

Asthma Management Webinar

2021 Provider Training

AGENDA

Asthma Management Guidelines

• Myron Liebhaber, MD, Sansum Clinic

Medications & Delivery Devices

• Adam Horn, Pharm.D., CenCal Health

CenCal Health Breathe SMART Program

 Rachel Ponce, Senior Population Health Specialist, CenCal Health

Q & A



www.cencalhealth.org/asthma



Asthma Management Guidelines



Myron Liebhaber, MD, Sansum Clinic

Asthma Management Guidelines

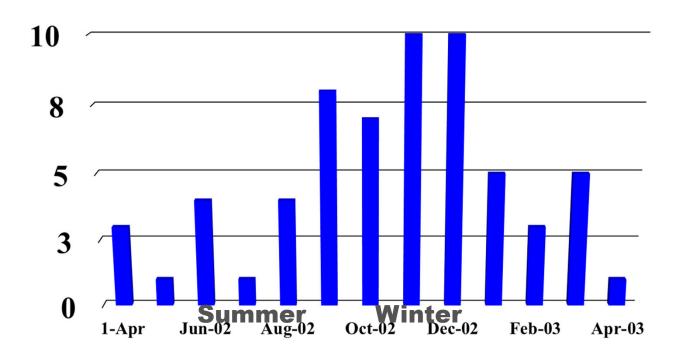
Six priority topic areas based on the state of science and needs assessment

- 1. Last updated 2013
- 2. 6 topics have significant new information
- 3. Used GRADE methodology and evidence based recommendations
- 3. Certainty of evidence: High, Moderate, Low, Very low
- 4. Strength of recommendations: Conditional, Strong
- 5. JACI, Dec 2020 volume 146 No. 6 Not included: Biologics

Systematic Review of Key Questions in Asthma Care

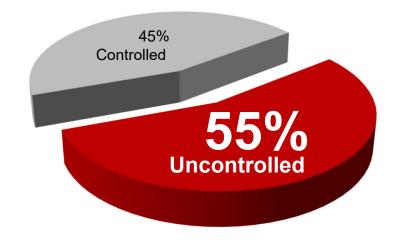
- **FeNO** what is the diagnostic accuracy, clinical utility, how does it measure response to medication?
- **Allergen mitigation** what is the effectiveness, in asthma control?
- ICS What is the comparative effectiveness of intermittent ICS use, and the comparative use of ICS/LAB controller and quick relief therapy?
- **LAMA** What is the effect as add-on therapy in individuals >12 years with persistent asthma
- **IMMUNOTHERAPY** What is the evidence of efficacy and safety of SLIT vs SCIT?
- **Bronchial thermoplasty** What is the benefit and harm in individuals over 18?

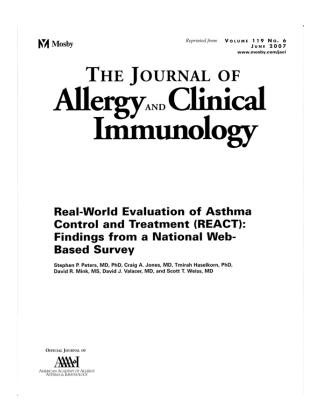
SANTA BARBARA COTTAGE HOSPITAL PEDIATRIC ASTHMA ADMITS FROM 4/01/02 TO 3/31/03



REACT Study1 Peters et al., 2007

Prevalence of Uncontrolled Asthma





Most Asthmatics Are Managed by **Primary Care**

76% of asthmatics are managed by Primary Care Clinicians¹

From AAFP:

"Primary care physicians are in an ideal position to consider the full spectrum of potential allergic and non-allergic triggers in their evaluation of patients who have asthma"2

^{1.} NCHS. Ambulatory care visits 2005. http://www.cdc.gov/nchs/Default.htm. Accessed July 6, 2009.

^{2.} Elward KS, et al. AAFP Asthma & Allergy Reference Guide. 2004.

In or Out of Control? Ask How Many!

The Rules of Two[®]¹

Asthma Control considered inadequate when:

- Patient requires rescue medication >2 times a week
- Patient is awakened by asthma symptoms >2 times a month
- Patient needs rescue inhaler Rx refilled >2 times a year
- PFT

Rules of Two is a registered service mark of Baylor Health Care System.

1. Baylor Health Care System Web site. http://www.baylorhealth.com/SpecialtiesServices/Asthma/Pages/Education.aspx. Accessed July 8, 2009.

Components of Control		Classification of Asthma Control (Children 5-11 years of age)					
		Well Controlled	Not Well Controlled	Very Poorly Controlled			
	Symptoms		≤2 days/week but not more than once on each day	>2 days/week or multiple times on ≤2 days/week	Throughout the	e day	
	Nighttime awakenings		≤1x/month	≥2x/month	≥2x/week		
Impairment	Interference with normal activity		None	Some limitation	Extremely limi	ited	
	Short-acting beta ₂ -agonist use for symptom control (not prevention of EIB)		≤2 days/week	>2 days/week Several tim		er day	
	Lung function						
	• FEV ₁ or peak flow		>80% predicted/ personal best	60-80% predicted/ personal best	<60% predicted/ personal best		
	• FEV ₁ /FVC		>80%	75-80%	<75%		
	Exacerbations requiring oral systemic corticosteroids		0–1/year ≥2/year (see note)				
			Consider severity and interval since last exacerbation				
Risk	Reduction in lung growth		Evaluation requires long-term followup.				
Risk	Treatment-related adverse effects		Medication side effects can vary in intensity from none to very troublesome and worrisome. The level of intensity does not correla to specific levels of control but should be considered in the overall assessment of risk.				
			Classification of Asthma Severity				
Lowest level of treatment required to maintain control (See figure 4-1b for treatment steps.)		Intermitte	ent	Persistent			
			Mild	Moderate	Severe		

The Features of An Essential Asthma Allergy Diagnostic Tools

- Clinicians need a convenient tool to identify allergic triggers
 - Skin testing requires special training, domain of specialists
- Accuracy: Skin prick testing versus in vitro testing^{1,2}
 - In vitro blood testing and skin prick testing (SPT) viewed as interchangeable³
 - Older RAST technology -- poor sensitivity/not reliable
- Convenience
 - Absence of risk to the patient
 - No special skill is required to administer the test
- Pulmonary function testing; spirometry with response to bronchodilator (airway responsiveness), FeNO (airway inflammation), IOS (impulse oscillometry (large vs small airway disease), methacholine challenge (airway responsiveness)

