Leukotriene Receptor Antagonist for the Treatment of Asthma

**Key Points**

- Inhaled corticosteroids are the most effective preventative therapy for persistent asthma in adults and children.

- For patients whose asthma is uncontrolled with an inhaled corticosteroid alone, the addition of a long-acting beta₂-agonist is more effective than the addition of a leukotriene receptor antagonist.

- For patients whose asthma is poorly controlled despite treatment with an inhaled corticosteroid and a long-acting beta₂-agonist, evidence indicates that the addition of a leukotriene receptor antagonist is no better than placebo.

- Monitoring, patient education, and treatment adherence are integral components in the management of asthma.

**Overview of Evidence & Recommendation**

1. **Inhaled corticosteroids (ICS) are the most effective preventative therapy for persistent asthma in both adults and children.**

   Available evidence clearly demonstrates that ICS is the preferred first-line treatment for persistent asthma. Results from published studies indicate that ICS is more effective than leukotriene receptor antagonist (LTRA) for first-line monotherapy of persistent asthma. Findings from a high quality systematic review comparing LTRA to ICS as first-line asthma therapy demonstrated that ICS was superior to LTRA for preventing asthma exacerbations, and for improving lung function, night awakenings, rescue medication use, symptom control and quality of life. The systematic review found no difference in the risk of side effects between ICS and LTRA.

   Moreover, a randomized controlled study showed that switching treatment (“step-down”) from an ICS to a LTRA may result in an increased risk of treatment failure (defined as the need for hospitalization, urgent medical visits for asthma, use of systemic corticosteroids, etc.).

   **Children**

   ICS is the preferred first-line treatment in both adults and children of all ages³. Evidence for the use of ICS as the preferred first-line treatment in children is further supported by a recent study. This study in children ages 6-14 years old with mild to moderate persistent asthma showed that ICS was superior to LTRA with respect to all measures of asthma control (e.g. asthma control days, exacerbation rate, and pulmonary function). Growth over the study duration of 48 weeks was not significantly different between the study group on ICS and the group on LTRA.

**Funding Status**

Montelukast (Singulair®) 4mg tablet will continue to be listed on the Ontario Drug Benefit Formulary as a Limited Use benefit for the treatment of asthma in patients aged 2-5 years old.

Montelukast (Singulair®) 5mg and 10mg tablets and zafirlukast (Accolate®) 20mg tablet will be funded through the Exceptional Access Program (EAP) according to the following revised criteria:

- For asthma patients who cannot manage the use of an inhalation device despite assistance with a spacer (e.g. physically or mentally challenged patients or pediatric patients).

The revised EAP criteria will take effect on October 15, 2008 for all new EAP requests. For patients with an existing EAP approval, coverage will remain effective until October 15, 2010, to allow adequate time for physicians to re-evaluate the patient’s treatment plan.

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1 Ducharme et al. Antileukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma in adults and children. Cochrane Database of Systematic Reviews 2004;(1):CD002314.


A common concern with the use of ICS in children is its effect on growth. It is important to note that children treated with ICS attain normal adult height but at a later age, while uncontrolled or severe asthma adversely affects growth and final adult height.3,

2. In patients whose asthma is inadequately controlled on ICS alone, the addition of a long-acting beta2-agonist (LABA) is superior to the addition of a LTRA.

In patients whose asthma is not controlled on ICS monotherapy, findings from a good quality systematic review5 showed that the addition of a LABA provided greater improvement in exacerbation rates, lung function, symptom control, use of rescue medication, quality of life and patient satisfaction as compared to the addition of a LTRA. The systematic review also found that withdrawals of treatment due to adverse events were not significantly different between patients who received add-on therapy with LABA and those who received add-on with LTRA.

3. For patients whose asthma is poorly controlled despite treatment with ICS and LABA, evidence indicates that add-on therapy with LTRA is no better than placebo.

A large, rigorous clinical study6 in patients with poorly controlled asthma despite ICS monotherapy or combination ICS plus LABA found that add-on therapy with LTRA was no better than placebo at improving the rate of poor asthma control, asthma symptoms or quality of life.

4. Monitoring, patient education, and treatment adherence are integral components in the management of asthma.

One of the most common reasons for a poor response to asthma therapy is non-adherence to treatment. The reported rates of non-adherence to asthma medication regimens range from 30-70%.3,7,8 Patients should be assessed for asthma control, medication technique and treatment adherence at regular intervals. Education has been shown to increase treatment adherence and improve important clinical outcomes in patients with asthma.

5. Role of LTRA in specific patient subgroups

Although LTRA has been shown to be effective against placebo in certain patient subgroups (e.g. patients with concomitant allergic rhinitis, aspirin-intolerant asthma, and exercise-induced asthma), direct head-to-head comparison studies against alternative treatments are lacking to establish the relative place in therapy of LTRA in these conditions.

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Committee to Evaluate Drugs

The Committee to Evaluate Drugs (CED) is an expert advisory group that makes recommendations to the Executive Officer of the Ontario Public Drug Programs. The CED's recommendations are based on an evaluation of the therapeutic value and cost-effectiveness of the drug relative to available alternatives. Membership on the CED includes practicing physicians, pharmacists, health economics experts, and patient representatives.

For more information about the Ontario Public Drug Programs and the Committee to Evaluate Drugs, please visit: www.health.gov.on.ca/english/providers/program/drugs/drugs_progrm_mn.html

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Ontario Ministry of Health and Long-Term Care

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