

Asthma: Controller (Long-Acting) Medications Washington Drug Archive Report

Washington P&T Committee

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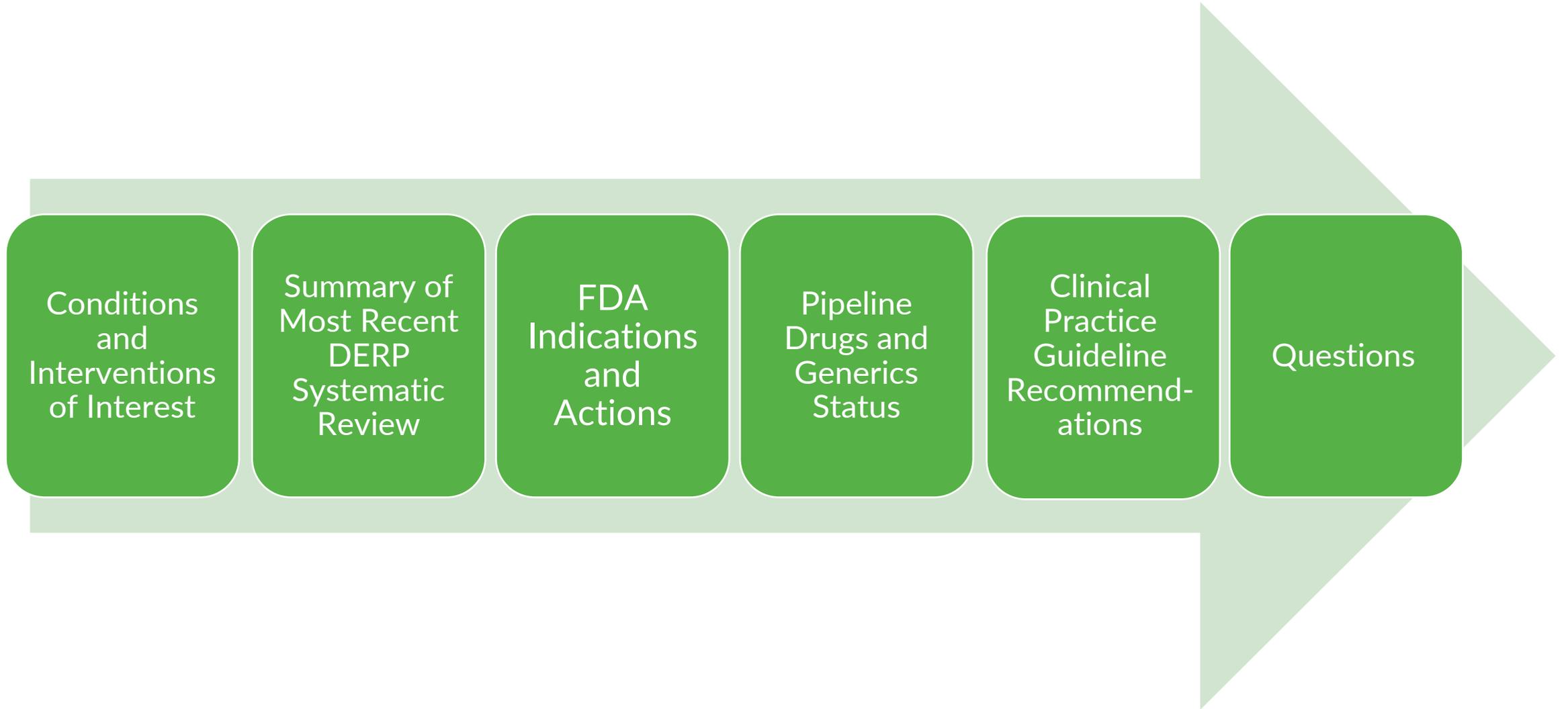


Aim of Project

- The Drug Effectiveness Review Project (DERP) aims to present information to the Washington State Pharmacy and Therapeutics (P&T) Committee with topic reports on 9 drug classes that are candidates to be archived from active review by the Committee
- The 9 drug classes identified by the Washington Health Care Authority (HCA) as archive candidates are:
 - Anticoagulants
 - Antiemetics
 - Antiplatelets
 - **Asthma controllers**
 - Asthma quick relief drugs
 - Long-acting opioids
 - Overactive bladder drugs
 - PCSK9 inhibitors
 - Statins

