Part VI: Summary of the risk management plan

Summary of risk management plan for Xembify

This is a summary of the risk management plan (RMP) for Xembify. The RMP details important risks of Xembify, how these risks can be minimised, and how more information will be obtained about Xembify risks and uncertainties (missing information).

Xembify SmPC (Summary of Product Characteristics) and its patient information give essential information to healthcare professionals and patients on how Xembify should be used.

Important new concerns or changes to the current ones will be included in updates of Xembify.

I. The medicine and what it is used for

Xembify is indicated for the replacement therapy in adults and children and adolescents (0-18 years) in:

- Primary immunodeficiency syndromes with impaired antibody production
- Hypogammaglobulinaemia and recurrent bacterial infections in patients with chronic lymphocytic leukaemia (CLL) in whom prophylactic antibiotics have failed or are contra-indicated.
- Hypogammaglobulinaemia and recurrent bacterial infections in multiple myeloma (MM) patients.

It contains unmodified human immunoglobulin G (IgG) as the active substance and is to be administered via the subcutaneous route.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Xembify, together with measures to minimise such risks are outlined below.

Measures to minimise the risks identified for medicinal products can be:

- Specific information (such as warnings, precautions, and advice on correct use) in the Package Insert and Patient Information addressed to patients and healthcare professionals;
- Important advice on the medicine's packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;

- The medicine's legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed, including PSUR assessment, so that immediate action can be taken as necessary. These measures constitute *routine pharmacovigilance activities*.

If important information that may affect the safe use of Xembify is not yet available, it is listed under 'missing information' below.

II.A List of important risks and missing information

Important risks of Xembify are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of a link with the use of IGSC 20%. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	• Infusion site reactions
Important potential risks	• Hypersensitivity reactions including anaphylactic reactions • Thromboembolic events • Aseptic Meningitis • Theoretical risk of pathogen infection • Interaction with live attenuated vaccines • Medication errors arising from self-administration
Missing information	• Use in women who are pregnant or lactating

II.B Summary of important risks

Important identified risk: Infusion site reaction	
Evidence for linking the risk to	Certain adverse reactions may be related to how to apply the

the medicine	infusion. The recommended use of administration and the dose given on PI must be closely followed. Patients must be closely monitored and carefully observed for any symptoms throughout the infusion period.
Risk factors and risk groups	All patients using subcutaneous injection are exposed to the risk. Some patients experience infusion site reactions when applying the product.
Risk minimisation measures	Routine risk communication: - *EU SmPC 4.8 Undesirable effects* Other routine risk minimisation measures beyond the Product Information: None proposed.

Important potential risk: Hypersensitivity reactions including anaphylactic reactions	
Evidence for linking the risk to the medicine	Hypersensitivity reactions, including life-threatening anaphylactic reactions can occur even when a previous administration has been tolerated (including a negative test). Caution is therefore needed with every dose, even if previous tests have been made.
Risk factors and risk groups	All patients using any subcutaneous protein product are exposed to the risk. Risk factors associated with anaphylactic reactions are IgA deficiency and history of hypersensitivity reactions. Most often, hypersensitivity reactions are associated with first-time exposure as well as with rapid infusion rate.
Risk minimisation measures	Routine risk communication: - *EU SmPC 4.3 Contraindications* - *EU SmPC 4.4 Special warnings and precautions for use* - *EU SmPC 4.8 Undesirable effects* Additional risk minimisation measures: None proposed.

Important potential risk: Thromboembolic events	
Evidence for linking the risk to the medicine	A link between the use of immune globulin products and thromboembolic events has been established and there is evidence that suggests that there are procoagulant proteins present in the medicine, in addition to other factors such as an increase in viscosity that could lead some patients to experience a thromboembolic event.
Risk factors and risk groups	Risk factors may include: advanced age, prolonged immobilization, hypercoagulable conditions, history of venous or arterial thrombosis, use of estrogens, indwelling central vascular catheters, hyperviscosity and cardiovascular risk factors. Thrombosis may occur in the absence of known risk factors.
Risk minimisation measures	Routine risk communication: - *EU SmPC 4.4 Special warnings and precautions for use* Other routine risk minimisation measures beyond the Product Information: None proposed.

Important potential risk: Aseptic Meningitis	
Evidence for linking the risk to the medicine	Aseptic meningitis syndrome has been reported to occur in association with intravenous use of human immune globulins immunoglobulin treatments. With the subcutaneous use the product does also arrive to the bloodstream and aseptic meningitis could be developed. This may occur more frequently in association with high-dose treatments.
Risk factors and risk groups	All patients receiving the infusion are exposed to the risk.
Risk minimisation measures	Routine risk communication: - *EU SmPC 4.4 Special warnings and precautions for use* Other routine risk minimisation measures beyond the Product Information: None proposed.
Important potential risk: Theoretical risk of pathogen infection	
Evidence for linking the risk to the medicine	Because this product is made from human blood, it may carry a risk of transmitting infectious agents. The risk that such products will transmit an infectious agent has been reduced by

	screening plasma donors for prior exposure to certain viruses, by testing for the presence of certain current virus infections, and by inactivating and/or removing certain viruses. Despite these measures, such products can still potentially transmit infectious agent, e.g. viruses and, theoretically, the Creutzfeld-Jakob disease (CJD) agent. The possibility of transmitting infective agents cannot be totally excluded. This also applies to unknown or emerging viruses and other pathogens.
Risk factors and risk groups	All patients receiving the infusion are exposed to the risk.
Risk minimisation measures	Routine risk communication: - *EU SmPC 4.4 Special warnings and precautions for use* Other routine risk minimisation measures beyond the Product Information: None proposed.

Important potential risk: Interaction with live attenuated vaccines	
Evidence for linking the risk to the medicine	Immunoglobulin administration may impair for a period of at least 6 weeks and up to 3 months the efficacy of live attenuated virus vaccines such as measles, rubella, mumps and varicella. After administration of this product, an interval of 3 months should elapse before vaccination with live attenuated virus vaccines. In the case of measles, this impairment may persist for up to 1 year. Therefore patients receiving measles vaccine should have their antibody status checked.
Risk factors and risk groups	All patients receiving the infusion are exposed to the risk.
Risk minimisation measures	Routine risk communication: - *EU SmPC 4.5 Interaction with other medicinal products and other forms of interaction* Other routine risk minimisation measures beyond the Product Information: None proposed.
Important potential risk: Medication errors arising from self-administration	
Evidence for linking the risk to the medicine	Since this product is intended to be administered in a home setting or a location away from the clinical setting, user errors could normally be associated with an incorrect use of the Patient

	Information instructions for the proposed administration use of the product.
Risk factors and risk groups	All patients receiving or self-administering the subcutaneous infusion are exposed to the risk.
Risk minimisation measures	Routine risk communication: - *EU SmPC 4.2. Posology and method of administration* - *EU Package Leaflet 3. How to use Xembify* Other routine risk minimisation measures beyond the Product Information: None proposed.

Missing information: Use in women who are pregnant or lactating	
Risk minimisation measures	Routine risk communication: - *EU SmPC section 4.6 Fertility, pregnancy and lactation* Other routine risk minimisation measures beyond the Product Information: None proposed.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Xembify.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Xembify.