EMA/515658/2015

Summary of the risk management plan (RMP) for Obizur (susoctocog alfa)

This is a summary of the risk management plan (RMP) for Obizur, which details the measures to be taken in order to ensure that Obizur is used as safely as possible. For more information on RMP summaries, see here.

This RMP summary should be read in conjunction with the EPAR summary and the product information for Obizur, which can be found on Obizur's EPAR page.

Overview of disease epidemiology

Obizur is a medicine used to stop bleeding in adults with acquired haemophilia caused by the spontaneous development of antibodies that inactivate factor VIII, one of the proteins needed for normal clotting of the blood. This form of haemophilia is significantly more rare than the inherited form, and affects approximately 1.5 people per million per year worldwide. Acquired haemophilia generally develops later in life, occurring very infrequently in children. Most patients are middle-aged or elderly and have other illnesses. The incidence is similar in males and females, with an increase of female cases in early adulthood in women who have recently given birth or are in later stages of pregnancy. There is often an underlying illness associated with acquired haemophilia caused by antibodies to factor VIII, including diseases where the body's immune system attacks itself (autoimmune conditions) and, cancer; the use of certain medicines and pregnancy may also be linked to the disease. In about half of patients, there is no clear underlying illness and the condition is considered to have started on its own without a known cause.

Summary of treatment benefits

Obizur contains the active substance susoctocog alfa which works similarly to natural factor VIII but is not as easily recognised by antibodies. It has been investigated in one main study involving 28 adult patients with acquired haemophilia caused by antibodies against factor VIII who were experiencing a severe bleeding episode. Obizur was not compared with any other medicine. The response to Obizur was considered positive if bleeding stopped or was reduced, while a negative response meant that the bleeding continued or worsened. All 28 patients showed a positive response within 24 hours of starting treatment with Obizur; in 24 patients, the bleeding stopped completely.

Unknowns relating to treatment benefits

Clinical studies did not include patients aged less than 18 years old. It is not known whether these patients would respond differently to Obizur compared with older patients. There is no information on the effects of Obizur on pregnancy, breastfeeding, or on fertility. There is insufficient information on off-label (unauthorised) use of this product, especially in patients born with haemophilia A who have developed antibodies (inhibitors) against factor VIII used for treatment.

Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Antibodies which may reduce the effectiveness of Obizur (inhibitory antibodies to Obizur)	Antibodies against Obizur may result in the medicine not working effectively with the potential for serious bleeding which may be life threatening.	If bleeding does not stop as expected, the doctor will do a blood test to check if there are sufficient levels of Obizur in the blood and also if the patient has developed antibodies (inhibitors) against Obizur.

Important potential risks

Risk	What is known
Allergic reactions to the main ingredient or any of the other components of the medicine (hypersensitivity and allergic reactions to the active substance, any of the excipients or to baby hamster kidney (BHK) proteins)	As with any intravenous protein product, potentially life-threatening reactions (anaphylaxis) and other allergic reactions (hypersensitivity) can occur. The infusion must be stopped and emergency medical care sought immediately if patients experience early signs of hypersensitivity/allergic reactions like hives, rash, tightness of the chest, wheezing, low blood pressure or anaphylaxis (severe allergic reaction that can cause difficulty in swallowing and/or breathing, red or swollen face and/or hands). Doctors should treat patients promptly for these reactions. Obizur should not be used in patients allergic to Obizur or any of the other ingredients of this medicine; because the active substance is produced in hamster cells it should also not be used in patients who are allergic to hamster proteins.
The medicine does not stop the bleeding (lack of efficacy due to neutralising inhibitory antibodies)	If a significant increase in the amount of Obizur is needed to control bleeding, doctors should check plasma factor VIII levels to confirm that adequate levels have been achieved and maintained if necessary.
Blood clots in veins that may detach and travel in the blood stream (thromboembolic events)	Problems from excessive blood clotting (thromboembolic episodes) have not been observed with Obizur, but may occur. These could include heart attack, stroke, blood clots in the veins or blood clots in the lung.
Problems related to the infusion catheter (catheter-related complications)	Obizur is given by infusion (drip) into a vein. Problems related to the infusion catheter have not been observed with Obizur, but may occur. These may include infection, blood clots (thrombosis), bruising, blood that collects and pools under the skin (haematoma), and injury to the arteries. It is possible for a blood clot to form in the vein at the tip of the catheter line. This may lead to a blocked catheter line requiring medication to dissolve the clot or removal of the line. If left untreated, blood clots in veins may detach and travel in the blood stream (thromboembolic events).
Errors prescribing and/or preparing the medicine	Obizur is intended for use in the hospital setting only and should be administered under the supervision of a physician experienced in the

Risk	What is known
(dose dispensing errors)	treatment of haemophilia. There have been no dose dispensing errors reported with use of Obizur. The healthcare professional should follow dosing and administration instructions for Obizur to avoid medication errors.