*Drug classes in **green** are presented in this report*

Overview

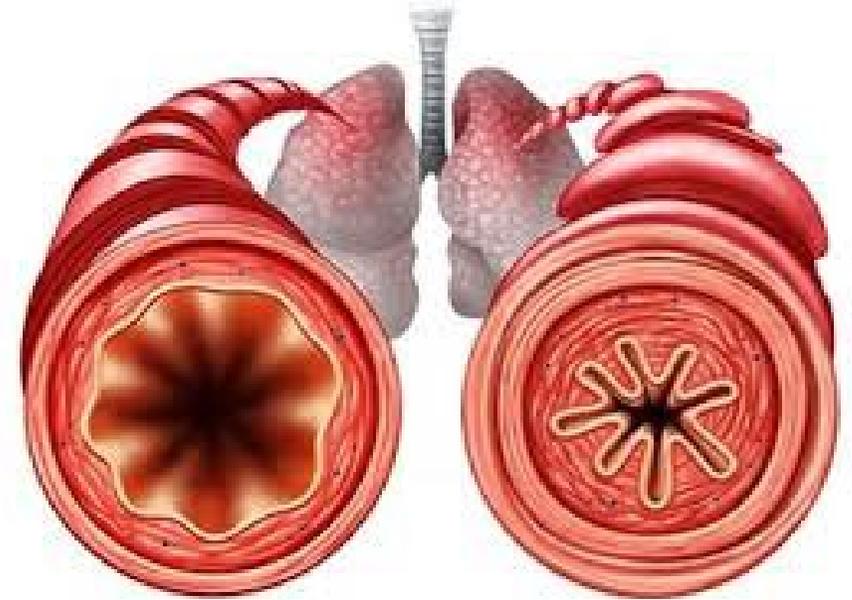


Abbreviations

- ACL: aclidinium
- ARF: arformoterol tartrate
- BEC: beclomethasone dipropionate
- BUD: budesonide
- CIC: ciclesonide
- COPD: chronic obstructive pulmonary disease
- ED: emergency department
- FDA: US Food and Drug Administration
- FLUN: flunisolide
- FF: fluticasone furoate
- FP: fluticasone propionate
- FOR: formoterol fumarate
- GLY: glycopyrrolate
- HCl: hydrochloride
- HFA: hydrofluoroalkane
- ICS: inhaled corticosteroids
- IND: indacaterol
- LABA: long-acting beta-2 agonists
- LAMA: long-acting muscarinic antagonists
- LM: leukotriene modifiers
- MOM: mometasone furoate
- MON: montelukast sodium
- NDA: new drug application
- OLO: olodaterol hydrochloride
- OTC: over-the-counter
- QoL: quality of life
- ROF: roflumilast
- SABA: short-acting beta-agonists
- SAL: salmeterol xinafoate
- SIL: zileuton
- TIO: tiotropium bromide
- UME: umeclidinium bromide
- VIL: vilanterol
- ZAR: zafirlukast

Asthma: Definition

- Asthma is a chronic inflammatory disorder of the lungs; this inflammation can cause:
 - ❑ Reversible airway obstruction (spontaneous reversal or with treatment)
 - ❑ Increased airway responsiveness
- Symptoms include:
 - ❑ Wheezing
 - ❑ Shortness of breath
 - ❑ Coughing
 - ❑ Chest tightness
- Long-term risks of severe asthma include:
 - ❑ Deterioration of lung function
 - ❑ Side effects of long-term medications such as oral corticosteroids



Source. www.urmc.rochester.edu

Asthma: Epidemiology

- Nearly [25 million individuals](#) (about 1 in 12) in the US have asthma
 - 3% to 13% have [severe asthma](#)
 - Asthma has the highest chronic disease prevalence in children (6.5%)
 - Male children are more likely to have asthma than female children, but this is reversed in adults
 - Non-Hispanic Black children are twice as likely to have asthma compared with White children
 - Exercise-induced asthma (bronchoconstriction) occurs in 5% to 30% of the general population; up to 90% of people with asthma have this symptom

Risk Factors for [Asthma](#)

- Family history/genetics
- Allergies
- Viral respiratory infections during childhood

- Occupational exposures
- Environmental exposures
 - Smoking
 - Air pollution
- Obesity

Treatments for Asthma

- No cure for asthma, but goal of treatment is to mitigate symptoms, prevent exacerbations, and reduce long-term complications
- Asthma is classified by whether symptoms are intermittent versus persistent, and then by symptom severity

Nonpharmacologic treatments

- Breathing exercises
- Increased physical activity
- Avoiding environmental triggers

Pharmacologic agents

- Quick-relief medications (bronchodilators)
- Controller medications
- Combination quick-relief and controller medications (newly approved/emerging market)
- Biologics (newer treatments for severe asthma, including omalizumab, mepolizumab, reslizumab)

Summary of Most Recent DERP Products (Controllers)

Last Report	2016
Date Presented	June 2016
Report Title	<u>Drugs to Treat Asthma and Chronic Obstructive Pulmonary Disease</u>
Search Dates	From inception (most databases) through October 2015
Authors	Pacific Northwest Evidence-based Practice Center
<u>Surveillance</u> Since Last Report	
June 2018	<i>Drugs to Treat Asthma or Chronic Obstructive Pulmonary Disease</i> • Search Dates: March 17 through May 2018
June 2017	<i>Drugs to Treat Asthma or Chronic Obstructive Pulmonary Disease</i> • Search Dates: October 2015 through May 2017

PICOS of Most Recent DERP Report (Controllers)

- *Population*

- Adult or pediatric patients (at least 12 months) with persistent or chronic asthma in outpatient settings
- **Adult patients with chronic obstructive pulmonary disease (COPD)**

- *Comparators*

- Head-to-head comparison of included interventions, including one drug, 2 devices
 - *Specifically excluded: add-on therapy (e.g., comparing fixed-dose combinations A/B to either included drug), fixed-dose combination products vs. components at same dose (A/B vs. A+B)*

- *Study Designs*

- Randomized controlled trials (≥ 12 weeks in duration and ≥ 100 participants), comparative effectiveness reviews, observational studies (for safety outcomes only)

PICOS of Most Recent DERP Report (Controllers; slide 1 of 3)

