

spasm due to exercise. The onset of activity is quick (1-2 minutes) and length of activity is 4-8 hours. The agents, when given as an HFA or a nebulizer solution, have similar effectiveness. It is important to note that 1.25 mg of levalbuterol base is equal to 2.5 mg of albuterol. The most common side effects of albuterol are excitement, nervousness, and tremor. Levalbuterol is more likely to cause headache and vomiting. All patients with asthma should have a short-acting  $\beta_2$ -agonist on hand in case they start to have airway spasms.<sup>1,8,30,35</sup>

### Long-Acting and Ultra-Long-Acting

The long-acting (Table 12) and ultra-long-acting  $\beta_2$ -adrenergic agonists should only be used with other agents, such as ICS, for treating chronic asthma. Using these agents alone can increase the chance of acute severe asthma attacks and asthma-related death.<sup>43</sup> In fact, there is a boxed warning against their use without ICS. A boxed warning is the Food and Drug Administration's (FDA) strictest warning to alert the public to serious adverse effects. Many long-acting and ultra-long-acting  $\beta_2$ -adrenergic agonists are supplied as combination products with ICS (Table 13).

Formoterol is only available in the US as a part of combination products.<sup>31,36</sup> Long-acting  $\beta_2$ -adrenergic agonists have a duration of activity of about 12 hours or more. This longer length of activity compared to short-acting  $\beta_2$ -adrenergic agonists allows for twice daily dosing and use as maintenance therapy. While the length of activity is similar, onset of activity differs. For example, formoterol starts to work in 1-2 minutes, while salmeterol's effects are typically seen around 10 minutes.

Vilanterol is the only ultra-long-acting  $\beta_2$ -adrenergic agonist that is approved for asthma in the US. It is only available as a combination product with fluticasone furoate.<sup>24</sup> Like albuterol, the onset of activity for vilanterol is 1-2 minutes. However, its length of activity is 24 hours or longer, which allows for once daily dosing. The long-acting and ultra-long-acting  $\beta_2$ -adrenergic agonists have mild side effects like headache and back or joint pain.<sup>24,31,36,44</sup>

### Combination Products

The long-acting and ultra-long-acting  $\beta_2$ -adrenergic agonists are available as combination inhaler products with corticosteroids (Table 13). This is easier for patients who need two different medications for their asthma.

Also, since the two classes of medications are within the same inhaler, it is not possible to stop the corticosteroid and only take the  $\beta_2$ -adrenergic agonist by itself. As a result, the boxed warning for long-acting and ultra-long-acting  $\beta_2$ -adrenergic agonists increasing acute severe asthma attack and asthma-related death was removed for combination products with ICS.<sup>45</sup>

**Table 11.**  
Correction updated 11/9/22.

Agent	Dosage Form	4-11 years	12 years or older
Albuterol (PROAIR HFA; PROVENTIL HFA; VENTOLIN HFA)	90 mcg/puff (200 puffs/canister)	1-2 puffs every 4-6 hours as needed	2 puffs every 4-6 hours as needed
Albuterol (ProAir RespiClick)	90 mcg/puff (200 puffs/inhaler)	2 puffs every 4-6 hours as needed	2 puffs every 4-6 hours as needed
Albuterol nebulizer solution (ACCUNEB)	0.63 mg/3 mL; 1.25 mg/3 mL; 2.5 mg/3 mL; 2.5 mg/0.5mL	5-11 years: 0.63-5 mg in 3 mL saline every 4-8 hours as needed	1.25-5 mg in 3 mL saline every 4-8 hours as needed
Levalbuterol (XOPENEX HFA)	45 mcg/puff (200 puffs/canister)	2 puffs every 4-6 hours as needed	2 puffs every 4-6 hours as needed
Levalbuterol nebulizer solution (XOPENEX)	0.31 mg/3 mL; 0.63 mg/3 mL; 1.25 mg/0.5 mL; 1.25 mg/3 mL	6-11 years: 0.31-1.25 mg in 3 mL saline every 4-8 hours as needed	0.63-1.25 mg in 3 mL saline every 6-8 hours as needed

Agent	Dosage Form	4 years or Older
Salmeterol (SEREVENT DISKUS)	50 mcg/blister (60 blisters/inhaler)	Contents of one blister every 12 hours

**Test Your Knowledge #13**

*True or False*

Formoterol is only available in the United States as a part of a combination product. \_\_\_\_\_

*Answers can be found on page 16.*