Asthma is a Complex Disease

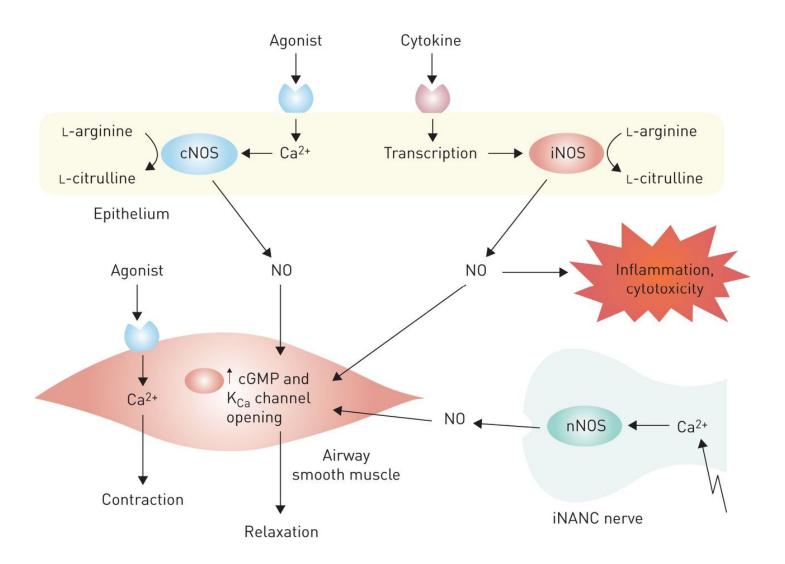
- The Asthma and Allergy Link
 - Over 60% of adult asthmatics have allergic asthma
 - Up to 90% of children with asthma also have allergies^{1,2}
- Steroids and Beta Agonists are essential but not sufficient
- Clear need for multifaceted interventions Ur
- Precision medicine: Urinary metabolites of eicosanoids (prostaglandin D2 mast cell, Leukotriene C4 eosinophils, Isoprostanes)
 - Milgrom H. Understanding allergic asthma. [AeAAAI News Release]. June 18, 2003. 2. Høst A, et al. Allergy. 2000;55:600-608.
 - 2. Am Jouranl of respiratory and critical care medicine 1/13/2021

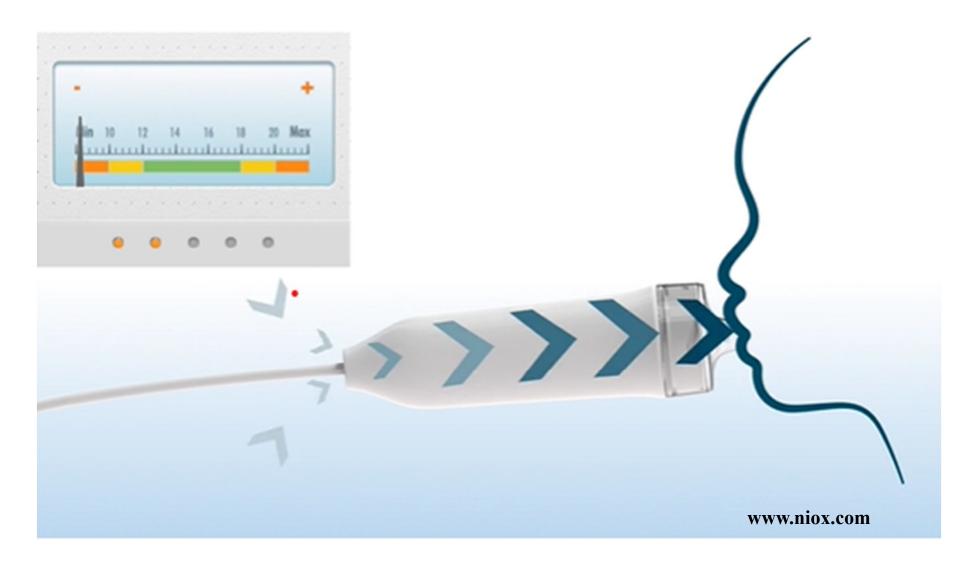
FeNO what is the diagnostic accuracy, clinical utility, how does it measure response to medication?

- **Allergen mitigation** what is the effectiveness, in asthma control?
- **ICS** What is the comparative effectiveness of intermittent ICS use, and the comparative use of ICS/LAB controller and quick relief therapy?
- LAMA What is the effect as add-on therapy in individuals >12 years with persistent asthma
- IMMUNOTHERAPY What is the evidence of efficacy and safety of SLIT vs SCIT?
- Bronchial thermoplasty What is the benefit and harm in individuals over 18?

Fractional Exhaled Nitric Oxide

- Indication of T2 (allergic) airway inflammation
- Measured in parts per billion (PPB)
- No data on diagnostic accuracy under the age of 4
- Requires trained personnel and specialized equipment





Fractional Exhaled Nitric Oxide

- Strong recommendation/low certainty to avoid use of FeNO to predict future risk of asthma in patients with wheezing under age 4
- Conditional recommendation/moderate certainty for the use of patients 5 years and older as an adjunct in the diagnostic process
 - Uncertain diagnosis or unable to perform spirometry
 - Likelihood ratio: increased by 2.8-7 if FeNO is elevated

Fractional Exhaled Nitric Oxide

- Conditional recommendation, low certainty for selecting medication options and monitoring treatment response in patients 5 and older
 - Monitoring can help decrease exacerbations with monitoring every 2-3 months
 - More helpful with history of atopy and uncontrolled disease
 - Does not help in monitoring adherence though responsiveness has been shown to ICSs, montelukast, and omalizumab
- Strong recommendation, low certainty against in utilization FeNO measurements in isolation to monitor asthma
 - No correlation with QOL or asthma control
 - No correlation with severity of exacerbation
- Concerns for cost-effectiveness, availability, and widening health disparities

