VI.2. Elements for a Public Summary

VI.2.1. Overview of Disease Epidemiology

Around 21% of the global population smokes, and smoking kills almost 6 million people a year. It is estimated that around half of all smokers die of smoking-related diseases (such as cancers, diabetes, and cardiovascular and chronic lung diseases). Based on current trends, tobacco-related deaths will reach more than 8 million yearly by 2030, and 80% of those deaths will occur in developing countries (Euromonitor; 2007, WHO; 2011, WHO; 2013, Doll et al; 2004, USDHHS; 2012).

VI.2.2. Summary of Treatment Benefits

The assessment of benefit of NRT is based on studies that compare nicotine with placebo (a pill without an active drug) or with comparators (other NRT drugs), and reviews of published papers and other literature. While there are differences in the methods, the majority of these studies were well-designed and involved patients with various backgrounds. The results obtained consistently showed that nicotine is effective for the treatment of tobacco dependence.

A paper by Cahill et al (2013) summarised and analysed the results of 12 systematic reviews which included around 150 clinical trials on NRT. The study showed that NRT is effective in aiding smoking cessation, and that NRT is more effective than placebo doing so. Additionally, the different types of NRTs (that is, patches, tablets, sprays, lozenges, and inhalers) have similar efficacies, and the use of multiple NRT types is more effective than using only 1 type.

VI.2.3. Unknowns Relating to Treatment Benefits

In general, all development studies for NRT excluded patients with a history of allergic or dermatologic disease, pregnant or breast feeding women, and in later development programmes patients with symptomatic cardiovascular disease. Studies also excluded patients <18 years of age. Otherwise, participants in the study were healthy volunteers.

In general, use in patients/consumers who are pregnant, breast feeding or have pre-existing conditions should be undertaken following consultation with a physician.

VI.2.4. Summary of Safety Concerns

Table 22: Important Identified Risks

Risk	What is known	Preventability
None	N/A	N/A

Table 23: Important Potential Risks

Risk	What is known	Preventability
None	N/A	N/A

Table 24: Missing Information

Risk	What is known
None	N/A

VI.2.5 Summary of Additional Risk Minimisation Measures by Safety Concern

All medicines have a Summary of Product Characteristics (SmPC) that provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. A shortened version of this in lay language is provided in the form of the Package Leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned Postauthorisation Development Plan

No post-authorisation development is planned for nicotine.

VI.2.7 Summary of Changes to the Risk Management Plan Over Time

Table 25: Major Changes to the Risk Management Plan over Time

Version	Date	Safety Concerns	Comment
1.0	27 Oct 2011	Identified Risks: none Potential Risks: none Missing information: Limited safety information in subpopulation of patients with cardiovascular disease	This is the first RMP combining all formulations of nicotine.
2.0	13 Feb 2014	No new safety concerns	- Update of RMP format to comply with Good Pharmacovigilance Practices (GVP) Module V - Risk management systems - Removal of the topic of "Harm Reduction" (UK only) which is now complete, and did not identify any potential risks associated with the indication of harm reduction.
3.0	16 Dec 2014	No new safety concerns	- Removal of quarterly monitoring of cardiovascular events as a routine risk minimisation measure, after fulfilling RMP commitments to monitor quarterly data from all sources in the subpopulation of patients experiencing cardiovascular events and who had a history of a cardiovascular condition or predisposing factors to its development (2011 to 2013). - Updated post marketing data up to 31 August 2014, which is the data lock date of the most recent PBRER/PSUR. Further update of RMP format to comply with GVP Module V - Risk management systems (EMA/465932/2013 Rev.1 - 25 July 2013)
4.0	05 Nov 2015	No new safety concerns	- . - Updated post marketing data up to 31 August 2015 throughout the document (SDE00124716). - Harm reduction information was moved from Part II, SVII.3.2 to Part III.3.

Table 25: Major Changes to the Risk Management Plan over Time

Version	Date	Safety Concerns	Comment
4.1	20 Jan 2016	Swedish HA comments provided in Day-40 PRAR have been added in section SV.1. Action Taken by Regulatory Authorities and/or Marketing Authorisation Holders for Safety Reasons. No changes made yet to the RMP as the Company is currently reviewing this assessment report.	
5.0	17 Mar 2016	Identified Risks: none Potential Risks: none Missing information: None	- The safety concern "Limited safety information in subpopulation of patients with cardiovascular disease" was removed as missing information. - Updated post marketing data up to 31 January 2016 throughout the document (SDE00148674).
5.1	29 Nov 2016	No update in safety concerns	Following requests from HAs during DCP/MRP procedures (SE/H/904/01/R/01 and SE/H/904/001/II/013, SE/H/904/002/DC)) and UK national procedures, the following 2 sections were updated: • Section SV.1. Action Taken by Regulatory Authorities and/or Marketing Authorisation Holders for Safety Reasons (Table 12 updated) • Section SV.3.1. Use in Paediatric Patients (details of serious cases added in Table 25 (this table)
	31 Jan 2017	No update in safety concers	No changes made to the safety aspects of the RMP. The RMP has only been reissued for submission of the version with updated Section SV.1. Action Taken by Regulatory Authorities and/or Marketing Authorisation Holders for Safety Reasons and Section SV.3.1. Use in Paediatric Patients for SE/H/1617/003-004/DC (fruit lozenges), SE/H/1617/001-001/DC (mint lozenges DCP1) and ES/H/0427/001-002/DC (mint lozenges DCP2). The cover page and product review have been updated to be more generic and cover any nicotine formulations/products/procedures.