- *Interventions*

Drug Name	Abbreviation	Brand Name	Formulation (Delivery)	Date of FDA Approval
Long-acting beta-2 agonist (LABA)				
Arformoterol tartrate	ARF	Brovana	Solution (inhalation)	October 6, 2006
Formoterol fumarate	FOR	Foradil	Powder (inhalation)	February 16, 2001
		Perforomist	Solution (inhalation)	May 11, 2007
		Foradil Certihaler	Powder (inhalation)	December 16, 2006
Indacaterol maleate	IND	Arcapta	Powder (inhalation)	July 1, 2011
Olodaterol HCl	OLO	Striverdi Respimat	Soft-mist spray (inhalation)	July 31, 2014
Salmeterol xinafoate	SAL	Serevent	Powder (inhalation)	September 19, 1997
Long-acting muscarinic antagonist (LAMA)				
Acclidinium	ACL	Tudorza Pressair	Powder (inhalation)	July 23, 2012
Glycopyrrolate	GLY	Seebri Breezhaler	Powder (inhalation)	October 29, 2015
Tiotropium bromide	TIO	Spiriva	Powder (inhalation)	January 30, 2004
		Spiriva Respimat	Soft-mist spray (inhalation)	September 15, 2015
Umeclidinium bromide	UME	Incruse Ellipta	Powder (inhalation)	April 30, 2014

Note. Drugs and brands in red are not indicated for asthma and are not of interest for this report presentation, but were included in the last report.

PICOS of Most Recent DERP Report (Controllers; slide 2 of 3)

- Interventions*

Drug Name	Abbreviation	Brand Name	Formulation (Delivery)	Date of FDA Approval
Inhaled corticosteroid (ICS)				
Beclomethasone dipropionate	BEC	Qvar	Aerosol (inhalation)	September 15, 2000
Budesonide	BUD	Pulmicort Respules	Suspension (inhalation)	August 8, 2000
		Pulmicort Flexhaler	Powder (inhalation)	July 12, 2006
Ciclesonide	CIC	Alvesco	Aerosol (inhalation)	January 10, 2008
Flunisolide	FLUN	Aerospan HFA	Aerosol (inhalation)	January 27, 2006
Fluticasone furoate	FF	Arnuity Ellipta	Powder (inhalation)	August 20, 2014
Fluticasone propionate	FP	Flovent Diskus	Powder (inhalation)	September 29, 2000
		Flovent HFA	Aerosol (inhalation)	May 14, 2004
Mometasone furoate	MOM	Asmanex Twisthaler	Powder (inhalation)	March 30, 2005
		Asmanex HFA	Aerosol (inhalation)	April 25, 2014
Inhaled corticosteroid/long-acting beta-2 agonist (ICS/LABA fixed-dose combination products)				
Budesonide/formoterol	BUD/FOR	Symbicort	Aerosol (inhalation)	July 21, 2006
Mometasone furoate/formoterol	MOM/FOR	Dulera	Aerosol (inhalation)	June 22, 2010
Fluticasone propionate/salmeterol xinafoate	FP/SAL	Advair Diskus	Powder (inhalation)	August 24, 2000
		Advair HFA	Aerosol (inhalation)	June 8, 2006
Fluticasone furoate/vilanterol	FF/VIL	Breo Ellipta	Powder (inhalation)	May 10, 2013

PICOS of Most Recent DERP Report (Controllers; slide 3 of 3)

- *Interventions*

Drug Name	Abbreviation	Brand Name	Formulation (Delivery)	Date of FDA Approval
Long-acting beta-2 agonist/long-acting muscarinic antagonist (LABA/LAMA, fixed-dose combination products)				
Indacaterol/ glycopyrrolate	IND/GLY	Utibron	Powder (inhalation)	October 29, 2015
Olodaterol HCl/ tiotropium bromide	OLO/TIO	Stiolto Respimat	Solution (inhalation)	May 21, 2015
Umeclidinium bromide/ vilanterol trifenate	UME/VIL	Anoro Ellipta	Powder (inhalation)	December 18, 2013
Leukotriene modifier				
Montelukast sodium	MON	Singulair	Tablet, chewable/granules (oral)	February 20, 1998
Zileuton	SIL	Zyflo	Tablet (oral)	May 30, 2007
		Zyflo CR	Tablet (ER oral)	May 30, 2007
Zafirlukast	ZAR	Accolate	Tablet (oral)	September 26, 1996
Phosphodiesterase-4 (PDE-4) inhibitor				
Roflumilast	ROF	Daliresp	Tablet (oral)	February 28, 2011

Note. Drugs in red are not indicated for asthma and are not of interest for this report presentation, but were included in the last report.

PICOS of Most Recent DERP Report (Controllers)

- *Outcomes*

- ❑ Asthma **and COPD** control (e.g., exacerbations, frequency of symptoms or rescue medication)
- ❑ Quality of life (QoL)
- ❑ Functioning (e.g., participation in work, school, physical activity)
- ❑ Health care service use (e.g., emergency department care visits, hospitalization)
- ❑ Mortality
- ❑ Adverse events (AEs; overall AEs, withdrawals due to AEs, specific AEs)

Note. Red text is not of interest for this archive report, but was included in last report

Key Questions in Most Recent DERP Report (Controllers)

- What is the comparative efficacy and effectiveness (KQ1), and harms (KQ2) of long-acting medications (within- and across-class) used to treat outpatients with asthma **or chronic obstructive pulmonary disease (COPD)**?
- Are there any differences in effectiveness or harms between patient subgroups (KQ3)?

