Serevent Diskus Product Profile Summary

This information is provided in response to your request for information about Serevent® Diskus® (salmeterol xinafoate inhalation powder).

DISEASE: CONSENSUS TREATMENT GUIDELINES

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Asthma: The National Asthma Education and Prevention Program (NAEPP) asthma management guidelines recommend the addition of a long-acting beta$_2$-agonist (LABA) to an inhaled corticosteroid (ICS) as one of the preferred treatments for patients ≥ 5 years of age with moderate to severe persistent asthma who are new to controller therapy. [1] A LABA plus an ICS is also recommended as one of the preferred treatments in patients whose asthma is no longer controlled by low-dose ICS alone.

Chronic Obstructive Pulmonary Disease (COPD): The GOLD Guidelines recommend 1) inhaled long-acting bronchodilator therapy in patients with a forced expiratory volume in 1 second (FEV_1) <80% predicted, and 2) the addition of an ICS to long-acting bronchodilator therapy in chronic obstructive pulmonary disease (COPD) patients with a post-bronchodilator FEV_1 of <50% predicted and a history of repeated exacerbations. [2] The ATS/ERS guidelines state that data from trials using concomitant LABA plus an ICS shows a significant additional effect on pulmonary function compared with the individual components alone and using different medication classes is a way of delivering treatment to obtain better results including improved lung function. [3]

BENEFITS OF *SEREVENT DISKUS* IN ASTHMA

• *Serevent Diskus* contains the LABA, salmeterol xinafoate, in a convenient *Diskus* device with a built-in dose counter. [4]

• *Serevent Diskus* is approved for use in children 4 years of age and older with asthma and was evaluated in over 2,500 children 4 to 11 years old, including 346 children treated for 1 year. [4]

• *Serevent Diskus* is approved for prevention of exercise-induced bronchospasm (EIB) in patients 4 years of age and older. [4]

• *Serevent Diskus* provided clinically significant improvements in FEV_1 (≥ 15%) on Day 1, which lasted 12 hours. Median time to onset post first-dose ranged from 30 to 48 minutes with maximum improvement within 3 hours. [4]

• *Serevent Diskus* has demonstrated efficacy for up to 1 year in adults, adolescents and children 4 years of age and older. [4]

• Salmeterol xinafoate, administered via inhalation aerosol, in combination with an ICS provided significantly greater improvements in lung function, symptom scores, and rescue albuterol use compared to double-dose ICS. [4]

• *Serevent Diskus* provided significantly greater improvements in pulmonary function, asthma symptoms, and patient satisfaction than montelukast when added to current ICS therapy in patients 12 years of age and older. [5]

BENEFITS OF *SEREVENT DISKUS* IN COPD

• *Serevent Diskus* provided significant improvements in pulmonary function on Day 1 (FEV_1 ≥ 12% and at least 200 mL) which lasted 12 hours. Significant improvements were noted at 2 hours post first-dose, which were maintained throughout 24 weeks of treatment. The mean time post-dose to peak bronchodilator effect ranged from 3.27 to 4.75 hours. [4]

• *Serevent Diskus* was designed to provide consistent dose delivery via the *Diskus* device at a flow rate of 60 L/min for 2 seconds. Studies have shown that the mean peak inspiratory flow (PIF) through a *Diskus* was 82.4 L/min in adult patients with obstructive lung disease and severely compromised lung function (FEV_1 20% to 30% of predicted). (4)

EFFICACY IN ASTHMA

• In two 12-week, pivotal trials, *Serevent Diskus* provided a significant, rapid, and well-maintained improvement in lung function without evidence of tachyphylaxis to the bronchodilator effects and without increasing asthma exacerbation rates compared with "as needed" albuterol in adult and adolescent patients with asthma. (4) (6)

• In two 12-week, pivotal trials, *Serevent Diskus* provided significant improvement in lung function, asthma symptom scores, and rescue albuterol use compared with placebo in children 4 to 11 years old with asthma. (4) (7)

• In 4 pivotal trials, single-doses of *Serevent Diskus* prevented EIB when inhaled 30 minutes prior to exercise in adults, adolescents and children 4 to 11 years old. For many patients, this protective effect against EIB was still apparent up to 8.5 hours after a single dose. (4) (8) (9) (10)

EFFICACY IN COPD

• In 2 pivotal trials, *Serevent Diskus* provided greater improvements in pulmonary function endpoints compared with placebo in patients with chronic bronchitis with airflow limitation, with or without emphysema. Significant improvements in secondary endpoints assessing COPD symptoms were not seen. (4) (11)

