VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Albumin is a naturally-occurring protein that is abundant in the blood. One of its main functions is to keep the fluid levels in the blood and tissues balanced. Low albumin causes fluids to move from the blood into tissues, disrupting the fluid balance and potentially resulting in organ failure. Albumeon / Human Albumin 20% Behring is a solution containing albumin that restores fluid lost from the blood in critically ill patients. The amount of blood circulating in the body may be reduced due to many causes (including injury [trauma], surgery, burns, severe infection, and severe liver disease), which can be corrected through treatment with Albumeon / Human Albumin 20% Behring. Three of the most common situations for use of Albumeon / Human Albumin 20% Behring are discussed below:

Burn injuries

Due to damage of the skin, fire-related burns increase the amount of fluid lost into wound tissues from the blood. Burns are a common injury around the world; each year, approximately 21 per every 100,000 people are admitted into hospitals with burns in the UK,

whilst 5 in every 100,000 people worldwide die from burn-related injuries. The young and elderly are particularly at risk of burn injuries, as are men, ethnic minority groups and people in certain occupations (such as firefighters, miners, and furnace operators). Some health conditions such as fits, mental and physical disabilities also carry a high risk of fire-related injuries.

Sepsis

The presence of infection and the severe whole-body reactions that occur as a result of infection is known as sepsis. Sepsis is brought about by the body's own defenses reacting to a serious infection, such as bacteria, viruses, or parasites. Severe low blood pressure is seen in about half of the patients with sepsis. Severe sepsis occurs when one or more organ systems (such as the heart and lungs), start to fail on functioning, which is potentially fatal. Sepsis is a major healthcare problem, affecting millions of people worldwide each year and approximately one-third of those affected are patients who had surgery. Patients with severe sepsis are more likely to die of the disease than those with mild sepsis. Some medical conditions such as HIV, cancer, and diabetes can increase the risk of sepsis. Other risk factors include older age, male gender, and non-white racial groups.

Severe liver disease

Severe liver disease such as liver scarring ('cirrhosis') is most commonly caused by hepatitis B, hepatitis C, and alcohol abuse, though it can also be caused by certain drugs and diseases. As albumin is made in the liver, any disruption to its function reduces the amount of albumin available in the blood. A lack of albumin can result in tissues becoming swollen, especially in the abdominal area (a condition called 'ascites'). Chronic liver disease is common throughout the world, with an estimated 4.5 to9.5percent of the population being affected.

VI.2.2 Summary of treatment benefits

Medicinal products containing human serum albumin have been used for more than half a century worldwide to treat the harmful effects of low blood volume. A number of clinical trials show that products containing human serum albumin (including Albumeon) are effective at replacing fluid lost from the blood in patients. This includes patients in intensive care with reduced blood volume due to severe injury (trauma), infections (sepsis), surgery, burn patients and patients with severe liver disease.

VI.2.3 Unknowns relating to treatment benefits

No significant unknown information relating to treatment benefits of Albumeon in licensed indications has been identified by the Company.

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
Anaphylactic reactions (an anaphylactic reaction is a serious allergic reaction of rapid onset that causes, for example, difficulty in breathing and dizziness; it may develop to a life-threatening response involving the whole body).	Anaphylactic reactions are a very rare, but known effect of therapy with human serum albumin products.	Yes, by monitoring of early symptoms. Potential complications can often be avoided by ensuring that patients are carefully monitored for any symptoms throughout the infusion period. Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of treatment.

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
Potential of transmission of infectious agents	This is a potential risk with all blood products, including plasma derived products like Albumeon®. However, transmission of infectious agents has not been reported for human serum albumin products manufactured according to the standards defined by the European Pharmacopeia and no confirmed cases have been reported for Albumeon®.
High blood volume (hypervolaemia)	A high blood volume may occur in patients treated with Human Albumin CSL Behring if the dosage and rate of infusion are too high. Certain underlying disorders (such as high blood pressure and kidney disease) may increase the risk of this occurring. Consequences can be severe and life threatening. The dosage and infusion rate of Albumeon is different for each person and needs to be adjusted to each patient's individual requirements. The treating physician will determine the best approach and dose for the patient.

Missing information

Risk	What is known
None identified	Not applicable

VI.2.5 Summary of additional risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimizing them. The measures in this document are known as routine risk minimization measures.

The Summary of Product Characteristics for Albumeon® can be found in the Annex 2.

Human Albumin 20% Behring has no additional risk minimization measures.

VI.2.6 Planned post authorisation development plan

Not applicable.

Studies which are a condition of the marketing authorisation

Not applicable.

VI.2.7 Summary of changes to the Risk Management Plan over time

Table 4: Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
1.0	03 August 2012	No identified risks No potential risks	Submitted to Reference Member State (Germany) in the context of a new licence application (approved April 22, 2013)
2.0	01 July 2013	Additions to safety concerns: Identified Risks: Anaphylactic reactions Potential Risks: Potential for transmission of infectious agents	Updated to new EMA format and update with new post-marketing data with DLP 31 March 2013
3.0	December 2014	Additions to safety concerns: Potential Risks: Hypervolaemia and haemodilution in high risk patients	Hypervolaemia and haemodilution in high risk patients is not a new risk and has been already reflected in the in the labelling texts for Albumeon. It has now been added as an potential risk on the request of a health authority