









Inhaled Corticosteroids (ICS)

ICS: Class Overview

<i>Indication</i>	<i>MOA</i>	<i>Common Side Effects (>3% reported frequency)</i>	<i>Warnings/Precautions</i>	<i>Counseling Points</i>
<ul style="list-style-type: none"> - Maintenance and prophylactic therapy for asthma in patients, as indicated by age. <p>NOT INDICATED FOR THE RELIEF OF ACUTE BRONCHOSPASM</p>	<p>ICS have been shown to have multiple anti-inflammatory effects that contribute to their efficacy in asthma, including inhibiting both inflammatory cells (mast cells, eosinophils, basophils, lymphocytes, macrophages, and neutrophils) and release of inflammatory mediators (histamine, eicosanoids, leukotrienes, and cytokines).</p>	<ul style="list-style-type: none"> - Dysphonia/hoarseness - Headache - Nausea - Oral candidiasis - Upper RTI - Allergic rhinitis 	<ul style="list-style-type: none"> - Hypersensitivity reactions: angioedema, rash, urticaria - Localized infection: Candida albicans infection of the mouth and throat - Immunosuppression: potential worsening of existing infections - Paradoxical bronchospasm - Adrenal suppression/Cushing's - Decrease in bone mineral density - Eye disorders: changes in vision - Growth effects: reduction in growth velocity in pediatrics 	<ul style="list-style-type: none"> - Treat acute asthma exacerbations with an inhaled, SABA (such as albuterol). - Rinsing the mouth with water without swallowing after inhalation is advised to help reduce the risk of thrush - The use of DPI inhalers is contraindicated in patients with severe hypersensitivity to milk proteins (avoid if lactose-intolerant)

ICS: Available Medications

Name (Brand)	Dosage Forms	Product Images	FDA-Approved Indicated Age	Dosage Strengths	CMKC Formulary (Y/N)
Beclomethasone (Qvar®)	RediHaler (breath-activated)		4 y+	40 mcg/puff	N
				80 mcg/puff	
Budesonide (Pulmicort®)	Flexhaler (DPI)		6 y+	90 mcg/puff	Y
	Respules (NEB)		12 mon – 8 y	0.25 mg/2mL	
				0.5 mg/2mL	
				1 mg/2mL	
Ciclesonide (Alvesco®)	HFA		12 y+	80 mcg/puff	N
				160 mcg/puff	
Fluticasone furoate (Arnuity®)	Ellipta (DPI)		5 y+	50 mcg/puff	N
				100 mcg/puff	
				200 mcg/puff	
Fluticasone propionate	HFA		4 y+	44 mcg/puff	Y
				110 mcg/puff	
				220 mcg/puff	
Mometasone (Asmanex®)	HFA		5 y+	50 mcg/puff	Y
				100 mcg/puff	
				200 mcg/puff	
	Twisthaler (DPI)		4 y+	110 mcg (100 mcg/puff)	Y
			220 mcg (200 mcg/puff)		

ICS: Pharmacokinetics¹

Name (Brand)	Particle Size ^{2,3} (µm)	Onset (h)	DDI/ Metabolism	Active Metabolite	Serum t _½ (h)	Protein binding (%)	PO Bioavailability (%)	Lung delivery (%)	Vd (L)	Systemic CL (L/hr)	Renal Excretion (%)
Beclomethasone (Qvar®)	~1.1	0.5	3A4	Beclomethasone-17-monopropionate	2.8	87	20/40 (metabolite)	50-60	20/424	150/120	<10
Budesonide (Pulmicort®)	2-3	1-2	3A4 (major)	16α-hydroxyprednisolone 6β-hydroxybudesonide	2-3	88	11	15-30: DPI 5-8: NEB	280	84	60
Ciclesonide (Alvesco®)	~1.1	Not reported	3A4 (minor)	Des-ciclesonide	6-7	99	<1	50	207/897	152/228	≤20
Fluticasone furoate (Arnuity®)	~4	0.5-1	3A4	N/A	24	99.6	1.3	13.9	661	66	1-2
Fluticasone propionate	<5	Variable	3A4 (major)	N/A	14.4	90	≤ 1	15-20: DPI	318-859	66	<5
Mometasone (Asmanex®)	~2	1-2.5	3A4 (minor)	N/A	5 (IV)	99	<1	11	152	53	8

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 µm) or in the oropharyngeal region (≥ 5 µm): smaller particles (0.5 – 3 µm) typically deposit peripherally in the lungs, such as alveolar space, and larger particles (3-5 µm) 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.

² Ali HS, York P, et al. *Iran J Pharm Res.* 2014;13(3):785-795.

³ Leach C, Colice GL, et al. *Journal of Allergy and Clinical Immunology.* 2009;124(6).

ICS: Comparative Dosing (mcg/day)									
Name (Generic)	Dosage Forms	Children 6-11 years				Adults and Adolescents (>12 years)			
		Low	Medium	High	Max daily dose	Low	Medium	High	Max daily dose
Beclomethasone (Qvar®)	RediHaler**	80-160	160-320	>320	160	80-240	240-480	>480	640
Budesonide (Pulmicort®)	Respules (NEB)	250-500	500-1000	>1000	1000	N/A	N/A	N/A	N/A
	Flexhaler (DPI)	90-180	180-400	>400	6-17 yr: 720	180-360	360-720	>720	6-17 yr: 720 18+ yr: 1440
Ciclesonide (Alvesco®)	HFA	80 [±]	80-160 [±]	>160 [±]	N/A	80-160	160-320	>320	640
Fluticasone furoate (Arnuity®)	Ellipta (DPI)	50	50	N/A	50	100	100	200	200
Fluticasone propionate (Flovent®)	HFA**	88-176	>176-352	>352	880	88-264	264-440	>440	1760
	Flovent Diskus (DPI)**	50-100	100-200	>200	200	100-250	250-500	>500	2000
Mometasone (Asmanex®)	HFA	100	100	200	200	200-400	200-400	>400	800
	Twisthaler (DPI)**	100	100	100	100	100-200	200-400	>400	800

[±] = Only FDA-approved for ages ≥ 12 years

** = FDA-approved for ages 4 years and up