermidis* polyclonal immunoglobulin for the prevention of late onset sepsis in premature infants of less than or equal to 32 weeks gestational age.

What is late onset sepsis in premature infants of less than or equal to 32 weeks gestational age?

Immunoglobulins are proteins produced by our body that help fighting infections. Newborns do not have the capacity to produce immunoglobulins themselves immediately after birth but have some immunoglobulins transferred from the mother during the last weeks of gestation. Premature babies, those born before the normal gestation duration (40 weeks), miss this period partially or completely and therefore they have a reduced amount of immunoglobulins or even lack them completely. For this reason they are more prone to suffer infections after birth as one of the natural defences of the body is not present. The risk of infection has been found to be particularly high for children born before or around 32 weeks of gestation. Late onset sepsis defines generalised infections that start 3 days after birth and in which the micro-organisms causing the infection can be identified from blood samples. Late onset sepsis in premature infants of less than 32 weeks gestational age is a life threatening condition as it increases the risk of death of premature babies.

What are the methods of prevention available?

Preventive measures against infections include adherence to the so-called universal precautions, such as limiting as much as possible any patient contact, using specialised hospital facilities for providing intensive nursing and medical care limited to premature babies (neonatal intensive care units), avoiding crowded intensive care units for premature babies, limiting the nurse-to-patient ratios, strict compliance with hand washing and very careful skin care of the premature babies. There are at present no products authorised for prevention of the condition.

What is the estimated number of patients at risk of developing the condition*?

Based on the information provided by the sponsor and previous knowledge of the Committee, the number of patients at risk of developing late onset sepsis in premature infants of less than or equal to

* 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 Lichtenstein. This represents a population of 459,700,000 (Eurostat 2004). This estimate is based on available information and calculations presented by the sponsor at the time of the application.

32 weeks gestational age was considered to be approximately 1.5 in 10,000 persons in the European Union, which, at the time of designation, corresponded to about 69,000 persons.

How is this medicinal product expected to act?

Staphylococcus aureus and *Staphylococcus epidermidis* are micro-organisms that are a normal component of the human flora, which are the microorganisms that normally live in areas of our body. However sometimes these micro-organisms can cause infections in human beings, particularly in patients with a compromised defence system (immunity) such as premature infants. Infections by *Staphylococcus aureus* and *Staphylococcus epidermidis* are amongst the most common causes of late onset sepsis in premature infants of less than 32 weeks gestational age. Human *Staphylococcus aureus* polyclonal immunoglobulin and human *Staphylococcus epidermidis* polyclonal immunoglobulin are immunoglobulins obtained from persons that have in their blood a very high content of immunoglobulin against both microorganisms. The administration of these immunoglobulins in premature babies would restore their defence system against these microorganisms. Therefore by replacing the missing immunoglobulins the product might protect the newborns against those infections.

What is the stage of development of this medicinal product?

At the time of submission of the application for orphan designation, clinical trials in premature babies of less than 32 weeks at risk of developing late onset sepsis were ongoing.

In the United States Orphan Drug status was granted for the reduction (prevention) of nosocomial bacteremia caused by *Staphylococci* in very low birth weight infants.

According to Regulation (EC) No 141/2000 of 16 December 1999, the Committee for Orphan Medicinal Products (COMP) adopted on 21 October 2005 a positive opinion recommending the grant of the above-mentioned designation.

Opinions on orphan medicinal products designations are based on the following cumulative criteria: (i) the seriousness of the condition, (ii) the existence or not of alternative methods of diagnosis, prevention or treatment and (iii) either the rarity of the condition (considered to affect not more than five in ten thousand persons in the Community) or the insufficient return of development investments.

Designated orphan medicinal products are still investigational products which were considered for designation on the basis of potential activity. An orphan designation is not a marketing authorisation. As a consequence, demonstration of the quality, safety and efficacy will be necessary before this product can be granted a marketing authorisation.

For more information:

Sponsor's contact details:
Omnicare Clinical Research
Wessex Business Centre
Bumpers Way
Bumpers Farm
Chippenham
Wiltshire SN14 6NQ
United Kingdom
Telephone: +44 12 49 44 42 12
Telefax: +44 12 49 44 41 89

Patients' association contact point:

BLISS (The premature baby charity)

