Therapeutic Class Overview
Short-acting β₂-Agonists

Therapeutic Class

- **Overview/Summary:** Respiratory short-acting β₂-agonists (SABAs) are Food and Drug Administration (FDA)-approved indications include asthma, chronic obstructive pulmonary disease, exercise-induced bronchospasm (EIB), and/or and reversible bronchospasm. Respiratory β₂-agonists act preferentially on the β₂-adrenergic receptors. Activation of these receptors on airway smooth muscle leads to the activation of adenylyl cyclase and an increase in intracellular cyclic-3',5'-adenosine monophosphate (cyclic AMP). The increase in cyclic AMP leads to activation of protein kinase A and the inhibition of myosin phosphorylation resulting in lower intracellular ionic calcium and smooth muscle relaxation. Increased cyclic AMP levels also inhibit the release of mediators from mast cells in the airways. The β₂-agonists can be divided into two categories: short-acting and long-acting. The short-acting respiratory β₂-agonists consist of albuterol (ProAir HFA®, ProAir RespiClick®, Proventil HFA®, Ventolin HFA®), 6-oxoalbuterol (Xopenex®, Xopenex HFA®), metaproterenol and terbutaline. Respiratory β₂-agonists elicit a similar biologic response in patients suffering from reversible airway disease, but differ in their dosing requirements, pharmacokinetic parameters and potential adverse events. As a result of the Clean Air Act and the Montreal Protocol on Substances that Deplete the Ozone Layer, the FDA made the decision to end production, marketing and sale of all albuterol metered dose inhalers (MDIs) containing chlorofluorocarbons (CFCs) as their propellant by December 31, 2008. These inhalers were replaced by MDIs which use hydrofluoroalkanes (HFAs). There is no difference in the safety or efficacy of the HFA inhalers compared to the CFC inhalers; however, there may small differences in taste and/or feel with the HFA inhalers. The deadline for removal of the pirbuterol (Maxair®) CFC inhaler is December 31, 2013.

**Table 1. Current Medications Available in the Therapeutic Class**¹⁻¹⁵

<table>
<thead>
<tr>
<th>Generic (Trade Name)</th>
<th>Food and Drug Administration Approved Indications</th>
<th>Dosage Form/Strength</th>
<th>Generic Availability</th>
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<tbody>
<tr>
<td><strong>Short-Acting β₂-agonists</strong></td>
<td>Relief of bronchospasm in patients with asthma†, treatment or prevention of bronchospasm in patients with reversible obstructive airway disease†‡§, prevention of exercise-induced bronchospasm†‡</td>
<td><strong>Dry Powder Inhaler:</strong> 90 µg</td>
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<td><strong>Meter dose aerosol inhaler (HFA):</strong> 120 µg albuterol sulfate#</td>
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<td><strong>Solution for nebulization:</strong> 0.63 mg 1.25 mg 2.5 mg 0.5% concentrated solution (3 mL unit dose vials)</td>
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<td><strong>Sustained-release tablet:</strong> 4 mg 8 mg</td>
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<td><strong>Syrup:</strong></td>
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### Therapeutic Class Overview: short acting β2-agonists

<table>
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<tr>
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</table>
| **Levalbuterol** (Xopenex®, Xopenex HFA<sup>®</sup>) | Treatment or prevention of bronchospasm in patients with reversible obstructive airway disease<sup>†</sup> | 2 mg/5 mL Tablet: 2 mg 4 mg  
Meter dose aerosol inhaler (HFA): 59 µg<sup>¶</sup> 
Solution for nebulization: 0.31 mg 0.63 mg 1.25 mg (3 mL vials) | ✔️ |
| **Metaproterenol**<sup>*</sup>         | Prevention and treatment of asthma and reversible bronchospasm, which may occur in association with bronchitis and emphysema | Syrup: 10 mg/5 mL  
Tablet: 10 mg 20 mg | ✔️ |
| **Terbutaline**<sup>*</sup>           | Prevention and treatment of asthma and reversible bronchospasm, which may occur in association with bronchitis and emphysema | Injection: 1 mg/mL (2 mL vial)  
Tablet: 2.5 mg 5 mg | ✔️ |

<sup>†</sup>Generic available in at least one dosage form or strength.  
<sup>‡</sup>Inhalation solution.  
<sup>¶</sup>Metered-dose inhaler.  
<sup>§</sup>Dry powder inhaler.  
<sup>‖</sup>Oral formulations.  
<sup>¶</sup>Delivering 45 µg levalbuterol base.  
<sup>#</sup>Delivering 108 µg of albuterol (90 µg albuterol base).

### Evidence-based Medicine
- Clinical trials have demonstrated the efficacy SABAs in providing relief from reversible bronchospasms and EIA.<sup>21-41</sup>
- Safety and efficacy of albuterol dry powder inhaler (ProAir Respiclick<sup>®</sup>) was evaluated in two 12-week randomized, double-blind, placebo-controlled studies. Forced expiratory volume in one second (FEV<sub>1</sub>) was significantly improved with albuterol dry powder inhaler compared with placebo (no P value reported).<sup>7</sup>
- In clinical trials that comparing albuterol to levalbuterol, inconsistent results have been reported and have not consistently demonstrated improved outcomes with levalbuterol compared to albuterol. Moreover, studies have shown no significant differences between the two agents in the peak change in FEV<sub>1</sub> or the number and incidence of adverse events.<sup>21-31</sup>

### Key Points within the Medication Class
- According to Current Clinical Guidelines:
  - Short-acting β<sub>2</sub>-agonists are recommended for patients in all stages of asthma, for symptomatic relief of reversible airway disease and for exercise-induced bronchospasm.<sup>17-20</sup>
  - Short-acting β<sub>2</sub>-agonists should be used on an as-needed or “rescue” basis.<sup>17-20</sup>
Anticholinergics may also be used for the treatment of acute exacerbations but are considered less effective than SABAs.17-20

The addition of a systemic corticosteroid may be required if patients do not respond immediately to treatment with a SABA or if the exacerbation is severe.17-20

The use of LABAs to treat acute symptoms or exacerbations of asthma is not recommended.17

Other Key Facts:

- Studies have failed to consistently demonstrate significant differences between products.
- Albuterol oral solution, oral tablets, and solution for nebulization, levalbuterol solution for nebulization, metaproterenol oral solution and oral tablets, and terbutaline oral tablets and solution for injection are available generically.
- There are currently branded albuterol hydrofluoroalkanes (HFA) inhalers and one dry-powder inhaler; however, no generic equivalents are available.

References