- **FeNO** what is the diagnostic accuracy, clinical utility, how does it measure response to medication?
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Predictive Value vs. Skin Prick Testing (SPT)1

Performance parameters	ImmunoCAP	SPT
Sensitivity (%)	87.2	93.8
Specificity (%)	90.5	80.1
PPV (%)	91.1	90.1
NPV (%)	86.4	87.1
Clinical Efficiency (%)	88.8	89.2

Authors concluded that ImmunoCAP Specific IgE blood test & SPT values both exhibited excellent efficiency¹

Allergen Mitigation

Dust mite

- Acaricides: dust mite pesticide
- Impermeable pillow and mattress covers
- Removal or cleaning of allergen reservoirs
- Pets: furry and feathered
 - HEPA filtration and vacuum cleaners
 - Removal of allergen reservoirs
 - Confinement to specific rooms or removal from the household



www.niehs.nih.gov/health/topics/agents/allerge

Allergen Mitigation

Integrated pest management:

- Cockroach, Mice
 - Traps and poison
 - Barriers to ingress
- Mold mitigation
 - Bleach-based cleaning products
 - Professional removal or demolition
 - Prevention of source
- Air filtration/air purifiers



www.niehs.nih.gov/health/topics/agents/

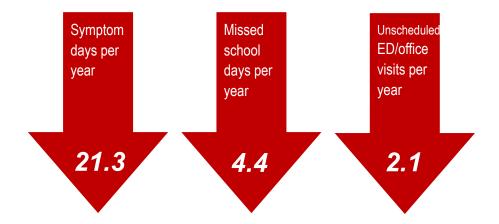
A Multifaceted Home-based Environmental Intervention

- Randomized controlled trial 937 innercity children with asthma and allergies
- Intervention activities tailored to child's sensitization profile
- Targeted allergen exposure reduction improves asthma control

Inner City Asthma Study¹ Morgan et al., 2004



- 2 years with Targeted Exposure Reduction
- Bedroom only interventions
- 34 fewer days of wheezing; effect similar to ICS therapy



Inner-City Asthma Study¹ Morgan et al., 2004

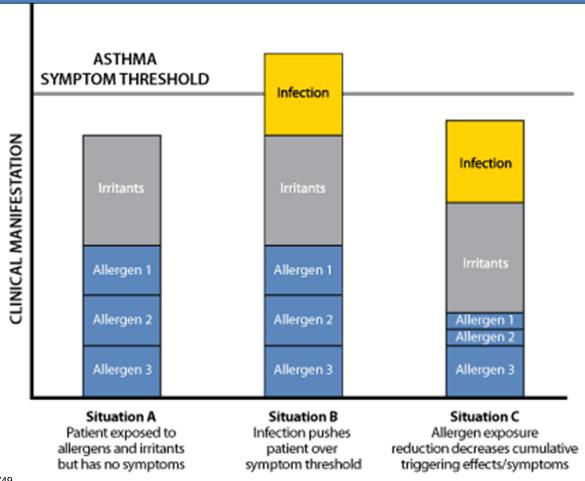


Create a "Safe Sleep Zone"

- Allergic disease severity is dose related
 - allergen concentration
 - duration of exposure¹
- Most allergic pet owners will not get rid of a pet
- Male vs Female dog, Purina Pro Plan for cats (anti-felD1)
- Allergen-control interventions in home settings, particularly the bedroom, have been proven effective^{1,2}
- Establish an *environmentally safe sleeping zone* tailored to objective test results²



Cumulative Triggers of Asthma1,2



^{1.} Fromer, L.J Family Pract 2004; April: S3-S14

^{2.} Simpson, A et al. J All Clin Immuno 2005;116:744-749.

Allergen Mitigation

- Improvement in symptoms but not exacerbations, QOL, or control
- Conditional recommendation, low certainty against interventions for asthmatics who do not have sensitization to indoor allergens
- Conditional recommendation, low certainty **for** asthmatics who have symptoms with exposure to undergo a multicomponent, allergen-specific mitigation
- Conditional recommendation, moderate certainty for impermeable pillow/mattress covers as part of a multicomponent allergen mitigation for asthmatics who are allergic to dust mite

- **FeNO** what is the diagnostic accuracy, clinical utility, how does it measure response to medication?
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AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Manag	2+ Years			
						STEP 6
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	SIEPO
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA	Daily and PRN combination low-dose ICS- formoterol A	Daily and PRN combination medium-dose ICS-formoterol •	Daily medium-high dose ICS-LABA + LAMA and PRN SABA A	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium- dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA, A or daily low-dose ICS + LTRA, and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton,* and PRN SABA	Daily medium- dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA * or Daily medium- dose ICS + LTRA,* or daily medium- dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA	
		Steps 2-4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherap in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy. ♣		dard pharmacotherapy controlled at the	Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

Assess Control



- First check adherence, inhaler technique, environmental factors, ▲ and comorbid conditions.
- Step up if needed; reassess in 2-6 weeks
- Step down if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Conditional recommendation/moderate certainty **for** use of either daily low-dose ICS with as needed SABA or as needed ICS and SABA concomitantly in mild persistent asthmatics 12 years and older

- Likely more beneficial in the setting of poor compliance with good symptom perception
- Combination ICS-SABA under development for US market
- No recommendation provided 0-11 due to insufficient evidence

Conditional recommendation/low certainty **against** short-term increase in ICS dose for loss of asthma control in asthmatics 4 years and older with mild to moderate persistent asthma and good adherence to daily ICS therapy

- Studies increased ICS by 2-5 times daily dose
- Improved time to severe exacerbation but no change in exacerbations, QOL, or symptoms
- Growth suppression noted but not statistically significant

Strong recommendation/high certainty **for** moderate to severe persistent asthmatics 12 years and older and moderate certainty for 4-11 years old for use of ICS-formoterol for daily controller and reliever therapy compared to either high-dose ICS as a daily controller and SABA for quick-relief therapy or the same dose ICS-LABA as controller therapy and SABA for quick-relief therapy