Missing information

Risk	What is known
Use during pregnancy and breastfeeding; effect on fertility	Acquired haemophilia caused by antibodies against factor VIII occurs equally in men and women and mostly develops later in life when women are likely not able to become pregnant anymore. However, acquired haemophilia caused by antibodies against factor VIII may also occur after pregnancy. There is no information on the use of Obizur in pregnant or breastfeeding women or on its impact on fertility.
Use in patients less than 18 years of age	Acquired haemophilia caused by antibodies against factor VIII typically occurs in middle age or later in life and very rarely occurs in children. It is not known whether patients younger than 18 years of age would respond differently to the medicine.
Use in patients born with haemophilia A (congenital haemophilia A) with antibodies against Obizur (use of Obizur in patients with congenital haemophilia A with inhibitors (CHAWI))	Obizur can be used in patients with acquired haemophilia caused by antibodies against factor VIII. However, there is the potential that patients who were born with haemophilia A (congenital haemophilia A) with antibodies against factor VIII given them for treatment may be given Obizur. There is not enough information from clinical studies with Obizur to demonstrate that Obizur is safe and effective for congenital haemophilia A with antibodies against factor VIII.

Summary of risk minimisation measures by safety concern

All medicines have a summary of product characteristics (SmPC) which provides physicians, pharmacists and other healthcare professionals with details on how to use the medicine, and also describes the risks and recommendations for minimising them. Information for patients is available in lay language in the package leaflet. The measures listed in these documents are known as 'routine risk minimisation measures'.

The SmPC and the package leaflet are part of the medicine's product information. The product information for Obizur can be found on Obizur's EPAR page.

This medicine has special conditions and restrictions for its safe and effective use (additional risk minimisation measures). Full details on these conditions and the key elements of any educational material can be found in Annex II of the product information which is published on Obizur's EPAR page; how they are implemented in each country however will depend upon agreement between the marketing authorisation holder and the national authorities.

These additional risk minimisation measures are for the following risks:

Dose dispensing errors

Risk minimisation measure: To inform healthcare professionals of the risk of dose dispensing errors with Obizur. Make tools available to healthcare professionals informing of the proper method for dose calculation and administration of the medicine.
Objective and rationale: Ensure that all healthcare professionals prescribing/ordering Obizur are provided with an educational brochure that shall inform about the method for calculation of the dose taking into account the patient's weight.
Description: Key points: • Healthcare professional brochure including a detailed calculation of the number of vials needed taking into account the patient's weight. • An on-line video to further elaborate on the required calculation and administration of the medicine.

Planned post-authorisation development plan

List of studies in post-authorisation development plan

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
241302: Post-marketing non-interventional safety evaluation of Obizur in the treatment of bleeding episodes for patients with acquired hemophilia A (United States)	Describe the immune profile during treatment of bleeding episodes. Assess the safety and effectiveness of Obizur in the treatment of bleeding episodes.	Inhibitory antibodies to Obizur Hypersensitivity and allergic reactions to the active substance, any of the excipients or to baby hamster (BHK) protein Thromboembolic events	Planned	Completion of final report: approximately 31 January 2020
241501:Prospective, Non-Interventional Study to Evaluate the Safety and Effectiveness of Obizur in Real Life Practice (EU)	Describe the immune profile during treatment of bleeding episodes. Assess the safety and effectiveness of Obizur in the treatment of bleeding episodes.	Inhibitory antibodies to Obizur Hypersensitivity and allergic reactions to the active substance, any of the excipients or to baby hamster (BHK) protein Thromboembolic events No data on pregnant and lactating women or fertility Insufficient data on off-	Planned	Completion of final report: 6 months after last subject out

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results
		label use of Obizur particularly in patients with congenital haemophilia A with inhibitors (CHAWI)		

Studies which are a condition of the marketing authorisation

The 'Prospective, Non-Interventional Study to Evaluate the Safety and Effectiveness of Obizur in Real Life Practice (EU)', to be conducted in the EU, is a condition of marketing authorisation.

Summary of changes to the risk management plan over time

Not applicable.

This summary was last updated in 09-2015.