Part VI: Summary of activities in the risk management plan

Overview of disease epidemiology

The prevalence of asthma has risen in affluent countries over the last 30 years but now appears to have stabilized, with approximately 10–12% of adults and 15% of children affected by the disease. In developing countries where the prevalence of asthma had been much lower, there is a rising prevalence, which is associated with increased urbanization. The prevalence of atopy and other allergic diseases has also increased over the same time, suggesting that the reasons for the increase are likely to be systemic rather than confined to the lungs. This epidemiologic observation suggests that there is a maximum number of individuals in the community, who are likely to be affected by asthma, most likely by genetic predisposition. Most patients with asthma in affluent countries are atopic, with allergic sensitization to the house dust mite *Dermatophagoides pteronyssinus* and other environmental allergens.

Summary of existing efficacy data

Inhaled corticosteroids are established drugs in the treatment of bronchial asthma. The inhaled corticosteroids attenuate bronchial inflammation and responsiveness to various trigger factors, improve the patient's clinical status and reduce the number of asthma attacks. Inhaled corticosteroids are the most potent and effective anti-inflammatory agents available for the treatment of patients with persistent asthma.

The results of randomised, placebo-controlled, double-blind studies have clearly demonstrated that nebulised budesonide is effective and can easily be delivered to infants and children who lack the coordination and understanding necessary to use pressurised metered-dose inhalers with a spacer or inhalation-driven devices.

Summary of safety concerns

The following identified and potential risks for budesonide are known and appropriately described with advice to patients and physicians for an appropriate use of the product:

Risk	**What is known**	**Preventability**
Systemic corticosteroid effects	Budesonide is a halogen-free glucocorticosteroid and share the actions of this class of hormones. Possible systemic effects include Cushing's disease. Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract, glaucoma, and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression or aggression (particularly in children).	Following normal medical and pharmacy practice, patients should be instructed on the proper use of Budesonide Nebuliser Suspension. The maintenance dose should be adjusted to the individual needs of the patient taking into account the severity of the disease and the clinical response of the patient. When therapeutic effects are obtained, the maintenance dose should be reduced to the lowest possible effective dose.
Risks in switching patients from oral corticosteroids to inhaled corticosteroids	Adrenal insufficiency may occur.	In patients being switched from systemic corticosteroids to inhaled budesonide, systemic corticosteroid therapy should be withdrawn gradually.
Concurrent use of CYP3A4 inhibitors	The metabolism of budesonide is primarily mediated by CYP 3A4. Inhibitors of this enzyme such as ketoconazole and itraconazole can, therefore, increase systemic exposure to budesonide several fold. Limited data about this interaction on high-dosed inhaled budesonide indicate that a considerable increase in the plasma concentration (on average four-fold) can occur if itraconazole 200 mg once daily is administered concomitantly with inhaled budesonide (1 mg single dose).	Concomitant use should be avoided. If this is not possible, the period between treatments should be as long as possible and a reduction of the budesonide could also be considered.

Summary of risk minimisation activities by safety concern

Please see the product information for details of routine risk minimisation measures.

Planned post-authorisation development plan

Not applicable.

Summary of changes to the risk management plan over time

Version	Date	Safety Concerns	Comment
1.0	26-July-2012 (initial submission of marketing authorisation application)	**Identified Risks:** - Systemic corticosteroid effects - Risks in switching patients from oral corticosteroids to inhaled corticosteroids **Potential Risks:** - Concurrent use of CYP3A4 inhibitors	Preapproval version. Returned to applicant for amendment.
1.1	18-March-2013	Safety concerns unchanged	Amended after receipt of assessment report.
2.0	4-November-2013	Safety concerns unchanged	Formal update as marketing authorisation is transferred to Teva