- Single Maintenance And Reliever Therapy (SMART)
- Rescue dosing (formoterol component with base dose of 4.5 mcg)
 - 4-11: 1-2 puffs as needed for max dose of 8 puffs (36 mcg) per day
 - 12+: 1-2 puffs as needed for max dose of 12 puffs (54 mcg) per day
- Appropriate for Step 3 and 4 therapy
- Do not combine with ICS-salmeterol

AGES 0-4 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 0-4 Years						
			STEP 4	STEP 5	STEP 6		
STEP 1	STEP 2	STEP 3	SIEP 4				
RN SABA d the start of RTI: dd short course illy ICS •	Daily low-dose ICS and PRN SABA	Daily low-dose ICS-LABA and PRN SABA or Daily low-dose ICS + montelukast,* or daily medium-dose ICS, and PRN SABA	Daily medium- dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA		
	Daily montelukast* or Cromolyn,* and PRN SABA		Daily medium- dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast*+ oral systemic corticosteroid and PRN SABA		
	_	Step 4 on Management	of Persistent Asthma				
			Step 4 on Management in Individuals Ages 5-11	For children age 4 years only, see Step 3 and Step 4 on Management of Persistent Asthma in Individuals Ages 5-11 Years diagram.	Step 4 on Management of Persistent Asthma in Individuals Ages 5-11 Years diagram.		

Assess Control

- First check adherence, inhaler technique, environmental factors, ▲ and comorbid conditions.
- Step up if needed; reassess in 4-6 weeks
- Step down if possible (if asthma is well controlled for at least 3 consecutive months)





Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta₂-agonist; SABA, inhaled short-acting beta₂-agonist; RTI, respiratory tract infection; PRN, as needed

- ▲ Updated based on the 2020 guidelines.
- Cromolyn and montelukast were not considered for this update and/or have limited availability for use in the United States. The FDA issued a Boxed Warning for montelukast in March 2020.

AGES 5-11 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 5-11 Years					
					STEP 5	STEP 6	
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	5.12.15		
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA	Daily and PRN combination low-dose ICS-formoterol A Ages 4-11	Daily and PRN combination medium-dose ICS-formoterol A	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA	
Alternative		Daily LTRA,* or Cromolyn,* or Nedocromil,* or Theophylline,* and PRN SABA	Daily medium- dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LTRA,* or daily low-dose ICS +Theophylline,* and PRN SABA	Daily medium- dose ICS-LABA and PRN SABA or Daily medium- dose ICS + LTRA* or daily medium- dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* or daily high-dose ICS + Theophylline,* and PRN SABA	Daily high-dose ICS + LTRA* + oral systemic corticosteroid or daily high-dose ICS + Theophylline* + oral systemic corticosteroid, and PRN SABA	
		immunotherapy as an a in individuals ≥ 5 years	s 2-4: Conditionally recommend the use of subcutaneous unotherapy as an adjunct treatment to standard pharmacotherapy lividuals ≥ 5 years of age whose asthma is controlled at the tion, build up, and maintenance phases of immunotherapy.		Consider On	nalizumab**▲	

Assess Control

- First check adherence, inhaler technique, environmental factors, ▲ and comorbid conditions.
- Step up if needed; reassess in 2-6 weeks
- Step down if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.



AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years					
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6	
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA	Daily and PRN combination low-dose ICS- formoterol A	Daily and PRN combination medium-dose ICS-formoterol A	Daily medium-high dose ICS-LABA + LAMA and PRN SABA *	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA	
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium- dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA,* or daily low-dose ICS + LTRA," and PRN SABA or Daily low-dose ICS + Theophylline" or Zileuton," and PRN SABA	Daily medium- dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA * or Daily medium- dose ICS + LTRA,* or daily medium- dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA		
		Steps 2-4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacothera in individuals > 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy.		dard pharmacotherapy controlled at the	(e.g., anti-IgE, a	: Asthma Biologics nti-IL5, anti-IL5R, 4/IL13)**	

Assess Control



- First check adherence, inhaler technique, environmental factors, ▲ and comorbid conditions.
- . Step up if needed; reassess in 2-6 weeks
- . Step down if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

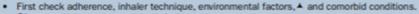
Conditional recommendation/high certainty **for** moderate to severe persistent asthmatics 12 and older using ICS-formoterol in a single inhaler as both a daily controller and reliever therapy compared to high-dose ICS-LABA as a daily controller with SABA for quick-relief therapy

- Adjustment in Step 4 therapy instead of progressing to Step 5
- Max daily dose: 12 puffs (54 mcg)
- Do not combine with ICS-salmeterol

AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma Management of Persistent Asthma in Individuals Ages 12+ Year					
			STEP 3	STEP 4	STEP 5	STEP 6
Treatment	STEP 1	STEP 2	SIEPS		ļ	
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA •	Daily and PRN combination low-dose ICS- formoterol A	Daily and PRN combination medium-dose ICS-formoterol •	Daily medium-high dose ICS-LABA + LAMA and PRN SABA *	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium- dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA, A or daily low-dose ICS + LTRA, and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton, and PRN SABA	Daily medium- dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA * or Daily medium- dose ICS + LTRA,* or daily medium- dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA,* and PRN SABA	
		Steps 2-4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals > 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy.			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**	

Assess Control





. Step down if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.



AGES 0-4 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Manag	ement of Persiste	ent Asthma in Inc	dividuals Ages 0-	4 Years
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6
Preferred	PRN SABA and At the start of RTI: Add short course daily ICS •	Daily low-dose ICS and PRN SABA	Daily low-dose ICS-LABA and PRN SABA or Daily low-dose ICS + montelukast,* or daily medium-dose ICS, and PRN SABA	Daily medium- dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic corticosteroid and PRN SABA
Alternative		Daily montelukast* or Cromolyn,* and PRN SABA		Daily medium- dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast*+ oral systemic corticosteroid and PRN SABA
			For children age 4 year Step 4 on Management in Individuals Ages 5-11	of Persistent Asthma		
	Step up Step do Consult with	of needed; reassess own if possible (if as the asthma specialist	technique, environme in 4-6 weeks thma is well controlled if Step 3 or higher	d for at least 3 conse	cutive months) der consultation at S	
	measures, se	If-reported control, a		ion are complementa	irment and risk. Use o ary and should be emp	