*Note. **Red text** is not of interest for this archive report, but was included in last report.*

Summary of Findings in Most Recent DERP Report (Controllers; slide 1 of 5)

- 2016 report^a
 - Included 87 studies, cumulative since original report; 77 RCTs, 5 observational studies, and 5 systematic reviews
- Summary of key findings (*for asthma only*):
 - Intraclass comparisons for inhaled corticosteroids
 - In adults, in general, no difference in effectiveness or harms outcomes; few studies reported health care utilization or QoL
 - Some evidence for lower risk of oral candidiasis (thrush) with CIC than with FP
 - In children, results are mostly similar to those seen in adults, but fewer intraclass studies identified
 - Some evidence for reduction in growth-velocity is less with FP than with BEC or BUD, and growth in height was greater with CIC than with BUD

Note. ^a Unable to identify number of trials for asthma versus COPD because of differences in reporting.

Summary of Findings in Most Recent DERP Report (Controllers; slide 2 of 5)

- Summary of key findings (*for asthma only*)
 - ▣ Intraclass comparisons for ICS/LABA
 - No difference in efficacy or harms between:
 - BUD/FOR and FP/SAL,
 - FP/SAL and MOM/FOR
 - No difference in QoL or harms between FP/SAL and FF/VIL

Summary of Findings in Most Recent DERP Report (Controllers; slide 3 of 5)

- Summary of key findings (*for asthma only*)
 - Interclass comparisons
 - ICS vs. leukotriene modifier
 - ICS therapy demonstrated greater effectiveness and QoL than leukotriene modifiers in adults and children, fewer emergency department (ED) visits in children, but no differences in withdrawals due to AEs in children
 - ICS vs. PDE-4 inhibitor^a:
 - ROF (a PDE-4 inhibitor) resulted in more exacerbation experiences and more withdrawals due to AEs
 - ICS/LABA vs. different ICS:
 - No differences in effectiveness, QoL, or harms between FF/VIL and FP
 - Exacerbations of asthma were greater, and AEs more common, with CIS than with FP/SAL, but QoL was more improved with CIC

Note. ^a Drug is not indicated for asthma at this time.

Summary of Findings in Most Recent DERP Report (Controllers; slide 4 of 5)

- Summary of key findings (*for asthma only*)
 - ▣ Interclass comparisons (cont.)
 - ICS/LABA vs. leukotriene modifier
 - In general, ICS/LABAs were more effective in adults and children, and no difference in withdrawals due to AEs
 - ICS/LABA vs. ICS/leukotriene modifier^a
 - In general, ICS/LABAs resulted in greater effectiveness, higher rates of SAEs, and no differences in QoL
 - ICS/LABA vs. LABA/leukotriene modifier^a
 - ICS/LABA had longer (better) time-to-treatment-failure in adolescents and adults

Note. ^a These studies were for leukotriene modifiers as add-on therapy to other drugs, not as fixed products; fixed-dose products for these combinations currently not available.

Summary of Findings in Most Recent DERP Report (Controllers; slide 5 of 5)

- Summary of key findings (*for asthma only*)
 - Population subgroup differences
 - Younger asthma patients (2 to 4 years) experienced more exacerbations and serious AEs with MON than with BUD
 - In a stratified analysis, African American patients experienced higher risk of withdrawals due to AEs and serious AEs with ARF^a compared with FOR^a; there was no difference in Caucasian patients
 - No differences in linear growth velocity between genders in children comparing MON, BUD, or FP, in 1 observational study

Note. ^a These drugs are not indicated for asthma at this time.

Summary of Findings in Most Recent Surveillance (Controllers; slide 1 of 2)

- Cumulative surveillance from most recent report through last 2018 scan (search through May 2019)
 - No new drugs or indications
 - New formulations
 - GLY (Lonhala Magnair): new solution for inhalation; approved for COPD in 2017 (since discontinued)
 - FF/UME/VIL (Trelegy Ellipta): new *fixed-dose combination*; approved 2017
 - BEC (Qvar RediHaler): new aerosol formulation for individuals at least 4 years of age; approved in 2017
 - FF (ArmonAir Digihaler): new powder formulation approved in 2020
 - FP/SAL (AirDuo RespiClick): new powder formulation approved in 2017
 - FOR/GLY (Bevespi Aerosphera): new fixed-dose combination (ICS + LAMA) approved for COPD in 2016

Note. The agents in *red text* are not indicated for asthma at this time.

Summary of Findings in Most Recent Surveillance (Controllers; slide 2 of 2)

- Cumulative surveillance from most recent report through last 2018 scan (search through May 2019)
 - ▣ **No new boxed warnings**
 - Boxed warning *removed* for ICS/LABA products (Advair Diskus, Advair HPA, Breo Ellipta, Dulera, Symbicort), December 2017
 - *LABA used in combination with ICS significantly increases the risk of asthma-related hospitalizations, intubation, and asthma-related deaths, compared with ICS alone*
 - ▣ **13 new studies^a**
 - 1 systematic review, 12 head-to-head RCTs for asthma (4 of the RCTs compare the same drug between different doses or with different delivery methods)

Note. ^a Only studies for asthma are included in this report (additional new studies for COPD are in the most recent surveillance).

