

## **Long-Acting Beta-Agonist Therapy in Asthma**

Asthma is a complex condition characterized by airflow obstruction, bronchial hyperresponsiveness, and underlying inflammation. The prevalence of asthma continues to increase, now affecting over 22 million Americans.

Pharmacologic therapy in asthma is used to prevent and control symptoms, improve quality of life, and reduce asthma exacerbations. Both quick-relief and long-term control medications are used in the management of asthma. Inhaled corticosteroids (ICS) are the most important long-term control medications in children and adults with asthma; however, long-acting beta-agonists (LABAs) are also important for improved asthma control. LABAs are indicated for maintenance treatment in asthma as well as bronchospasm associated with chronic obstructive pulmonary disease (COPD). Salmeterol (Serevent) and formoterol (Foradil) are the two currently approved LABAs in the United States. Each is also available in combination products with inhaled steroids, salmeterol/fluticasone (Advair), formoterol/budesonide (Symbicort).

### **Key Points**

- Inhaled corticosteroids (ICSs) are the most important long-term control medications in children and adults with asthma
- Long-acting beta-agonists (LABAs) **should not be used as monotherapy** for long-term control of persistent asthma and should **always be combined with an ICS**
- Doses of LABAs should not exceed 2 puffs every 24 hours (100 mcg/day of salmeterol or 24 mcg/day of formoterol)
- LABAs may increase the risk of severe asthma exacerbations and/or asthma related deaths in certain patients
- Use of LABAs for the treatment of acute symptoms or exacerbations is not recommended
- Addition of a LABA in patients inadequately controlled with ICSs has been shown to improve lung function, decrease symptoms, and reduce exacerbations and use of short-acting beta-agonists
- Combination LABA with low- to medium-dose ICS is preferred over high-dose ICS alone in patients  $\geq 5$  years of age with moderate to severe persistent asthma
- Salmeterol and formoterol are approved for use in Idaho Medicaid patients with moderate to severe persistent asthma receiving ICSs
- Salmeterol/fluticasone (Advair) is approved for use in Idaho Medicaid patients with documented moderate to severe persistent asthma provided prior authorization criteria are met; formoterol/budesonide (Symbicort) is currently non-preferred

*Idaho Drug Utilization Review Program  
Educational Leaflet for Physicians, Pharmacists, and other Healthcare Practitioners*

In October 2007, the US National Asthma Education and Prevention Program (NAEPP) released the Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma.<sup>1</sup> These guidelines recommend that in patients who have moderate persistent asthma or asthma inadequately controlled on low-dose ICSs, increasing the dose of ICS should be given equal weight to adding a LABA. In patients who have severe persistent asthma the combination of LABA and ICS is preferred. The addition of a LABA in patients whose asthma is not controlled on low- or medium-dose ICS has been shown to improve lung function, decrease symptoms, and reduce exacerbations and use of short-acting beta-agonists to a greater extent than doubling the dose of ICSs.<sup>2,3</sup>

Although beneficial effects of LABAs have been shown for a majority of patients who require more than low dose ICSs to control asthma symptoms, clinical trial data has demonstrated LABAs may increase the risk of severe asthma exacerbations and/or asthma related deaths in certain patients. LABAs do not have any apparent anti-inflammatory activity; and therefore, should not be used as monotherapy for long-term control of persistent asthma. One study showed that discontinuation of ICS therapy following initiation of LABA resulted in an increase in asthma exacerbations.<sup>4</sup> Recently life-threatening and fatal reports of severe exacerbations have been associated with regular use of LABAs.<sup>5,6</sup> Studies show that the increased risk of exacerbations may be greater in the African-American population, patients receiving high-dose LABAs, and patients on LABA monotherapy without ICS.

The exact mechanism by which LABAs potentially increase asthma exacerbations has not yet been established. These drugs may have a direct adverse effect on bronchial smooth muscle, resulting in more severe obstruction following a bronchoconstrictive stimulus. LABAs may also provide maintenance of lung function despite worsening underlying inflammation, leading either to increases in obstruction or patients delaying appropriate medical attention for a severe exacerbation.<sup>1</sup>

#### References

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