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta,-agonist; SABA, inhaled short-acting beta,-agonist; RTI, respiratory tract infection; PRN, as needed

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Adjustable Medication Dosing in Recurrent Wheezing and Asthma

- Recurrent wheezing:
 - 3+ episodes of wheezing triggered by respiratory tract infections (RTI) in a child's lifetime or 2 episodes in the past year
 - Well between episodes
- ICS: low-high dosing, with or without long-acting beta₂-agonist (LABA)
- Quick-relief therapy: medications taken as needed for acute asthma symptoms, typically short-acting beta₂-agonist (SABA)
- Intermittent dosing: temporary initiation or escalation of ICS with or without LABA based on selected symptom threshold
- Controller therapy: daily medications to control asthma symptoms

Adjustable Medications in Recurrent Wheezing

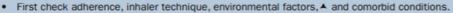
Conditional recommendation/high certainty **for** starting a short course of daily ICS with SABA as needed at the onset of an RTI in children 0-4 years old with recurrent wheezing compared to SABA as needed alone

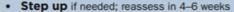
- Especially if not on daily ICS
- Various regiments reported, typically for 7-10 days
- Can be started at home if education is provided
- Growth monitoring required
- 33% relative risk reduction in exacerbations requiring systemic corticosteroids

AGES 0-4 YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 0-4 Years					
				STEP 4	STEP 5	STEP 6	
Treatment	STEP 1	STEP 2	STEP 3	SIEP 4			
	PRN SABA and	Daily low-dose ICS and PRN SABA	Daily low-dose ICS-LABA and PRN SABA▲	Daily medium- dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA and PRN SABA	Daily high-dose ICS-LABA + oral systemic	
Preferred	At the start of RTI: Add short course daily ICS •		or Daily low-dose ICS + montelukast,* or daily medium-dose ICS, and PRN SABA			corticosteroid and PRN SABA	
Alternative		Daily montelukast* or Cromolyn,* and PRN SABA		Daily medium- dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast* and PRN SABA	Daily high-dose ICS + montelukast*+ oral systemic corticosteroid and PRN SABA	
			For children age 4 year Step 4 on Management in Individuals Ages 5-11	t of Persistent Asthma			

Assess Control





Step down if possible (if asthma is well controlled for at least 3 consecutive months)



Consult with asthma specialist if Step 3 or higher is required. Consider consultation at Step 2.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Abbreviations: ICS, inhaled corticosteroid; LABA, long-acting beta₂-agonist; SABA, inhaled short-acting beta₂-agonist; RTI, respiratory tract infection; PRN, as needed

▲ Updated based on the 2020 guidelines.

Cromolyn and montelukast were not considered for this update and/or have limited availability for use in the United States. The FDA issued a Boxed Warning for montelukast in March 2020.

Montelukast Boxed Warning

- Issued by the FDA in March 2020: significant risk of neuropsychiatric side effects including suicidal ideation
 - Completed suicides reported
 - Onset or persistence after discontinuation less common
- Should only be used for allergic rhinitis in which other therapies do not work
- Screening for psychiatric issues required beforehand with appropriate counseling
- Caution and alternative therapies advised in asthma

AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years					
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6	
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA	Daily and PRN combination low-dose ICS- formoterol A	Daily and PRN combination medium-dose ICS-formoterol •	Daily medium-high dose ICS-LABA + LAMA and PRN SABA A	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA	
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium- dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA, * or daily low-dose ICS + LTRA," and PRN SABA or Daily low-dose ICS + Theophylline" or Zileuton," and PRN SABA	Daily medium- dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA * or Daily medium- dose ICS + LTRA,* or daily medium- dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA," and PRN SABA		
		Steps 2-4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy ♣			Consider adding Asthma Biologics (e.g., anti-IgE, anti-ILS, anti-ILSR, anti-IL4/IL13)**		

Assess Control



- First check adherence, inhaler technique, environmental factors, ▲ and comorbid conditions.
- Step up if needed; reassess in 2-6 weeks
- . Step down if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

Medications for SMART

Budesonide-Formoterol (Symbicort®)

Low dose: 80 mcg-4.5 mcg

- Medium dose: 160 mcg-4.5 mcg

Mometasone-Formoterol (Dulera®)

Low dose: 50 mcg-5 mcg

Medium dose: 100 mcg-5 mcg

Ongoing development: ICS-SABA





- **FeNO** what is the diagnostic accuracy, clinical utility, how does it measure response to medication?
- **Allergen mitigation** what is the effectiveness, in asthma control?
- **ICS** What is the comparative effectiveness of intermittent ICS use, and the comparative use of ICS/LAB controller and quick relief therapy?
- LAMA What is the effect as add-on therapy in individuals >12 years with persistent asthma
- IMMUNOTHERAPY What is the evidence of efficacy and safety of SLIT vs SCIT?
- Bronchial thermoplasty What is the benefit and harm in individuals over 18?

LAMAs as Add-on Therapy to ICS

- Long-acting muscarinic antagonist (LAMA)
 - *Tiotropium (Spiriva Respimat®, Spiriva Handihaler®)
 - Umeclidinium (Incruse Ellipta®)
 - Aclidinium (Tudorza Pressair[®])
 - Glycopyrrolate (Lonhala Magnair®)
 - Revefenacin (Yupelri®)
- Adverse effects
 - Urinary retention
 - Glaucoma



LAMAs as Add-on Therapy to ICS

- Conditional recommendation/moderate certainty against adding LAMA to ICS compared to LABA to ICS in asthmatics 12 years and older with uncontrolled persistent asthma
- Conditional recommendation/moderate certainty for adding LAMA to ICS in asthmatics 12 years and older who cannot or will not use LABA as opposed to ICS alone
 - Part of Step 4 therapy
 - Slight improvement in exacerbations
- Conditional recommendation/moderate certainty for adding LAMA to ICS-LABA in uncontrolled persistent asthma 12 years and older opposed to continuing the same dose of ICS-LABA

