Part VI: Summary of the risk management plan

Summary of risk management plan for Plasbumin®/ Albutein®/ Human Albumin Grifols®/ Albumina Grifols®/ Albumina Humana Grifols®/ Probumin®.

This is a summary of the risk management plan (RMP) for Albutein®/ Human Albumin Grifols®/ Albumina Grifols®/ Albumina Humana Grifols®/ Probumin®.
The RMP details important risks of Albutein®/ Human Albumin Grifols®/ Albumina Grifols®/ Albumina Humana Grifols®/ Probumin ®, how these risks can be minimised, and how more information will be obtained about Albutein®/ Human Albumin Grifols®/ Albumina Grifols®/ Albumina Humana Grifols®/ Probumin® 's risks.
Albutein®/ Human Albumin Grifols®/ Albumina Grifols®/ Albumina Humana Grifols®/ Probumin®'s summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Human albumin should be used.
Important new concerns or changes to the current ones will be included in updates of Albutein®/ Human Albumin Grifols®/ Albumina Grifols®/ Albumina Humana Grifols®/ Probumin®'s RMP.

I. The medicine and what it is used for

The authorized indications for Albutein®/ Human Albumin Grifols®/ Albumina Grifols®/ Albumina Humana Grifols®/ Probumin® depend on the country. However, it can be considered that, in general, the product is indicated for restoring and maintaining the circulating blood volume where volume deficiency has been demonstrated and the use of a colloid is appropriate (see SmPC or PI for the full indication). It contains Human albumin solution as active substance and it is given as a solution for Infusion, with 5%, 20% or 25% strength.

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

Important risks of Albutein®/ Human Albumin Grifols®/ Albumina Grifols®/ Albumina Humana Grifols®/ Probumin®, together with measures to minimise such risks and the proposed studies for learning more about Albutein®/ Human Albumin Grifols®/ Albumina Grifols®/ Albumina Humana Grifols®/ Probumin®'s 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 leaflet and SmPC 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 Albutein®/ Human Albumin Grifols®/ Albumina Grifols®/ Albumina Humana Grifols®/ Probumin® is not yet available, it would be listed under 'missing information'.

II.A List of important risks and missing information

Important risks of Human albumin 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 Human albumin. 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;

List of important risks and missing information	
Important identified risks	- Hypersensitivity including anaphylactic reactions - Hypervolemia
Important potential risks	- Theoretical risk of pathogen transmission - Medication errors resulting in haemolysis
Missing information	None proposed

II.B Summary of important risks

Important identified risk: Hypersensitivity 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 intravenous 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	Routine risk minimisation measures:

measures	Adequately addressed in sections 4, 5 (5.1), 6 and 17 of PI; and sections 4.3, 4.4, and 4.8 of EU SmPC.

Important identified risk: Hypervolemia	
Evidence for linking the risk to the medicine	Hypervolemia may occur in instances where there is an elevation of intravascular volume levels. This may be due to shifts in fluids from the interstitium to plasma, reduced excretion of sodium and water, excessive intravenous fluids, and excessive retention of water and sodium from chronic renal stimuli attempting to conserve both. An elevation of the extracellular fluid volume produces circulatory overload and subsequently, an abnormally amplified cardiac contractility, increased mean artery pressure (MAP), and an elevated capillary hydrostatic pressure. The latter, as consequence, causes shifts of fluids to the interstitial space, and hence, producing edema.
Risk factors and risk groups	All patients using any intravenous protein product are exposed to the risk. Conditions where hypervolemia and its consequences could represent a special risk for the patient: - Decompensated cardiac insufficiency - Hypertension - Oesophageal varices - Pulmonary oedema - Haemorrhagic diathesis - Severe anaemia Renal and post-renal anuria.
Risk minimisation measures	Routine risk minimisation measures: Adequately addressed in sections 5(5.2) and 17 of the PI; and sections 4.4 and 4.9 of EU SmPC.

Important potential risk: Theoretical risk of pathogen transmission	
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	The patients had other risk factors which prevent a complete assessment. Other risk factors for these patients, such as risk sexual behaviour or drug use are unknown.
Risk minimisation measures	Routine risk minimisation measures: Adequately addressed insection 5(5.8) and 17 of the PI; and section 4.4 and 4.8 of EU SmPC.

Important potential risk: Medication errors resulting in haemolysis	
Evidence for linking the risk to the medicine	This risk is the result of a medication error. As with any hyperoncotic protein solution likely to be administered in large volumes, severe haemolysis may result from the inappropriate use of Sterile Water for Injection as a diluent for Albumin (Human).
Risk factors and risk groups	All patients receiving the infusion are exposed to the risk.
Risk minimisation measures	Routine risk minimisation measures: Adequately addressed in section 5(5.7) of the PI; and sections 4.4 and 6.6 of EU SmPC.

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 for Human albumin.

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

There are no studies required for Human albumin.