

Indiana Medicaid Therapeutics Committee Therapeutic Class Review Summary

Therapeutic class:

Long-acting Beta Agonist and Corticosteroid Combinations

Overview:

Beta₂-agonists are the most potent and rapidly acting bronchodilators available. The principal action of β₂-agonists is to relax airway smooth muscle by stimulating beta₂-receptors, which increases cyclic adenosine monophosphate (AMP) and produces functional antagonism to bronchoconstriction. In addition to their bronchodilatory effects, β₂-agonists also prevent bronchoconstriction, regardless of the stimulus (allergen, exercise, or cold air). The long-acting β₂-agonists have a duration of bronchodilation of at least 12 hours. The glucocorticoid component has potent anti-inflammatory activity.

Long-acting inhaled β₂-agonists and corticosteroid combinations should not be used for acute exacerbations, but should instead be used for the long-term maintenance treatment of asthma. Studies have shown that the maintenance use of long-acting β₂-agonists does not compromise the bronchodilator response to short-acting β₂-agonists during acute episodes of asthma. In general, inhaled long-acting beta agonists are preferred over oral sustained-release agents because they are longer acting and have fewer side effects.

Inhaled long-acting β₂-agonists have an important role in treating chronic asthma as adjunct therapy to inhaled corticosteroids. In randomized, controlled trials, the addition of salmeterol or formoterol to inhaled corticosteroid therapy resulted in statistically significant improvements in pulmonary function and asthma symptoms, and statistically significant reductions in supplemental short-acting β₂-agonist use. Data from a large, placebo-controlled US study that compared the safety of salmeterol or placebo added to usual asthma therapy showed a small but significant increase in asthma-related deaths in patients receiving salmeterol versus those on placebo. Subgroup analysis suggests the risk may be greater in African-American patients compared to Caucasians. As a result of this study, a black-box warning has been added to the product labeling for all long-acting beta agonists. Additionally, long-acting beta-agonists may increase the chance of severe asthma episodes and death when severe asthma episodes occur; a medication guide is now required for these agents. Advair Diskus[®] and Advair[®] HFA, the combination of both salmeterol and inhaled corticosteroid fluticasone, are also available. A new long-acting β₂-agonist and corticosteroid combination of budesonide and formoterol (Symbicort[®]) was recently approved.

Generic Name	Trade Name	Indications		Manufacturer
		Asthma	COPD	
Salmeterol and Fluticasone	Advair Diskus [®] , Advair [®] HFA	X	X (Advair Diskus)	GlaxoSmithKline
Formoterol and Budesonide	Symbicort [®]	X		AstraZeneca

Summary:

Salmeterol and formoterol are effective as adjunctive therapy to inhaled corticosteroids in the maintenance of asthma. Long-acting β_2 -agonists are not recommended as monotherapy because these agents do not affect the underlying inflammatory process of asthma. Advair Diskus[®], a combination of both salmeterol and fluticasone, is available for maintenance treatment of asthma in addition to COPD. The budesonide and formoterol combination product, Symbicort[®], has also been approved for the long-term maintenance treatment of asthma in adult patients. Data from a large, placebo-controlled US study that compared the safety of salmeterol or placebo added to usual asthma therapy showed a small but significant increase in asthma-related deaths in patients receiving salmeterol versus those on placebo. As a result of this study, a black-box warning has been added to salmeterol's labeling. Long-acting beta-agonists may increase the chance of severe asthma episodes and death when severe asthma episodes occur. A medication guide is now required for the long-acting beta agonists (ie, formoterol and salmeterol). Selection of an agent for the preferred drug list should be based upon FDA-approved indications, efficacy, safety, and cost.