SAFETY

• **BOXED WARNING:** Long acting $beta_2$-adrenergic agonists, such as salmeterol, the active ingredient in *Serevent Diskus*, may increase the risk of asthma-related death. Therefore, when treating patients with asthma, *Serevent Diskus* should only be used as additional therapy for patients not adequately controlled on other asthma controller medications (e.g., low- to medium-dose inhaled corticosteroids) or whose disease severity clearly warrants initiation of treatment with 2 maintenance therapies, including *Serevent Diskus*. Data from a large placebo-controlled US study that compared the safety of salmeterol (Serevent® Inhalation Aerosol) or placebo added to usual asthma therapy showed an increase in asthma-related deaths in patients receiving salmeterol (13 deaths out of 13,176 patients treated for 28 weeks on salmeterol versus 3 deaths out of 13,179 patients on placebo). (4) (12)

• The data from the Salmeterol Multicenter Asthma Research Trial (SMART) are not adequate to determine whether concurrent use of ICSs or other asthma-controller therapy modifies the risk of asthma-related death. No studies have been conducted that were adequate to determine whether the rate of death in patients with COPD is increased by LABAs. (4)

• It is important to watch for signs of worsening asthma, such as increasing use of inhaled, short-acting $beta_2$-agonists (SABAs) or a significant decrease in peak expiratory flow (PEF) or lung function. Such findings require immediate evaluation. (4)

• *Serevent Diskus* should not be used to treat acute symptoms. (4)

• *Serevent Diskus* should not be initiated in patients with significantly worsening or acutely deteriorating asthma, which may be a life-threatening condition. (4)

• *Serevent Diskus* is not a substitute for inhaled or oral corticosteroids. Corticosteroids should not be stopped or reduced when *Serevent Diskus* is initiated. (4)

• The most common adverse events ≥ 5%) reported in asthma clinical trials with *Serevent Diskus* (and placebo) in patients ≥ 12 years of age were: headache 13% (9%), nasal/sinus congestion 9% (6%), tracheitis/bronchitis 7% (4%), rhinitis 5% (4%), and influenza 5% (2%). (4)

• The most common adverse events (≥ 5%) reported in asthma clinical trials with *Serevent Diskus* (and placebo) in patients 4 to 11 years of age were: headache 17% (14%) and pharyngitis 6% (3%). (4)

• The most common adverse events (≥ 5%) reported in COPD clinical trials with *Serevent Diskus* (and placebo) were: headache 14% (11%), musculoskeletal pain 12% (10%), throat irritation 7% (6%), and cough 5% (4%). (4)

INDICATIONS

• **Asthma:** *Serevent Diskus* is indicated for long-term, twice-daily (morning and evening) administration in the maintenance treatment of asthma and in the prevention of bronchospasm in patients 4 years of age and older with reversible obstructive airway disease, including patients with symptoms of nocturnal asthma. LABAs, such as salmeterol, the active ingredient in *Serevent Diskus*, may increase the risk of asthma- related death. Therefore, when treating patients with asthma, *Serevent Diskus* should only be used as additional therapy for patients not adequately controlled on other asthma-controller medications (e.g., low- to medium-dose ICSs) or whose disease severity clearly warrants initiation of treatment with 2 maintenance therapies, including *Serevent Diskus*. It is not indicated for patients whose asthma can be managed by occasional use of inhaled SABAs or for patients whose asthma can be successfully managed by ICSs or other controller medications along with occasional use of inhaled SABAs. (4)

• **Prevention of Exercise-Induced Bronchospasm:** *Serevent Diskus* is also indicated for prevention of EIB in patients 4 years of age and older. (4)

• **COPD:** *Serevent Diskus* is indicated for the long-term, twice-daily (morning and evening) administration in the maintenance treatment of bronchospasm associated with COPD (including emphysema and chronic bronchitis). (4)

DOSING

• **Asthma:** For maintenance of bronchodilatation and prevention of symptoms of asthma, including the symptoms of nocturnal asthma, the usual dosage for adults and children 4 years of age and older is 1 inhalation (50 mcg) twice daily (morning and evening, approximately 12 hours apart). It is not indicated for patients whose asthma can be managed by occasional use of inhaled SABAs or for patients whose asthma can be successfully managed by ICSs or other controller medications along with occasional use of inhaled SABAs. If a previously effective dosage regimen fails to provide the usual response, medical advice should be sought immediately as this is often a sign of destabilization of asthma. Under these circumstances, the therapeutic regimen should be reevaluated. If symptoms arise in the period between doses, an inhaled SABA should be taken for immediate relief. (4)

• **COPD:** For maintenance treatment of bronchospasm associated with COPD (including chronic bronchitis and emphysema), the usual dosage for adults is 1 inhalation (50 mcg) twice daily (morning and evening, approximately 12 hours apart). (4)

• **Prevention of EIB:** One inhalation of *Serevent Diskus* at least 30 minutes before exercise has been shown to protect patients against EIB. When used intermittently as needed for prevention of EIB, this protection may last up to 9 hours in adolescents and adults and up to 12 hours in patients 4 to 11 years of age. Additional doses of salmeterol should not be used for 12 hours after the administration of this drug. Patients who are receiving *Serevent Diskus* twice daily should not use additional salmeterol for prevention of EIB. If regular, twice daily dosing is not effective in preventing EIB, other appropriate therapy for EIB should be considered. (4)

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