AGES 12+ YEARS: STEPWISE APPROACH FOR MANAGEMENT OF ASTHMA

	Intermittent Asthma	Management of Persistent Asthma in Individuals Ages 12+ Years					
Treatment	STEP 1	STEP 2	STEP 3	STEP 4	STEP 5	STEP 6	
Preferred	PRN SABA	Daily low-dose ICS and PRN SABA or PRN concomitant ICS and SABA	Daily and PRN combination low-dose ICS- formoterol A	Daily and PRN combination medium-dose ICS-formoterol A	Daily medium-high dose ICS-LABA + LAMA and PRN SABA A	Daily high-dose ICS-LABA + oral systemic corticosteroids + PRN SABA	
Alternative		Daily LTRA* and PRN SABA or Cromolyn,* or Nedocromil,* or Zileuton,* or Theophylline,* and PRN SABA	Daily medium- dose ICS and PRN SABA or Daily low-dose ICS-LABA, or daily low-dose ICS + LAMA, A or daily low-dose ICS + LTRA, and PRN SABA or Daily low-dose ICS + Theophylline* or Zileuton, and PRN SABA	Daily medium- dose ICS-LABA or daily medium-dose ICS + LAMA, and PRN SABA * or Daily medium- dose ICS + LTRA,* or daily medium- dose ICS + Theophylline,* or daily medium-dose ICS + Zileuton,* and PRN SABA	Daily medium-high dose ICS-LABA or daily high-dose ICS + LTRA," and PRN SABA		
		Steps 2-4: Conditionally recommend the use of subcutaneous immunotherapy as an adjunct treatment to standard pharmacotherapy in individuals ≥ 5 years of age whose asthma is controlled at the initiation, build up, and maintenance phases of immunotherapy ▲			Consider adding Asthma Biologics (e.g., anti-IgE, anti-IL5, anti-IL5R, anti-IL4/IL13)**		

Assess Control



- First check adherence, inhaler technique, environmental factors, ▲ and comorbid conditions.
- Step up if needed; reassess in 2–6 weeks
- Step down if possible (if asthma is well controlled for at least 3 consecutive months)

Consult with asthma specialist if Step 4 or higher is required. Consider consultation at Step 3.

Control assessment is a key element of asthma care. This involves both impairment and risk. Use of objective measures, self-reported control, and health care utilization are complementary and should be employed on an ongoing basis, depending on the individual's clinical situation.

- **FeNO** what is the diagnostic accuracy, clinical utility, how does it measure response to medication?
- **Allergen mitigation** what is the effectiveness, in asthma control?
- **ICS** What is the comparative effectiveness of intermittent ICS use, and the comparative use of ICS/LAB controller and quick relief therapy?
- LAMA What is the effect as add-on therapy in individuals >12 years with persistent asthma
- IMMUNOTHERAPY What is the evidence of efficacy and safety of SLIT vs SCIT?
- Bronchial thermoplasty What is the benefit and harm in individuals over 18?

Allergen Immunotherapy for Inhalant Allergy

- Administration of allergen in gradually increasing doses to induce tolerance to the allergen and reduction of symptoms with exposure
- Subcutaneous allergen immunotherapy (SCIT)
 - AKA allergy shots
 - Weekly build-up to 3-5 years of monthly maintenance dosing
- Sublingual allergen immunotherapy (SLIT)
 - Aqueous drops (not standardized) or tablets taken daily
 - Few FDA-approved options for allergic rhinoconjunctivitis: ragweed, dust mite, grass
 - Daily dosing starting 3 months before the season and continued until season completed

Allergen Immunotherapy

- Conditional recommendation/moderate certainty for utilizing
 SCIT as an adjunct treatment in mild to moderate allergic asthmathat is controlled
 - Potential to be disease-modifying
 - Risk assessment needed
- Conditional recommendation/moderate certainty against SLIT as an adjunct treatment in allergic asthma
 - Only approved for the treatment of allergic rhinitis and allergic conjunctivitis
 - FDA-approved therapies less relevant for pediatrics in Nebraska

Allergy Immunotherapy

Allergy shots

- Pro- effective therapy for pollen allergy
- Con- expensive and very time consuming, with some discomfort
- Biologicals
- -Anti IgE: Xolair

Oral desensitization

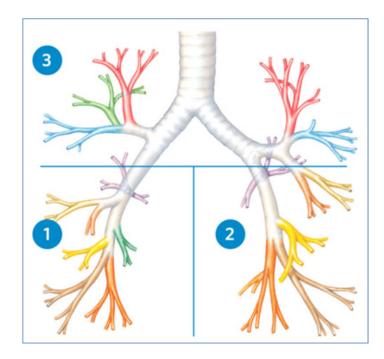
- Pro effective therapy for certain foods and grass, no discomfort
- Con- requires daily therapy, insurance issues, only one allergen at a time.



- **FeNO** what is the diagnostic accuracy, clinical utility, how does it measure response to medication?
- **Allergen mitigation** what is the effectiveness, in asthma control?
- **ICS** What is the comparative effectiveness of intermittent ICS use, and the comparative use of ICS/LAB controller and quick relief therapy?
- LAMA What is the effect as add-on therapy in individuals >12 years with persistent asthma
- IMMUNOTHERAPY What is the evidence of efficacy and safety of SLIT vs SCIT?
- Bronchial thermoplasty What is the benefit and harm in individuals over 18?