68 South Lambeth Road

London SW8 1RL

Telephone: +44 20 78 20 94 71

Parent Support Helpline FREEPHONE for UK citizens 0500 618140

Telefax: +44 20 78 20 95 67

E-mail: information@bliss.org.uk

**Translations of the active ingredient and indication in all EU languages
and Norwegian and Icelandic**

Language	Active Ingredient	Indication
English	Human <i>Staphylococcus aureus</i> polyclonal immunoglobulin and human <i>Staphylococcus epidermidis</i> polyclonal immunoglobulin	Prevention of late onset sepsis in premature infants of less than or equal to 32 weeks of gestational age
Czech	Polyklonální imunoglobulin proti lidskému Zlatému a epidermálnímu stafylokoklu	Prevence pozdní sepse u kojenců narozených v 32. týdnu těhotenství či dříve
Danish	Humant polyklonalt immunoglobulin rettet mod <i>Staphylococcus aureus</i> og humant polyklonalt immunoglobulin rettet mod <i>Staphylococcus epidermidis</i>	Forebyggelse af sent indsettende sepsis hos præmature spædbørn født før eller i 32. gestationsuge
Dutch	Humaan polyklonaal immunoglobine gericht tegen <i>Staphylococcus aureus</i> en humaan polyklonaal immunoglobuline gericht tegen <i>Staphylococcus epidermidis</i>	Preventie van laattijdig optredende sepsis in premature zuigelingen met een zwangerschapsleeftijd van minder of gelijk aan 32 weken.
Estonian	Inimese <i>Staphylococcus aureus</i> polükloonaalne immuunoglobuliin ja inimese <i>Staphylococcus epidermidis</i> polükloonaalne immuunoglobuliin	32. või väiksema rasedusnädalaga enneaegsete imikute hilise algusega sepsise ennetamine
Finnish	Ihmisen <i>Staphylococcus aureus</i> polyklonaalinen immuunoglobuliini ja ihmisen <i>Staphylococcus epidermidis</i> polyklonaalinen immuunoglobuliini	Viivästyneen ("late onset") sepsiksen ehkäisy keskosilla, joiden sikiöikä ("gestational age") on ≤ 32 viikkoa
French	Immunoglobuline polyclonale humaine pour <i>Staphylococcus aureus</i> et immunoglobuline polyclonale humaine pour <i>Staphylococcus epidermidis</i>	Prévention de sepsis de survenue retardée chez les nouveau-nés prématurés de 32 semaines ou moins d'âge gestationnel
German	Humanes polyclonales <i>Staphylococcus aureus</i> Immunoglobulin und humanes polyclonales <i>Staphylococcus epidermidis</i> Immunoglobulin	Prävention einer <i>late onset</i> Sepsis bei Frühgeborenen mit einem Gestationsalter von weniger oder gleich 32 Wochen
Greek	Ανθρώπινη πολυκλωνική ανοσοσφαιρίνη <i>Staphylococcus aureus</i> και ανθρώπινη πολυκλωνική ανοσοσφαιρίνη <i>Staphylococcus epidermidis</i>	Πρόληψη της νοσοκομειακής σήψης βραδείας εκδήλωσης σε πρόωρα βρέφη με κινητική ηλικία ≤ 32 εβδομάδες στη γέννηση.

Hungarian	<i>Staphylococcus aureus</i> ellen termelt humán poliklonális immunglobulin és <i>Staphylococcus epidermidis</i> ellen termelt humán poliklonális immunglobulin	Későn jelentkező szepszis megelőzése ≤ 32 hetes gesztációs idejű koraszülötteknél
Italian	Immunoglobulina umana policlonale per <i>Stafilococco aureus</i> e immunoglobulina umana policlonale per <i>Stafilococco epidermidis</i>	Prevenzione della sepsi nei neonati prematuri di ≤ 32 settimane d'età gestazionale
Latvian	Cilvēka <i>Staphylococcus aureus</i> poliklonāls imūnglobulīns un cilvēka <i>Staphylococcus epidermidis</i> poliklonāls imūnglobulīns	Sepses ar vēlu sākumu profilaksei jaundzimušiem ar gestācijas vecumu mazāku vai vienādu ar 32 nedēļām
Lithuanian	Žmogaus <i>Staphylococcus aureus</i> polikloninis imunoglobulinas ir žmogaus <i>Staphylococcus epidermidis</i> polikloninis imunoglobulinas	Vėlyvos pradžios neišnešiotų naujagimių 32 savaitių ar mažesnės gestacijos sepsio prevencija
Polish	Poliklonalna immunoglobulina ludzka przeciw <i>Staphylococcus aureus</i> i, poliklonalna immunoglobulina ludzka przeciw <i>Staphylococcus epidermidis</i>	Zapobieganie opóźnionej posocznicy u wcześniaków urodzonych przed lub w 32 tygodniu ciąży
Portuguese	Inmunoglobulina policlonal humana para <i>Staphylococcus aureus</i> e immunoglobulina policlonal humana para <i>Staphylococcus epidermidis</i>	Prevenção de sépsis de início tardio em prematuros com 32, ou menos, semanas de idade gestacional
Slovak	Ľudský polyklónový <i>Staphylococcus aureus</i> imunoglobulín a ľudský <i>Staphylococcus epidermidis</i> imunoglobulín	Prevenca sepsy s neskorým začiatkom u predčasne narodených detí s gestačným vekom 32 týždňov alebo menej
Slovenian	Človeški poliklonalni imunoglobulin za <i>Staphylococcus aureus</i> in človeški poliklonalni imunoglobulin za <i>Staphylococcus epidermidis</i>	Preprečevanje poznega nastanka sepse pri novorojenčkih gestacijske starosti 32 tednov ali manj
Spanish	Inmunoglobulina policlonal humana para <i>Staphylococcus aureus</i> e immunoglobulina policlonal humana para <i>Staphylococcus epidermidis</i>	Prevención de la sepsis de inicio tardío en neonatos prematuros con edad gestacional igual o menor a 32 semanas
Swedish	Human <i>Staphylococcus aureus</i> polyklonal immunoglobulin och human <i>Staphylococcus epidermidis</i> polyclonal immunoglobulin	Profylax av sen debut ('late-onset') sepsis hos prematurt nyfödda barn under eller lika 32 veckors gestationsålder

Norwegian	Immunoglobulin mot <i>Staphylococcus aureus</i> (polyklonalt, humant) og immunoglobulin mot <i>Staphylococcus epidermidis</i> (polyklonalt, humant)	Forebygging av sen sepsis hos premature spedbarn med gestasjonsalder ≤ 32 uker
Icelandic	Manna <i>Staphylococcus aureus</i> fjölstofna ónæmisglóbúlín og manna <i>Staphylococcus epidermidis</i> fjölstofna ónæmisglóbúlín	Forvörn gegn spítala-sýklasótt hjá fyrirburum eftir ≤ 32 vikna meðgöngu við fæðingu