New FDA Drugs and Indications Since Last DERP Report (Controllers)

- **No new drugs**

- *Triple therapy, Trelegy Ellipta, is a new fixed-combination drug of individual agents already approved for asthma or COPD*

- **New indications, with or without new formulations**

- Tiotropium bromide (TIO; brand name Spiriva Respimat)
 - In February 2017, the indication was expanded to include maintenance treatment of asthma in patients 6 and older
- Beclomethasone (BEC; brand name Qvar RediHaler)
 - In August 2017, this new formulation's indication was expanded to include pediatric patients at least 4 years
- Fluticasone furoate (FF; brand name Arnuity Ellipta)
 - In May 2018, indication was expanded to include patients 5 and older

New FDA Indications Since Last DERP Report (Controllers)

- **New indications, with or without new formulations (cont.)**
 - Mometasone furoate (MOM; brand name Asmanex HFA)
 - In August 2019, indication was expanded to include patients 5 years and older
 - Budesonide/formoterol (BUD/FOR; brand name Symbicort)
 - In January 2018, indication was expanded to include patients 6 and older
 - Mometasone/formoterol (MOM/FOR; brand name Dulera)
 - In August 2019, indication was expanded to include patients 5 and older
 - Fluticasone furoate/vilanterol (FF/VIL; brand name Breo Ellipta)
 - In May 2023, the indication was expanded to include maintenance treatment of asthma in patients 5 and older

FDA-Approved Indications (Controllers; slide 1 of 3)

- Indications of agents^a as of January 24, 2024

Drug Name (Brand)	Abbreviation	Treatment of, and Prophylaxis for, Asthma	Treatment of Asthma as Add-On to Long-Term Asthma Control Agent	Prevention of Exercise-Induced Bronchospasm in Children and Adults	Maintenance Treatment for COPD
Long-acting beta-2 agonists (LABA)					
Formoterol fumarate (Foradil , Perforomist , Foradil Certihaler)	FOR		✓ (≥ 5 years; Foradil, Foradil Certihaler)	✓ (Foradil)	✓ (Perforomist)
Salmeterol xinafoate (Serevent)	SAL		✓ (≥ 4 years)	✓ (≥ 4 years)	
Long-acting muscarinic antagonists (LAMA)					
Tiotropium bromide (Spiriva , Spiriva Respimat)	TIO	✓ (≥ 12 years; Spiriva Respimat)			✓
Inhaled corticosteroid/long-acting muscarinic antagonist/long-acting beta-2 agonist (fixed-dose triple therapy)					
Fluticasone furoate/umeclidinium bromide/vilanterol trifenate (Trelegy Ellipta) ^b	FF/UME/VIL	✓ (adults ≥ 18 years)		✓	

Notes. ^a Only drugs indicated for asthma are included; ^b New since last report.

FDA-Approved Indications (Controllers; slide 2 of 3)

- Indications of agents^a as of January 24, 2024

Drug Name (Brand)	Abbreviation	Treatment of, and Prophylaxis for, Asthma
Inhaled corticosteroid (ICS)		
Beclomethasone dipropionate (Qvar , Qvar RediHaler)	BEC	✓ (≥ 5 years)
Budesonide (Pulmicort Respules and Flexhaler)	BUD	✓ (≥ 6 years for Flexhaler, 12 months to 8 years for Respules)
Ciclesonide (Alvesco)	CIC	✓ (≥ 12 years)
Flunisolide (Aerospan HFA)	FLUN	✓ (≥ 6 years)
Fluticasone furoate (Arnuity Ellipta)	FF	✓ (≥ 5 years)
Fluticasone propionate (Flovent Diskus , & HFA , ArmonAir Digihaler & RespiClick)	FP	✓ (≥ 4 years)
Mometasone furoate (Asmanex HFA & Twisthaler)	MOM	✓ (≥ 5 years)

Note. ^a Only drugs indicated for asthma are included.

FDA-Approved Indications (Controllers; slide 3 of 3)

- Indications of agents^a as of January 24, 2024

Drug Name (Brand)	Abbreviation	Treatment of, and Prophylaxis for, Asthma	Prevention of Exercise-Induced Bronchospasm in Children and Adults	Maintenance Treatment for COPD
Inhaled corticosteroid/long-acting beta-2 agonist (ICS/LABA fixed-dose combination products)				
Budesonide/formoterol (Symbicort)	BUD/FOR	√ (≥ 6 years)		√
Mometasone furoate/Formoterol (Dulera)	MOM/FOR	√ (≥ 5 years)		
Fluticasone propionate/salmeterol xinafoate (Advair Diskus , Advair HFA , AirDuo Digihaler and RespiClick)	FP/SAL	√ (Advair Diskus, ≥ 4; Advair HFA & AirDuo RespiClick / Digihaler, ≥ 12)		√ (Advair Diskus)
Fluticasone furoate/vilanterol (Breo Ellipta)	FF/VIL	√ (≥ 5 years)		√
Leukotriene modifiers				
Montelukast sodium (Singulair)	MON	√ (≥ 12 years)	√ (≥ 6 years)	
Zileuton (Zyflo , Zyflo CR)	SIL	√ (≥ 12 years)		
Zafirlukast (Accolate)	ZAR	√ (≥ 5 years)		

Note. ^a Only drugs indicated for asthma are included.