Bronchial Thermoplasty

- Delivers radiofrequency energy to the airways via a catheter to decrease smooth muscle
 - Performed over 3 outpatient bronchoscopies
 - In conjunction with standard asthma medications
- FDA-Approved 18 years and older
- Risks: short-term worsening of symptoms, infection, hemoptysis, bronchiectasis
- Benefits: Improved QOL, small reduction in exacerbations
 - Duration unclear

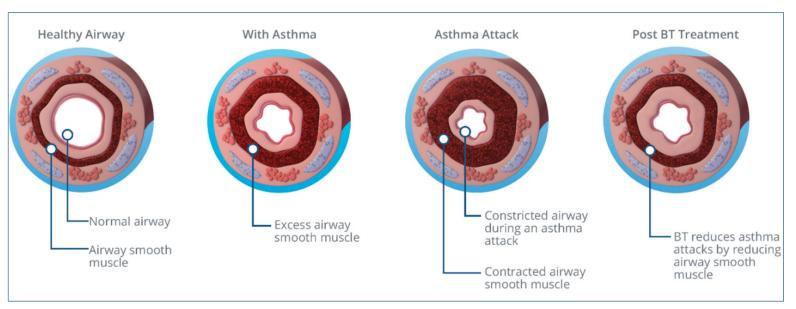


www.btforasthma.com

Bronchial Thermoplasty

Conditional recommendation/low certainty **against** BT in persistent asthmatics 18 years and older

Should be avoided with FEV1<60% predicted



www.btforasthma.com

Biologic Therapy in Pediatric Asthma

- Omalizumab (Xolair®)
- Mepolizumab (Nucala®): anti-IL-5 monoclonal antibody
 - Approved 6 years and up in moderate to severe persistent asthma
 - Requires peripheral blood eosinophils ≥ 150 cells/mcL
 - Dosing based on age
 - Subcutaneous injection every 4 weeks
 - Auto-injectors for at-home administration
- Benralizumab (Fasenra®)
- Dupilumab (Dupixent®)

Highlights of Medication Changes in EPR-4

0-4 years

- Step 1: Adds short course of daily ICS to RTI
- Step 3: Adds daily low dose ICS-LABA with prn SABA to preferred treatment options
- Step 3: Adds daily low dose ICS and montelukast to preferred treatment options
- Steps 2, 4, and 5: Montelukast changes to alternative instead of preferred therapy

4-11 years

- Step 3: Preferred therapy is low dose ICS-formoterol daily and as needed
- Step 4: Preferred therapy is medium dose ICS-formoterol daily and as needed

12 years and up

- Step 2: Adds prn ICS and SABA to preferred therapy
- Step 3: Preferred therapy is low dose ICS-formoterol daily and as needed
- Step 4: Preferred therapy is medium dose ICS-formoterol daily and as needed
- Step 5: Addition of LAMA as an add-on treatment

Q2. An 8-year-old patient presents for evaluation of new-onset asthma. Based on symptoms and spirometry, he is diagnosed with moderate persistent asthma.

What is the preferred initial treatment based on EPR-4?

- A. Start a daily low-dose inhaled corticosteroid and montelukast with Albuterol as needed
- B. Start a daily low-dose inhaled corticosteroid with Albuterol as needed
- C. Start a daily low-dose inhaled corticosteroid-formoterol daily with Albuterol as needed
- D. Start a daily low-dose inhaled corticosteroid-formoterol daily and as needed
- E. Start a daily medium-dose inhaled corticosteroid-formoterol daily and as needed

Answer:

D. Start a daily low-dose inhaled corticosteroid-formoterol daily and as needed

Medications & Delivery Devices



Adam Horn, Pharm.D.
Clinical Pharmacist, CenCal Health

Objectives



- Review Asthma Medications
- Asthma Medication Adherence, Technique, & Devices



Asthma Medication Therapy

Controller Medications

- Inhaled Corticosteroids (ICS)
- Long-acting Beta-Agonists (LABA)
- Combination Inhalers (ICS/LABA)
- Leukotriene Receptor Antagonists
- Biologic Treatments
- Theophylline

Rescue medications

- Short Acting Beta Agonists (SABA)
- Inhaled Anticholinergics

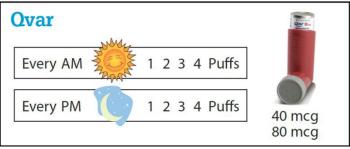


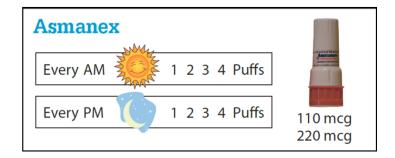


Inhaled Corticosteroids (ICS)

- Beclomethasone HFA (QVAR HFA® /QVAR Redihaler®)*
- Budesonide DPI (Pulmicort Flexhaler®)
- Fluticasone Propionate (Flovent HFA®/Flovent Diskus®/ArmonAir RespiClick®)*
- Fluticasone Furoate (Arnuity Ellipta®)
- Flunisolide (Aerospan®)
- Mometasone DPI (Asmanex Twisthaler®/Asmanex HFA®)*
- Ciclesonide (Alvesco®)







Rescue Inhalers: Bronchodilators

- Albuterol Sulfate (ProAir HFA®/ProAir RespiClick®, Proventil HFA®, Ventolin HFA®)
- Levoalbuterol Tartrate (Xopenex HFA®)
- Ipratropium Bromide(Atrovent ®, Combivent Respimat ®)

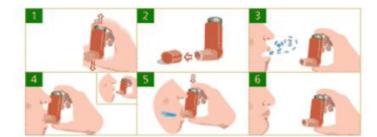






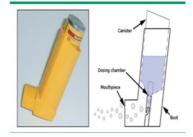
Metered Dose Inhalers (Standard HFA)

- 1. Shake the inhaler well before use (3 or 4 shakes)
- 2. Remove the cap
- 3. Breathe out, away from your inhaler



- 4. Bring the inhaler to your mouth. Place it in your mouth between your teeth and close your mouth around it.
- 5. Start to breathe in slowly. Press the top of your inhaler once and keep breathing in slowly until you have taken a full breath
- 6. Remove the inhaler from your mouth, and hold your breath for about 10 seconds, then breathe out.





