

## **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. Human Albumin CSL 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 Human Albumin CSL Behring. Three of the most common situations for use of Human Albumin CSL Behring are discussed below:

#### ***Burn injuries***

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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 to 9.5 percent 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 Human Albumin CSL Behring) 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.

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**VI.2.3 Unknowns relating to treatment benefits**

No significant unknown information relating to treatment benefits of Human Albumin CSL Behring in licensed indications has been identified by the Company.

**VI.2.4 Summary of safety concerns**

Reactions associated with Human Albumin CSL Behring include flushes, hives, fever, and nausea. These reactions are mostly mild in severity, do not require special treatment, and have little impact on daily living. Allergic reactions (also known as hypersensitivity reactions) may occur and on rare occasions, may be serious enough to cause shock.

**Table 12: Important identified risks**

| <b>Risk</b>  | <b>What is known</b>   | <b>Preventability</b>   |
|--|--|---|
| Serious, potentially life-threatening allergic reaction. (Anaphylactic reaction) | Anaphylactic reactions are a very rare, but known class 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.<br><br>Suspicion of allergic or anaphylactic type reactions requires immediate discontinuation of treatment and the person has to be treated appropriately according to the kind and severity of the unwanted effect. |

**Table 13: Important potential risks**

| <b>Risk</b>  | <b>What is known (Including reason why it is considered a potential risk)</b>  |
|--|--|
| The medicine could have a virus or other infectious agents in it | Human Albumin CSL Behring is made from human plasma. When medicines are made from human blood or plasma, several steps are taken to prevent infections from being passed on to people treated with the medicine. These steps include: <ul style="list-style-type: none"> <li>Careful selection of blood and plasma donors to make</li> </ul> |

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| Risk                             | What is known (Including reason why it is considered a potential risk)   |
|----------------------------------|--|
|                                  | <p>sure donations are not taken from anyone who may have an infection,</p> <ul style="list-style-type: none"> <li>• testing of each donation for signs of viruses, and</li> <li>• treating the blood and plasma during the manufacturing process to inactivate or remove any viruses that might be present.</li> </ul> <p>Despite all these steps, when people are treated with medicines prepared from human blood or plasma, the possibility of passing on infection cannot be totally excluded. However, no confirmed cases of viral infection have been reported with Human Albumin CSL Behring.</p> |
| High blood volume (hypervolemia) | <p>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.</p> <p>The dosage and infusion rate of Human Albumin CSL Behring 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.</p>                                     |

**Table 14: 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.

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The Summary of Product Characteristics (SmPC) for Human Albumin CSL Behring 5% 20%, and 25% can be found in the [Annex 2](#).

Human Albumin CSL 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 15: Major changes to the Risk Management Plan over time**

| <b>Version</b> | <b>Date</b>       | <b>Safety Concerns</b>  | <b>Comment</b>   |
|----------------|-------------------|---|--|
| 1.0            | 20 August 2007    | No identified risks<br>No potential risks   | Submitted to Reference Member State (Austria) in the context of a Mutual Recognition Procedure (approved February 04, 2008/)   |
| 2.0            | 05 December 2013  | Additions to safety concerns:<br><br>Identified Risks:<br>Anaphylactic reactions<br><br>Potential Risks:<br>Potential for transmission of infectious agents | Updated to new EMA format and update with new post-marketing data with data lock point (DLP) 01 Sep 2013<br><br>These risks are not new safety issues as they have been known for decades for human albumin (HA) products.               |
| 3.0            | 12 September 2014 | Additions to safety concerns:<br><br>Potential Risks:<br>Hypervolemia and haemodilution in high risk patients   | Hypervolemia and haemodilution in high risk patients is no new risk and has been already reflected in the labelling texts for Human albumin CSL Behring. It has now been added as an potential risk on the request of a health authority |