6.2 Elements for a Public Summary

6.2.1 Overview of disease epidemiology

As people continue to live longer, there is an increasing number of people who develop wrinkles or lines on the face. These wrinkles or lines on the face may be due to advancing age, exposure to sun, increased and continuous facial muscle contraction and sleep lines. These lines are a major source of worry for some patients and may lead them to have depression and other emotional instability, including low self-esteem. Because of these reasons, more people are demanding treatment for these conditions.

6.2.2 Summary of treatment benefits

Azzalure causes relaxation of muscles; as some wrinkles are caused by repetitive contraction of the muscles underneath the facial skin, relaxation of muscle contraction by Azzalure can reduce wrinkles and improve facial appearance. Azzalure injections are one of the most commonly performed aesthetic procedures in the world. Clinical studies to establish the benefit of Azzalure have included more than 2600 patients with facial wrinkles. In the key clinical studies, Azzalure

injections significantly reduced the severity of facial wrinkles for up to 4 months. Data from these studies showed that 90% of patients responded to treatment with Azzalure.

6.2.3 Unknowns relating to treatment benefits

Not applicable.

6.2.4 Summary of safety concerns

6.2.4.1 Important identified risks

Risk	**What is known**	**Preventability**
Eye disorders	Treatment with Azzalure can lead to ocular events, which are rarely serious and usually result from local muscle weakness.	To reduce the risk of patients developing ocular events, clinicians are advised to follow the advice on the technique of administration, the recommended dose for administration, and reconstitution of the product specified in the product label.
Remote distribution of the effects of the toxin	Serious but reversible reactions in muscles other than those targeted by the administration of Azzalure can occur, although the risk is considered to be low.	Clinicians are advised about the possibility of such undesirable effects and how to reduce the likelihood of occurrence, especially in patients with pre-existing risk factors.

6.2.4.2 Important potential risks

Risk	**What is known (Including reason why it is considered a potential risk)**
Neutralising antibodies	Injections of Azzalure at more frequent intervals or higher doses may lead to the development of antibodies that neutralise the activity of the product, resulting in non-response to treatment.

6.2.4.3 Missing information

Risk	**What is known**
Use in pregnancy and lactation	The experience with Azzalure in pregnancy and lactation is limited.
Use in children	The experience with Azzalure in children is limited.

6.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics, which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the Package Leaflet. The measures in these documents are known as routine risk minimisation measures. The Summary of Product Characteristics and the Package leaflet for Azzalure can be found in the European public assessment report page of the European Medicines Agency.

6.2.6 Planned post-authorisation development plan

Not applicable.

6.2.7 Summary of changes to the Risk Management Plan over time

Table 23 Summary of changes to the Risk Management Plan over time

Version	Date	Safety concerns	Comment
1.1	Data Lock Point 30 June 2007	• Produced following evaluation by the European Pharmacovigilance Working Party (PhVWP) in July 2006 of the risk of adverse events potentially related to the pharmacological action of BTX A HAC. • Update due to finalisation of submission, SmPC and responses to questions	None
2.0	Data Lock point 31 December 2008	• Update of post-marketing data to new data-lock-point	None
2.1	Data Lock Point 11 August 2009	• Utilisation Survey protocol approval • Update of post-marketing data to new data-lock-point	None
3.0	Data Lock Point 31 December 2011	• To further align the document with the EU template • To add information on the proposed LCL indication • Update of post-marketing data to new data-lock-point	None
4.0	Data Lock Point 31 May 2013	• Alignment of the RMP with the new European Guideline (EMA/816292/2011) on Good Pharmacovigilance Practices (Module V). • Update of post-marketing data to new data-lock-point	Reformatting of existing RMP into new template.
5.0	Data Lock Point 31 December 2013	• Update of the risk minimisation sections following the results of the Risk Minimisation Effectiveness Survey. • Amendments to the definitions of Missing information terms throughout the Module • Update of post-marketing data to new data-lock-point	None.