New FDA Warnings Since Last DERP Report (Controllers)

- **New boxed or serious warnings**

- 1 new boxed warning

- Montelukast sodium (brand name Singulair)

- Serious neuropsychiatric events added in April 2020

- Boxed warning *removals*

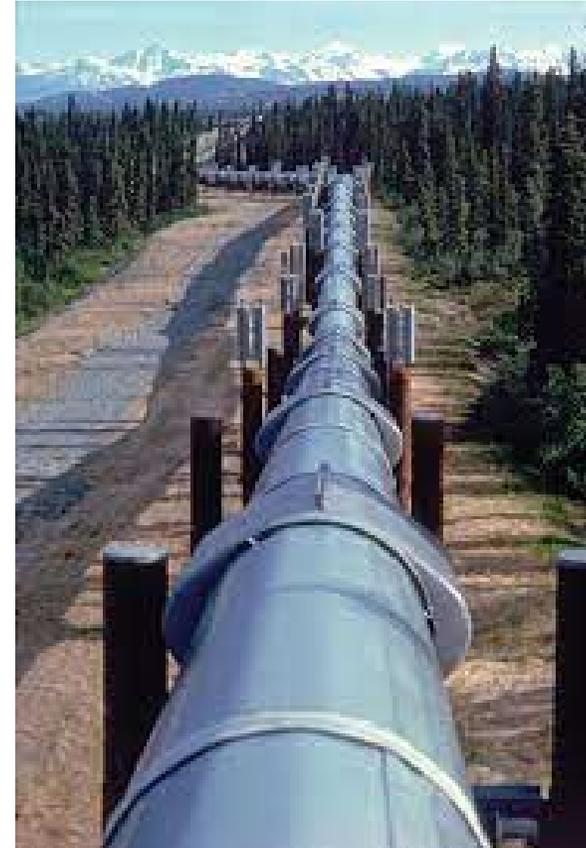
- 1 for ICS/LABA products in 2017 (see slide 34) reported in the surveillance report

- 1 for all LABAs around late 2018/early 2019, the warning for increased risk of asthma-related deaths was demoted

- This warning is currently listed as less serious, and for monotherapy only (no warning when in combination with ICS)

Pipeline Therapies (Controllers)

- Breztri Aerosphere HFA (BUD/FOR/GLY)
 - ICS/LABA/LAMA; solution formulation (inhaled)
- Fostair (BEC/FOR)
 - ICS/LABA; solution formulation (inhaled)
- PT001 (GLY)
 - LAMA; inhaled
- QMF149 (MOM/IND)
 - ICS/LABA



Source. [Britannica.com](https://www.britannica.com)

All pipeline drugs are in phase 3 trials

Generic Drug Status & Brand Discontinuations (Controllers; slide 1 of 3)

Name	Abbreviation	Generic Availability	Status
Inhaled corticosteroid (ICS)			
Beclomethasone dipropionate	BEC	No	Earliest possible generic launch to be determined (in litigation)
Budesonide	BUD	YES	<i>Newly available as generic since last report</i> <ul style="list-style-type: none"> <i>For nebulized solution; unclear if powder formulation is available</i>
Ciclesonide	CIC	No	Exclusivity lost, but no manufactures have applied for generic versions
Flunisolide	FLUN	Unclear	Medication has been phased out by FDA, but may be available for allergy; status unclear <ul style="list-style-type: none"> <i>Aerospan HFA brand discontinued</i>
Fluticasone furoate	FF	No	Loss of exclusivity in 2031
Fluticasone propionate	FP	YES	<i>Newly available as generic since last report</i>
Mometasone furoate	MOM	No	Exclusivity lost, but no manufactures have applied for generic versions

Generic Drug Status & Brand Discontinuations (Controllers; slide 2 of 3)

Name	Abbreviation	Generic Availability	Status
Long-acting beta-2 agonist (LABA)			
Formoterol fumarate	FOR	YES	<i>Newly available as generic since last report</i> • <i>Foradil brand discontinued</i>
Salmeterol xinafoate	SAL	No	Exclusivity lost; 2 manufacturers have applied for generic versions but no estimate date of generic entry
Long-acting muscarinic antagonist (LAMA)			
Tiotropium bromide	TIO	No	Estimated date of generic launch November 2025
ICS/LAMA/LABA fixed-dose triple therapy			
Fluticasone furoate/ umeclidinium bromide/ vilanterol trifenatate	FF/UME/ VIL	No	Estimated date of generic launch October 2030

Generic Drug Status & Brand Discontinuations (Controllers; slide 3 of 3)

Name	Abbreviation	Generic Availability	Status
Inhaled corticosteroid/long-acting beta-2 agonist (ICS/LABA fixed-dose combination products)			
Budesonide/formoterol	BUD/FOR	YES	<i>Newly available as generic since last report</i>
Mometasone furoate/Formoterol	MOM/FOR	Unclear	Estimated date generic launch: 2023 (may be held up due to litigation; some conflicting information between sources)
Fluticasone propionate/salmeterol xinafoate	FP/SAL	YES	<i>Newly available as generic since last report</i>
Fluticasone furoate/vilanterol	FF/VIL	YES	<i>Newly available as generic since last report</i>
Leukotriene modifiers			
Montelukast sodium	MON	Yes	Likely already available as generic with last report
Zileuton	SIL	Yes	Likely already available as generic with last report • <i>Zyflo CR brand discontinued</i>
Zafirlukast	ZAR	Yes	Likely already available as generic with last report

