VI.2 Elements for a public summary

VI.2.1 Overview of disease epidemiology

GRAZAX® is an allergy immunotherapy tablet to be placed under the tongue developed for treatment of grass allergy. The aim with the treatment is to increase the body's tolerance towards grass pollens, thereby reducing symptoms of AR and conjunctivitis (hay fever-like symptoms).

Allergic diseases in general are very common, and respiratory allergy is estimated to affect 20-25% of people in Europe. Grass pollen allergy is one of the most common allergic diseases, affecting up to 44% of patients with allergy.

Main treatment options for grass allergy are to avoid grass pollens, use symptom-relieving medication or allergy immunotherapy.

VI.2.2 Summary of treatment benefits

GRAZAX® is intended for use in patient who have a positive grass allergy test and who have persistent allergic symptoms despite using symptom-relieving medication such as oral antihistamine or nasal steroids.

The benefits and risks associated with GRAZAX® have been investigated in 18 completed controlled clinical trials comparing the effects and safety profile of GRAZAX® to placebo (a substance with no medical effect). More than 3200 patients aged 5 to 65 years have been exposed to the marketed dose of GRAZAX® in these trials. The trials showed that GRAZAX® improved the patients' symptoms substantially. In adults treated with GRAZAX® daily for three years, a disease-modifying effect was observed; meaning that the positive effect of GRAZAX® was present 2 years after treatment with GRAZAX® was terminated.

VI.2.3 Unknowns relating to treatment benefits

The effect of GRAZAX® has not been properly investigated in clinical trials in children below the age of 5 years, in elderly above the age of 65 years, or in pregnant or lactating women. Experience from other products within the same drug class and experience from use of GRAZAX® in the market has not indicated any specific safety concerns in these patient groups.

VI.2.4 Summary of safety concerns

Table 29 Important identified risks

Risk	What is known	Preventability
Serious allergic reactions affecting the body in general, including potentially life-threatening allergic reactions	Serious allergic reactions are well known adverse effects of allergy immunotherapy in general. In rare cases, these reactions may become life-threatening. For GRAZAX®, serious allergic reactions mainly occur in relation to intake of the first tablet, and the vast majority of the reactions occur within 30 minutes after taking GRAZAX®.	As a precaution, the treating physician should keep the patient under careful observation for at least 30 minutes after the patient takes the first GRAZAX® tablet so that possible adverse effects can be treated immediately. The patient should be told to contact a physician and stop treatment in case of any severe symptoms.
Progression of allergic reactions in the mouth to the throat	Mild allergic reactions in the mouth may occur in relation to treatment with GRAZAX®. In some cases these reactions may worsen and progress into the throat. This may potentially become serious as this could lead to swelling of the throat and thereby difficulty to breathe. This is a known potential adverse effect of allergy immunotherapy to be placed under the tongue.	As a precaution, the treating physician should keep the patient under careful observation for at least 30 minutes after the patient takes the first GRAZAX® tablet so that possible adverse effects can be treated immediately. The patient should be told to contact a physician and stop treatment in case of any severe symptoms.
Acute asthma	Many patients with grass pollen allergy also have allergic asthma, and asthma may be triggered by grass pollen exposure in these patients.	Patients at high risk of this adverse effect should not start treatment with GRAZAX®. If patients with concomitant asthma experience symptoms and signs indicating worsening of asthma, treatment should be discontinued and the patient should consult a physician immediately in order to evaluate the continuation of treatment.

Table 30 Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
No important potential risk identified	Not applicable

Table 31 Missing information

Risk	What is known
Limited information on use in children below the age of 5 years	Use of GRAZAX® in children below the age of 5 years has not been investigated sufficiently in clinical trials, and information available on benefits and risk in this group of patients is therefore limited.

Risk	What is known
	Reports from use of GRAZAX® in the market have not indicated any specific safety concerns in children below the age of 5 years.
Limited information on use in elderly patients above the age of 65 years	Use of GRAZAX® in patients above the age of 65 years has not been investigated sufficiently in clinical trials, and information available on benefits and risk in this group of patients is therefore limited. Reports from use of GRAZAX® in the market have not indicated any specific safety concerns in patients above the age of 65 years.
Limited information on use in pregnant and lactating women	Use of GRAZAX® has not been investigated in pregnant or lactating women in clinical trials. Treatment with GRAZAX® should not be initiated during pregnancy as some of the medications used to treat potential serious allergic adverse effects may be harmful in connection with pregnancy. If pregnancy occurs while treatment with GRAZAX® is ongoing, the patient should contact her physician who will decide whether it is safe to continue treatment.

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

All medicines have a Summary of Product Characteristics (SmPC) which provides the 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 (PL). The measures in these documents are known as routine risk minimisations measures.

The risks associated with GRAZAX® are evaluated to be sufficiently handled by routine risk minimisation measures. No additional risk minimisation activities are planned for GRAZAX®.

VI.2.6 Planned post-authorisation development plan

A number of studies are ongoing with GRAZAX®, including a large study investigating the use of GRAZAX® in children. None of the ongoing studies are performed as a condition of the marketing authorisation, and no additional studies are planned.

VI.2.7 Summary of changes to the risk management plan over time

Table 32 Major changes to the risk management plan over time

Version	Date	Safety Concerns
8.0	09-Mar-2015	Anaphylactic reaction updated from potential to identified risk based on a single case of anaphylactic shock reported post-marketing
6.0	15-Sep-2009	Systemic allergic reactions upgraded from potential to identified risk based on cases reported post-marketing