

## **VI.2 Elements for a Public Summary**

### **VI.2.1 Overview of disease epidemiology**

#### Asthma

Asthma is a common chronic inflammatory disease of the airways characterized by variable and recurring symptoms, reversible airflow obstruction, and bronchospasm. Common symptoms include wheezing, coughing, chest tightness, and shortness of breath.

It is one of the most common chronic diseases worldwide. There are an estimated 300 million affected individuals and 250,000 annual deaths worldwide by asthma. Asthma occurs in all countries regardless of the level of development. Prevalence appears to range from 1% to 18% in different countries, increasing in some and stabilised in others.

#### Pseudocroup (laryngitis subglottica)

Acute laryngotracheobronchitis (croup) is a common cause of acute upper airway obstruction in childhood, with an incidence of approximately 3 cases per 100 children less than 6 years of age. Croup refers to an infection of the upper airway, which obstructs breathing and causes a characteristic barking cough. The cough and other symptoms of croup are the result of swelling around the vocal cords (larynx), windpipe (trachea) and bronchial tubes (bronchi). When a cough forces air through this narrowed passage, the swollen vocal cords produce a noise similar to a seal barking. Likewise, taking a breath often produces a high-pitched whistling sound (stridor).

### **VI.2.2 Summary of treatment benefits**

Budesonide belongs to a group of steroids called glucocorticosteroids which can be used to reduce or prevent inflammatory reactions (swelling) in the lungs. This medicine can be used in adults, adolescents, children and infants aged 6 months and older.

Budesonide nebuliser suspension is used for the treatment of asthma. It is used in patients where other types of inhaler, such as a pressurised inhaler or an inhaler containing a dry powder are unsatisfactory or inappropriate.

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 major advantage of inhaled therapy is that drugs are delivered directly into the airways, producing higher local concentrations with significantly less risk of systemic side effects compared to oral use.

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.

Budesonide Nebuliser suspension is also indicated for treatment of very serious pseudocroup (laryngitis subglottica) in infants and children who are in hospital. Corticosteroids, such as dexamethasone and budesonide, have been shown to improve outcomes in children with all severities of croup. A number of studies in children with croup have compared Budesonide Nebuliser Suspension with placebo resulting with a reduction in the length of hospital stay and symptoms improvement.

### VI.2.3 Unknowns relating to treatment benefits

The efficacy of Budesonide Nebuliser Suspension in infants aged less than six months has not yet been established.

There are limited data available on the efficacy of Budesonide Nebuliser Suspension in overweight or obese children, however, weight loss is a key target that must be considered.

### VI.2.4 Summary of safety concerns

#### Important identified risks

| Risk                                                                                                                                                                                              | What is known                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              | Preventability                                                                                                                                                                                                                                                                                                                                                                                         |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Systemic corticosteroid effects (systemic means that the medicine is carried throughout the body in the bloodstream from the site of application and have general rather than only local effects) | <p>The following side effects have been reported:</p> <ul style="list-style-type: none"> <li>• Suppression of the adrenal gland (a small gland next to the kidney) can occur. The major symptoms of adrenal suppression include headaches, tiredness, feeling and being sick, weight loss, stomach pains and lack of appetite.</li> <li>• Feeling restless, nervous and irritable (these effects are more likely to occur in children).</li> <li>• Decrease in bone mineral density (thinning of the bones).</li> <li>• Glaucoma (increased pressure in the eye), aggression, sleeping problems and excitability</li> <li>• Anxiety</li> <li>• Depression</li> <li>• Clouding of the lens in the eye (Cataract)</li> </ul> | <p>The dose of inhaled corticosteroid should be titrated to the lowest dose at which effective control of asthma is achieved. Patients should always use this medicine exactly as the doctor has prescribed. Patients should check with their doctor or pharmacist if they are not sure.</p> <p>The doctor will advise patients of the correct dose, which will depend on how bad their asthma is.</p> |
| Risks in switching patients from oral corticosteroids to inhaled corticosteroids                                                                                                                  | The transfer of patients treated with oral corticosteroid to the inhaled corticosteroid and their subsequent management requires special care. If adrenal insufficiency occur doctor may consider adding steroid tablets to                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                | If patients have been taking steroid tablets for the asthma, their doctor may reduce the number of tablets that they take once they start to use                                                                                                                                                                                                                                                       |

| Risk | What is known                                                                                                                                                                                                                                                                                                                                                             | Preventability                                                                                                                                                                                                                   |
|------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|      | <p>the treatment during periods of stress (e.g. if patient has an infection, before surgery or worsening asthma attacks).</p> <p>During transfer from oral therapy to inhaled, patients might experience some symptoms as a result of this including a stuffy or runny nose, a lack of energy, depression, eczema (a type of skin rash) and joint and/or muscle pain.</p> | Budesonide Nebuliser Suspension. Patients should contact their doctor if any of the following symptoms persist: a stuffy or runny nose, a lack of energy, depression, eczema (a type of skin rash) and joint and/or muscle pain. |

### Important potential risks

| Risk                                | What is known (Including reason why it is considered a potential risk)                                                                                                                                                                                                                                                                                                                                                            |
|-------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Concurrent use of CYP3A4 inhibitors | <p>Inhibitors of the enzyme CYP3A4 such as medicines for the treatment of a fungal infection such as ketoconazole or itraconazole some medicines for HIV: ritonavir, cobicistat can increase systemic exposure to budesonide several fold.</p> <p>Patients are advised to tell their doctor or pharmacist if they are taking or have recently taken any other medicines, including medicines obtained without a prescription.</p> |

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

No additional risk minimisation measures are proposed.

### VI.2.6 Planned post authorisation development plan

Not applicable.

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

Major changes to the Risk Management Plan over time

| Version | Date                                                   | Safety Concerns                                                                                                                                                                                                                                                                                                    | Comment                                                                          |
|---------|--------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| 1.0     | 26 July 2012<br>(initial submission of MA application) | <p>Identified Risks:</p> <ul style="list-style-type: none"> <li>Systemic corticosteroid effects</li> <li>Risks in switching patients from oral corticosteroids to inhaled corticosteroids</li> </ul> <p>Potential Risks:</p> <ul style="list-style-type: none"> <li>Concurrent use of CYP3A4 inhibitors</li> </ul> | NA                                                                               |
| 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                  |
| 3.0     | 01 June 2017                                           | Safety concerns unchanged                                                                                                                                                                                                                                                                                          | Annex II updated with most recent version.<br>RMP translated to GVP EMA template |