Clinical Practice Guidelines (Controllers; slide 1 of 5)

Overall asthma management

- Patient education and action plans are key
 - Learn skills to self-monitor for symptoms and control, appropriately use inhalers/medications, avoid environmental triggers
- Initiating pharmacotherapy
 - All patients with asthma should have immediate access to an inhaled bronchodilator (quick-relief agent)
 - SABA (albuterol or levalbuterol) is most common/traditional
 - For patients with moderate or severe asthma, or those with history of severe attacks, consider concomitant (or combination inhalers) **low-dose glucocorticoid**
 - Initial maintenance therapy is based on asthma severity, and adjustment of therapy is based on asthma control

Clinical Practice Guidelines (Controllers; slide 2 of 5)

- Maintenance therapy; step-care approach (steps 1 to 4+)
 - Adults and adolescents
 - Step 1 (intermittent and mild) – treatment as needed
 - SABA only (according to the National Asthma Education and Prevention Program [NAEPP] guidelines); low-dose ICS-SABA or low-dose ICS-formoterol (combined or as used together; according to the Global Initiative for Asthma [GINA] guidelines)
 - Step 2 (mild persistent) – treatment as needed
 - Low-dose ICS alone, or plus SABA (NAEPP); low-dose ICS-formoterol (GINA)
 - Leukotriene modifiers are alternatives when avoidance of ICS is necessary (lower efficacy)

Clinical Practice Guidelines (Controllers; slide 3 of 5)

- Maintenance therapy; step-care approach (steps 1 to 4+)
 - Adults and adolescents (cont.)
 - Step 3 (moderate persistent)
 - Low-dose **ICS-formoterol** preferred (both guidelines), and SABA or **ICS-SABA** as needed
 - Inhaled **LAMA (tiotropium)** can be equally effective as **ICS-LABA** and appropriate for any patient intolerant to **formoterol/LABA**
 - Step 4 (severe persistent)
 - Medium-dose **ICS-formoterol** preferred (both guidelines); other **ICS-LABA** treatments recommended as alternatives, with SABA as needed
 - Additional therapy with **leukotriene modifiers, LAMAs**, or biologic agents may be needed (consider new **triple inhaler** product for severe persistent asthma)
 - In rare situations, systemic glucocorticoids may be needed, but caution due to long-term effects; biologics may be newer option with fewer long-term AEs

Clinical Practice Guidelines (Controllers; slide 4 of 5)

- Maintenance therapy for children
 - Oral systemic corticosteroids are recommended if asthma attacks/exacerbations occur:
 - More than 2 days per week in children 2 to 3 years
 - Throughout the day in children > 3 to 12 years
 - Step-care approach
 - Step 1: SABA as needed; short course daily ICS and SABA as needed (> 4 years)
 - Step 2: Daily low dose ICS, and SABA as needed; daily low dose ICS (< 4 years)
 - Step 3: Daily and as need, low-dose ICS-formoterol; daily low-dose ICS-LABA or ICS plus LMs (< 4 years)
 - Step 4 and higher: Daily and as needed medium or high dose ICS-formoterol, or ICS-LABA (< 4 years) , and SABA as needed for serious cases; biologics considered for most severe cases

Clinical Practice Guidelines (Controllers; slide 5 of 5)

- Exercise-induced asthma (bronchoconstriction)
 - ▣ Exercise to improve cardiovascular fitness actually reduces risk for bronchoconstriction
 - ▣ This symptom in most patients with well-controlled asthma is often treated by:
 - Avoiding exercise in cold or dry air
 - Pharmacotherapy
 - SABA or combination ICS and formoterol pretreatment (5 to 20 minutes prior to activity)
 - SABA plus LMs or ICS for patients who require daily therapy for this symptom
 - ▣ If symptom persists, consider step-up treatment of underlying asthma condition

Key Clinical Practice Guidelines

Focus	Date	Title of Guideline
British Thoracic Society (BTS) and Scottish Intercollegiate Guidelines Network (SIGN)		
General asthma treatment	2019	British guideline on the management of asthma
Canadian Thoracic Society (CTS)		
General asthma treatment	2021	Diagnosis and management of asthma in preschoolers, children and adults
Global Initiative for Asthma (GINA)		
Management and prevention	2023	Global Strategy for Asthma Management and Prevention
National Asthma Education and Prevention Program (NAEPP) and National Heart, Lung, and Blood Institute (NHLBI)		
Update	2020	Focused Updates to the Asthma Management Guidelines
Diagnosis and management	2007	Guidelines for the Diagnosis and Management of Asthma
US Department of Veterans Affairs/Department of Defense (VA/DoD)		
Management in adults	2019	The Primary Care Management of Asthma

Questions?



