



Penguins marching towards 4<sup>th</sup> Stanley Cup

## PIC QUESTION OF THE WEEK: 4/12/10

Q: What are the current recommendations regarding the use of long-acting beta agonists in the management of asthma?

A: Long-acting beta agonists (LABAs) are bronchodilators possessing a duration of action of at least 12 hours following administration of a single dose. The two LABAs now available in the United States are salmeterol (Serevent) and formoterol (Foradil). These agents are contained in a variety of formulations and combination products, many of which are FDA-approved for the treatment of asthma, COPD, or both. The 2007 *National Heart Lung Blood Institute (NHLBI) Guidelines for the Diagnosis and Management of Asthma* recommends these agents, in combination with inhaled corticosteroids, for the treatment of moderate to severe persistent asthma. Using the stepwise approach to treatment, the guidelines include LABAs as a step 3 or higher option in children  $\geq 5$  years old and adults and as step 4 or higher in children 0-4 years old. On February 18, 2010, the FDA announced it would require label changes for all LABAs following release of data from a meta-analysis that questioned the safety of these agents when used in asthma. The data revealed an increased risk for exacerbation of asthma and death in those patients, including children, who use LABAs. There is conflicting evidence as to whether the combined use of LABAs and inhaled corticosteroids carries the same risk as using an LABA alone. Several ongoing studies are focusing on this issue. The mechanism by which LABAs increase the risk of exacerbation of asthma and death is still unclear. Some theorize these adverse events may be based on increased sensitivity to bronchoconstrictive stimuli or the masking of symptoms of worsening asthma. In addition to revised labeling changes, the FDA now requires distribution of an updated Medication Guide with all LABAs. A summary of the updated FDA recommendations is presented below:

- **LABAs are not to be used as monotherapy in the treatment of asthma. If used, they must be administered in combination with another controller medication.**
- **LABAs should not be used to control asthma symptoms if such symptoms can be managed using a different controller medication.**
- **If LABAs must be used, they should be administered for the shortest time possible; once control is achieved, the patient should be maintained on another controller medication. (This conflicts with current NHLBI guidelines that recommend step-down therapy be initiated by decreasing the dose of inhaled corticosteroids prior to discontinuing the LABA.)**
- **Patients who require the use of a LABA and inhaled corticosteroids should use a combination product containing both agents to ensure compliance with both medications.**

### References:

- Chowdhury B, Pan G. The FDA and safe use of long-acting beta-agonists in the treatment of asthma. *N Engl J Med.* 2010; 362:1169-71.
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