

New Drug Bulletin:
Budesonide and Formoterol (Symbicort® -AstraZeneca)

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Symbicort® is a combination of budesonide and formoterol labeled for the long-term, maintenance treatment of asthma. Budesonide (Pulmicort®) and formoterol (Foradil®) are individually available for the treatment of asthma.

Budesonide is a synthetic corticosteroid that suppresses pulmonary inflammation through a variety of mechanisms. Formoterol is a long-acting beta2-agonist 200 times more selective for beta2 receptors compared to beta1 receptors. Activation of beta₂ receptors in the lungs relaxes bronchial smooth muscle and decreases release of inflammatory mediators.

Budesonide is rapidly absorbed from the lungs. When taken orally, it exhibits extensive first pass metabolism. Its volume of distribution is 3 L/kg, and it is 85-90% plasma protein bound. It is metabolized via cytochrome-P450 (CYP) 3A4 to 2 major metabolites. The metabolites are excreted in the urine and feces. Budesonide has a half life of 2-3 hours. Formoterol is rapidly absorbed when inhaled. The plasma protein binding is 46-58%. The primary metabolic pathways are glucuronidation and oxidation via CYP 2D6 and CYP 2C. Formoterol is excreted in the urine and feces. Dosage adjustments of Symbicort® are not required for geriatric patients. Safety has not been established in patients less than 12 years old.

In clinical studies, Symbicort® was more effective in most clinical endpoints compared to budesonide or formoterol alone. It showed similar results compared to budesonide and formoterol given via separate inhalers. One trial comparing Symbicort® to Advair® in adults with asthma showed no clinically significant differences between groups.

Formal drug interaction studies with Symbicort® are not available. Some potential drug interactions include inhibitors of CYP 2C, CYP 2D6, or CYP 3A4, diuretics, monoamine oxidase inhibitors, and tricyclic antidepressants. Common adverse reactions (≥3% incidence or greater incidence than placebo) to Symbicort® include nasopharyngitis, headache, upper respiratory tract infection, pharyngolaryngeal pain, sinusitis, influenza, back pain, nasal congestion, stomach discomfort, vomiting, and oral candidiasis. Rare adverse events reported include anaphylactic reaction, bronchospasm, hypocorticism, glaucoma, cataracts, and psychiatric symptoms.

Symbicort® is contraindicated as the primary treatment of status asthmaticus or acute episodes of asthma. Similar to Advair®, Symbicort® carries a black box warning regarding increased risk of death with long acting beta2-agonists. Symbicort® may cause paradoxical bronchospasm; discontinue the medication if paradoxical spasm occurs. Do not initiate Symbicort® during acute asthma exacerbations. Do not use

salmeterol, another long-acting beta₂ agonist, or additional formoterol while using Symbicort®. Use Symbicort® in caution in patients with cardiovascular disorders such as: coronary insufficiency, cardiac dysrhythmias, or hypertension. Use with caution in patients transferring from systemic corticosteroid therapy because of potential hypothalamic-pituitary-adrenal axis suppression.

Symbicort® is dosed twice daily. The maximum dose per day is 640 mcg budesonide/18 mcg formoterol. Before initial use and when not used for more than 7 days, prime the inhaler by releasing 2 test sprays. Shake the inhaler well for 5 seconds prior to each use. Symbicort® is a metered-dose inhaler available in strengths of 160 mcg budesonide/4.5 mcg formoterol and 80 mcg budesonide/4.5 mcg formoterol. Inhalers contain 120 inhalations or 60 inhalations (institutional pack). Discard inhaler after 120 inhalations or 3 months after opening. A “float” test is not effective for determining if contents remain in the inhaler. Store Symbicort® at room temperature 20-25°C (68-77°F) with the mouth piece down and the canister vertical.

A cost comparison of Symbicort® and Advair® is presented in the table below.

Table. Wholesale Acquisition Cost Comparison of Symbicort® and Advair®

Agent	Regimen	Cost per inhaler	Inhalations per inhaler	Cost per inhalation
Symbicort® (Budesonide / Formoterol)				
80 / 4.5	2 inhalations twice	\$212	120	\$1.76
160 / 4.5	daily	\$242	120	\$2.01
Advair HFA® (Fluticasone / Salmeterol)				
45 / 21	2 inhalations twice	\$212	120	\$1.76
115 / 21	daily	\$263	120	\$2.19
230 / 21		\$360	120	\$3.00
Advair Diskus® (Fluticasone / Salmeterol)				
100 / 50	1 inhalation twice daily	\$220	60	\$3.67
250 / 50		\$274	60	\$4.57
500 / 50		\$375	60	\$6.25

In summary, Symbicort® contains budesonide a corticosteroid and formoterol a long-acting beta₂ agonist. One clinical trial comparing Symbicort® to Advair® in adult patients with asthma shows no differences between the two products. Symbicort® must be dispensed with the patient Medication Guide.

References

1. AstraZeneca. Budesonide/formoterol (Symbicort) package insert. Wilmington, DE: AstraZeneca;2006
2. Dahl R, Chuchalin A, Gor D, et al. A randomized trial comparing salmeterol/fluticasone propionate and formoterol/budesonide combinations in adults with persistent asthma. *Respir Med.* 2006;100(7):1152-1162.

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