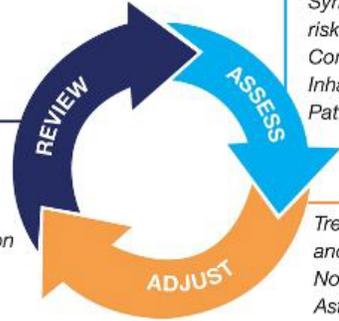


**Adults & adolescents
12+ years**

Personalized asthma management

Assess, Adjust, Review
for individual patient needs

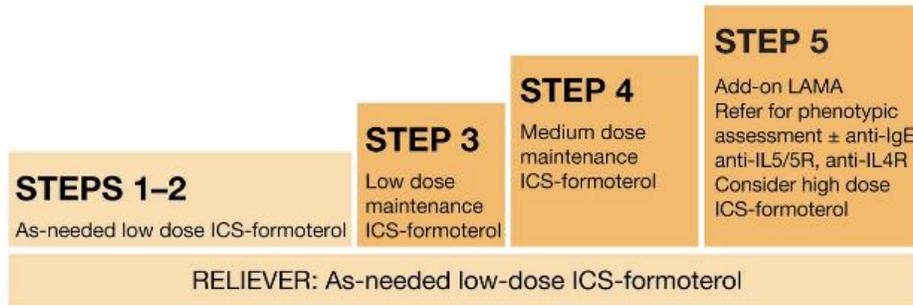
Symptoms
Exacerbations
Side-effects
Lung function
Patient satisfaction



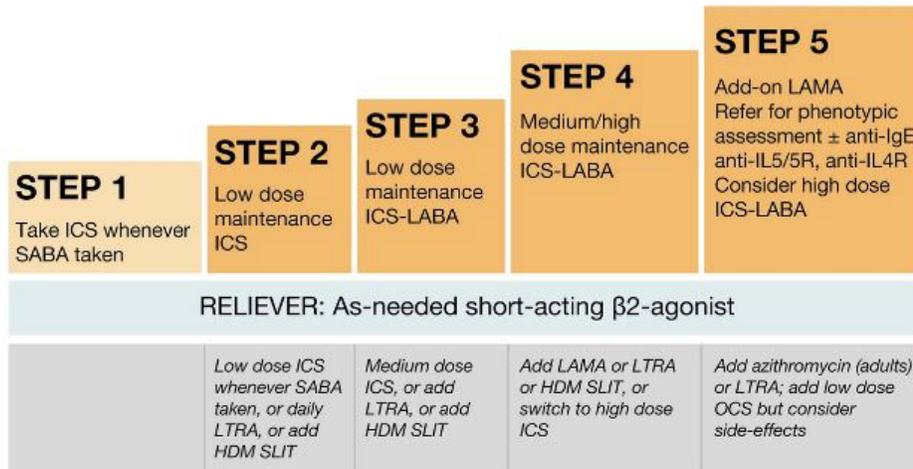
Confirmation of diagnosis if necessary
Symptom control & modifiable
risk factors (including lung function)
Comorbidities
Inhaler technique & adherence
Patient preferences and goals

Treatment of modifiable risk factors
and comorbidities
Non-pharmacological strategies
Asthma medications (adjust down/up/between tracks)
Education & skills training

**CONTROLLER and
PREFERRED RELIEVER**
(Track 1). Using ICS-formoterol
as reliever reduces the risk of
exacerbations compared with
using a SABA reliever



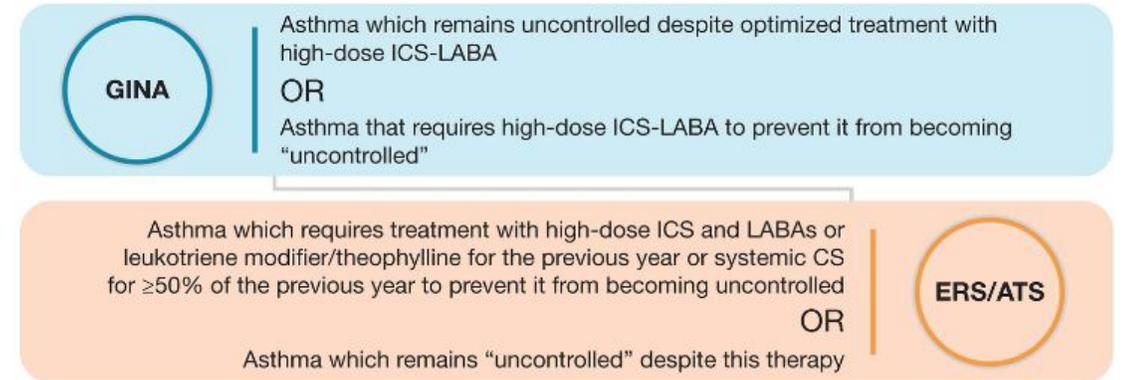
**CONTROLLER and
ALTERNATIVE RELIEVER**
(Track 2). Before considering a
regimen with SABA reliever,
check if the patients is likely to
be adherent with daily controller



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Source. [Calhoun et al., 2022](#)

Severe Asthma



a GINA recommended stepwise asthma treatment. **b** Severe asthma definition [1, 2]. ATS American Thoracic Society, BDP budesonide propionate, CS corticosteroids, ERS European Respiratory Society, FEV₁ forced expiratory volume in 1 s, GINA Global Initiative for Asthma, HDM house dust mite, ICS inhaled corticosteroids, IgE immunoglobulin E, IL interleukin, LABA long-acting β₂-agonist, LAMA long-acting muscarinic antagonist; LTRA leukotriene receptor antagonist, OCS oral corticosteroids; SABA short-acting β₂-agonist; SLIT sublingual immunotherapy