Short-Acting Beta Agonists (SABA)

SABA: *Class Overview*				
Indication	***MOA***	***Common Side Effects (>3% reported frequency)***	***Warnings/Precautions***	***Counseling Points***
- Treatment or prevention of bronchospasm - Prevention of exercise-induced bronchospasm (only albuterol HFA/DPI)	Activation of beta$_2$-adrenergic receptors leads to the activation of adenylyl cyclase and to an increase in the intracellular concentration of cyclic-3', 5'-adenosine monophosphate (cyclic AMP). This increase of cyclic AMP is associated with the activation of protein kinase A, which in turn inhibits the phosphorylation of myosin and lowers intracellular ionic calcium concentrations, resulting in muscle relaxation. Albuterol/Levalbuterol relaxes the smooth muscle of all airways, from the trachea to the terminal bronchioles.	Headache Tachycardia Pain Dizziness Pharyngitis Rhinitis Cough	- Hypersensitivity reactions: angioedema, rash, urticaria - Hypokalemia and changes in blood glucose may occur - Cardiovascular effects may occur - Paradoxical bronchospasm - Overdosage - Asthma Deterioration: monitor need for more doses	- Do not exceed recommended dose - The use of DPI inhalers, such as ProAir Respiclick, is contraindicated in patients with severe hypersensitivity to milk proteins (avoid if lactose-intolerant)

SABA: *Available Medications*

Name (Brand)	Dosage Forms	Product Images	FDA-Approved Indicated Age	Dosage Strengths
Albuterol Sulfate (ProAir)	HFA		4+ yrs	90 mcg/puff (200 puffs)
	RespiClick (DPI)		12+ yrs	90 mcg/puff (200 puffs)
Albuterol Sulfate (Proventil)	HFA		4+ yrs	90 mcg/puff (200 puffs)
Albuterol Sulfate (Ventolin)	HFA		4+ yrs	90 mcg/puff (60 puffs) 90 mcg/puff (200 puffs)
Albuterol Sulfate (AccuNeb)	Nebulizer		2-12 yrs	0.63 mg/3 mL (0.021%) 1.25 mg/3 mL (0.042%) 2.5 mg/3 mL (0.083%) 2.5 mg/0.5mL (0.5%)
Levalbuterol (Xopenex)	HFA		4+ yrs	45 mcg/puff (200 puffs)
	Nebulizer		6+ yrs	0.31 mg/3 mL 0.63 mg/3 mL 1.25 mg/3 mL 1.25mg/0.5mL

Children's Mercy

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SABA: *Pharmacokinetics*[1]

Name (Brand)	Particle Size (µm)	Onset (minutes)	DDI/ Metabolism	Active Metabolite	Serum t ½ (h)	Protein binding (%)	PO Bioavailability (%)	Lung delivery (%)	Renal Excretion (%)
Albuterol Sulfate (ProAir, Proventil, Ventolin)	3.39	5-8	MAO-I TCA Digoxin Beta-blockers Loop/thiazide diuretics	R/S-albuterol sulfate	4-6	10	10-20	50-60	80-100
Albuterol Sulfate (AccuNeb)	<5	<5	MAO-I TCA Digoxin Beta-blockers Loop/thiazide diuretics	R/S-albuterol sulfate	4-6	10	10-20	<20	80-100
Levalbuterol (Xopenex)	3.05	5-10	MAO-I Loop/thiazide diuretics Digoxin Beta-blockers	R-albuterol sulfate	3.3-4	10	10-20	N/A	80-100

[1] Medications delivered via inhalation are directly delivered to the target organ, typically yielding high pulmonary efficacy with minimal systemic side effects. However, the efficacy of inhaled drugs depends on pulmonary-specific pharmacokinetic processes and the ability for the drug particles to deposit throughout the lungs. This table reflects the relevant pharmacokinetic parameters for inhaled formulations. Particle size determines the likelihood of the drug depositing in the lungs (0.5 – 5 um) or in the oropharyngeal region ($\geq$ 5 um): smaller particles (0.5 – 3 um) typically deposit peripherally in the lungs, such as alveolar space, and larger particles (3-5 um) typically deposit in the upper conducting airways. The particle size and associated site of deposition impacts the drug's absorption into the lungs, onset of action, systemic clearance, and oral bioavailability. Due to differences in surface area, perfusion, and epithelial thickness, absorption of inhaled drugs is generally faster in the alveoli (the deposition site for smaller particles) and slower in the conducting airways (the deposition site for larger particles), which impacts the drug's time to onset. Moreover, mucociliary clearance is fastest in the larger conducting airways, ultimately clearing larger drug particles the most quickly and allowing smaller particles a longer duration. Generally, high systemic clearance and a low oral bioavailability is key to minimizing systemic exposure of inhaled formulations. An inhaled drug with a high oral bioavailability implies absorption of swallowed particles that deposited in the conducting airways or oropharyngeal region instead of depositing in the alveolar space, which is the optimal deposition site for maximal absorption and airway selectivity. Similarly, inhaled drugs with low systemic clearance have higher systemic exposure and are associated with poor airway selectivity.

SABA: *HFA/DPI Comparative Dosing*

Name (Brand)	Dosage Forms	Dosing for Bronchospasms	Dosing for Exercise-Induced Bronchospasms	Max Daily Dose	Priming	Clinical Pearls
Albuterol Sulfate (ProAir)	HFA	2 puffs by mouth q4-6 hours	2 puffs by mouth 5-20 min prior to exercise	12 puffs/day	- Prime before using for the first time - If not used for >2 weeks, prime by spraying **3** sprays into the air, away from the face	
	RespiClick	2 puffs by mouth q4-6 hours	2 puffs by mouth 5-20 min prior to exercise	12 puffs/day	- No priming required for DPI	- Do not use with spacer
Albuterol Sulfate (Proventil)	HFA	2 puffs by mouth q4-6 hours	2 puffs by mouth 5-20 min prior to exercise	12 puffs/day	- Prime before using for the first time - If not used for >2 weeks, prime by spraying **4** sprays into the air, away from the face	
Albuterol Sulfate (Ventolin)	HFA	2 puffs by mouth q4-6 hours	2 puffs by mouth 5-20 min prior to exercise	12 puffs/day	- Prime before using for the first time - If not used for >2 weeks, spray **4** sprays into the air away from the face	
Levalbuterol (Xopenex)	HFA	2 puffs by mouth q4-6 hours	NOT indicated	12 puffs/day	- Prime before using for the first time - If not used for **>3 days**, prime by spraying **4 sprays** into the air, away from the face	- Levalbuterol is the therapeutically active, R-enantiomer of albuterol[1]

[1]Albuterol is a racemic mixture of (S)-albuterol and (R)-albuterol (levalbuterol), where (S)-albuterol is considered inert with side effects such as cytokine production and increased immune cell proliferation. As the therapeutically active component of albuterol, levalbuterol is administered as a single isomer to avoid the potential unwanted side effects of (S)-albuterol. However, levalbuterol costs more than racemic albuterol and incidences of paradoxical bronchospasms have been documented with levalbuterol usage. Moreover, reviews of recent literature have not demonstrated the superiority of levalbuterol to albuterol in efficacy and safety for patients with acute asthma (Jat KR, Khairwa A. Pulm Pharmacol Ther. 2013).