Metered Dose Inhalers (RediHaler)



- 1. Do not shake the inhaler before use as it may activate the device.
- 2. Open the cap and breathe out fully. Do not open the cap until you are ready to take a dose.
- 3. Place the mouthpiece in your mouth and close your lips around it so a good seal is formed.
- 4. Inhale deeply to release the medicine.
- 5. Remove inhaler, holding your breath for 5 to 10 seconds, then breath out slowly away from the inhaler. Remember, hold the inhaler upright.
- 6. Close the white cap and you are ready for the next inhalation





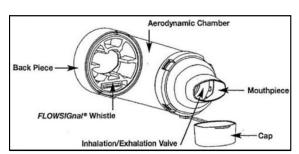
Metered Dose Inhalers with a Holding Chamber

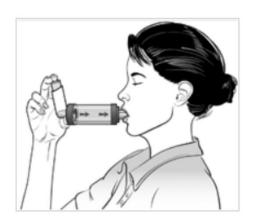
Using an MDI with a valved holding chamber (figure 1)

- 1. Remove the cap from the MDI and chamber.
- Shake well for 5 seconds.
- 3. Insert the MDI into the open end of the chamber (opposite the mouthpiece).
- Breathe out all the way.
- 5. Keep your chin up.
- Place the mouthpiece of the chamber between your teeth and seal your lips tightly around it.
- 7. Press the canister once.
- Breathe in slowly through your mouth to completely fill your lungs. If you hear a "horn-like" sound, you are breathing too quickly and need to slow down.
- 9. Hold your breath for 10 seconds (count to 10 slowly) to allow the medication to reach the airways of the lung.
- 10. Repeat steps 2-8 for each puff ordered by your doctor. Wait about 1 minute in between puffs.
- 11. Replace the cap on your MDI when finished.
- If you are using a corticosteroid MDI, rinse your mouth and gargle using water or mouthwash after each use. You should always use a chamber with a steroid MDI.









Metered Dose Inhalers Patient Reminders

- Prime inhaler at initial use and after 2 weeks of no use
- ICS USE = RINSE mouth with water after each use
- Clean mouthpiece at least once a week
 - DO NOT wash the medicine canister
 - Let the mouthpiece dry overnight









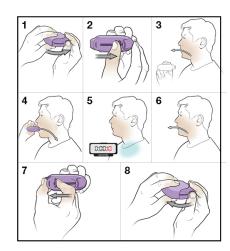




Dry Powder Inhalers (Diskus)

- 1.Open DPI Diskus: hold it in the palm of your hand, put the thumb of your other hand on the thumb grip and push the thumb grip until it "clicks" into place.
- 2. Slide the lever away from you as far as it will go.
- 3.Breathe out away from the device.
- 4. Place the mouthpiece gently in your mouth and close your lips around it.
- 5.Breathe in DEEPLY until you have taken a full breath.
- 6. Hold your breath for about 10 seconds, then breathe out.







Dry Powder Inhalers (RespiClick)

- 1.Open RespiClick Inhaler: Hold the inhaler upright as you open the cap fully. Pull the cap all the way back until you feel and hear a click. The inhaler is now ready to use.
- 2.Before you inhale, breathe out (exhale) though your mouth and push as much air from your lungs as you can. Put the mouthpiece in your mouth and close your lips tightly around it.
- 3.Breathe in quickly and deeply though your mouth to deliver the dose of medicine to your lungs. Hold your breath for about 10 seconds, or as long as you comfortably can.
- 4.Close the cap firmly over the mouthpiece. Always close the cap after each inhalation so that your inhaler will be ready for your next dose. If you need another dose, close the cap and repeat all of the steps.







Dry Powder Inhalers (Ellipta)

- 1. Open Ellipta Inhaler: Slide the cover down until you hear a "click".
- 2. While holding the inhaler away from your mouth, breathe out as far as is comfortable.
- 3. Put the mouthpiece between your lips, and close lips firmly around it.
- 4. Take one long, steady, deep breath in and hold this breath for at least 3-4 seconds
- 5. Remove the inhaler from your mouth and breathe out slowly and gently
- 6. Slide the cover upwards as far as it will go to cover the mouthpiece

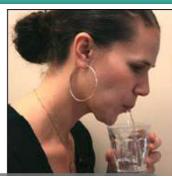




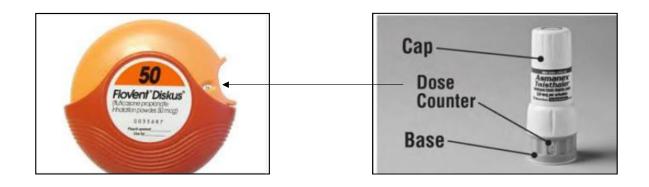
Dry Powder Inhalers (DPI) Patient Reminders

- DO NOT SHAKE your DPI
- Close the diskus/respiclick/ellipta after use
- Be mindful of how many doses remain on your inhaler
- Rinse with water and spit out after EACH use









CenCal Health Asthma Formulary Options

- Bronchodilators (Rescue Inhalers)
 - Albuterol Sulfate (Generic Proventil HFA®, Generic Proair HFA®/ ProAir RespiClick®, Generic Ventolin HFA®)
- Inhaled Corticosteroids (Controller Inhalers)
 - Beclomethasone (QVAR HFA® /QVAR Redihaler®)
 - Budesonide (Pulmicort Flexhaler®)
 - Ciclesonid (Alvesco®)
 - Fluticasone Propionate (Flovent HFA®/Flovent Diskus®/ArmonAir RespiClick®)
 - Fluticasone Furoate (Arnuity Ellipta®)
 - Flunisolide (Aerospan®)
 - Mometasone furoate (Asmanex twisthaler®/Asmanex HFA®)

- Combination Inhalers (ICS/LABA)
 - Generic AirDuo RespiClick®
 - Generic Advair Diskus®
- Please find the CenCal Health formulary at https://www.cencalhealth.org/providers/pharmacy/





Breathe SMART



Rachel Ponce Senior Population Health Specialist, CenCal Health

Breathe SMART

Goal:

- Improve asthma controller medication adherence
- Ensure patients understand their controller medications verses rescue inhalers

Incentive Payment

 \$100 per member who fills controller medication at least 8 times/calendar year

cencalhealth.org/providers/quality-of-care/provider-incentives



Breathe SMART

Best Practices

- Identify High Risk Members
 - Portal Page
 - Encourage more frequent visits
 - Hands on education for inhaler use
- Complete Asthma Action Plans
 - Individualized treatment plans
 - CPT Code 99402
 - Reimbursed at \$75/year per member
 - AAP Webinar
 - Asthma Action Plan



cencalhealth.org/asthma

CenCal Health Contact Information

Population Health Team

populationhealth@cencalhealth.org

Health Education & Promotion

healtheducation@cencalhealth.org

Provider Relations & Training

psrgroup@cencalhealth.org

Pharmacy Services

pharmacyteam@cencalhealth.org



