Drug Use Research & Management Program
Oregon State University, 500 Summer Street NE, E35
Salem, Oregon 97301-1079
Phone 503-947-5220 | **Fax** 503-947-2596

Drug Class Literature Scan: Inhalers for Asthma/COPD

Date of Review: June 2026

Date of Last Review: June 2024
Literature Search: 12/01/2023 – 03/25/2026

Current Status of PDL Class:
See **Appendix 1**.

Plain Language Summary:

- This review focuses on new information for inhalers in people who have asthma or chronic obstructive pulmonary disease (COPD).
- Inhaled medicines to treat asthma and COPD includes medicines called inhaled corticosteroids (ICS), long-acting beta-agonists (LABA), long-acting muscarinic antagonists (LAMAs), short-acting beta-agonists (SABA), short-acting muscarinic antagonists (SAMAs) and combinations of these medicines called ICS/LABA, LAMA/LABAs and ICS/LABA/LAMA.
- A review of studies in patients with COPD found that a combination LABA/LAMA inhaler called umeclidinium/vilanterol and a combination ICS/LABA/LAMA inhaler called umeclidinium/vilanterol/fluticasone furoate helped improve breathing problems, also known as exacerbations, compared to other similar inhaler therapy.
- A recent review that compiled data from many studies found that people who have moderate to severe COPD had fewer exacerbations when they added an ICS inhaler to their LAMA/LABA therapy.
- For people with COPD, the 2026 Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommends inhalers that align with fee-for-service (FFS) policy.
- For people with asthma, the Global Strategy for Asthma Management and Prevention (GINA), the British Thoracic Society (BTS), the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), and the Veterans Administration and Department of Defense (VA/DOD) recommend inhalers that align with FFS policy.
- Two new studies showed that adding an ICS inhaler helps improve breathing in people with asthma who still have symptoms when using a LABA or SABA inhaler alone.
- The Drug Use Research and Management (DURM) group recommends continuing with the current policy for inhaler therapy offered to patients with asthma or COPD.

Conclusions:

- There were 2 systematic reviews and meta-analyses, 4 high quality guidelines and 2 randomized controlled trials (RCTs) included in this literature scan.
- A high-quality systematic review and meta-analysis found dual umeclidinium (UMEC)/vilanterol (VI) and triple UMEC/VI/fluticasone furoate (FF) therapy improved lung function and symptoms in patients with COPD, when compared to active treatment, or placebo.[1]

Author: Kathy Sentena, PharmD

- A Cochrane review evaluated addition of an inhaled corticosteroid (ICS) to a long-acting muscarinic antagonist (LAMA) and long-acting beta-agonist (LABA), known as triple therapy, in patients who have moderate to severe COPD.[2] Triple therapy decreased severe exacerbations compared to LAMA/LABA therapy based on low-quality evidence (relative risk [RR] 0.75; 95% confidence interval [CI], 0.67 to 0.84). The risk of pneumonia was increased with triple therapy compared to LAMA/LABA , 3.3% versus 1.9% (odds ratio [OR] 1.74; 95% CI, 1.39 to 2.18).[2]
- The GOLD guidance for management of COPD was updated in 2026.[3] Guideline recommendations for inhalers align with the current FFS policy.
- A collaborative guideline from the British Thoracic Society (BTS), National Institute for Health and Care Excellence (NICE) and Scottish Intercollegiate Guidelines Network (SIGN) on the management of asthma for children and adults was published in 2024. Using anti-inflammatory therapy with reliever therapy is advocated as initial asthma management.[4] These recommendations align with other guidelines.[4]
- In 2025, GINA updated guidance for asthma management in individuals of all ages.[5] Recommendations for inhalers are consistent with the FFS policy and preferred drug list (PDL).
- The VA/DOD updated guidance on the management of asthma in primary care in 2025.[6] Updated guidance includes initiating therapy with an anti-inflammatory and rapid-acting LABA inhaler. Clinical guideline recommendations align with the current PDL.
- A RCT compared efficacy of FF/VI to FF monotherapy in patients 5 to 17 years. Patients were randomized to dual therapy or continuation of ICS (e.g., FF).[7] The combination of FF/VI was more effective at improving forced expiratory volume in one second (FEV_1) than FF monotherapy (treatment difference [TD] 0.083 L; 95% CI, 0.037 to 0.129; p<0.001), a difference that was both statistically and clinically significant.[7]
- A RCT evaluated combination therapy with albuterol/budesonide compared to albuterol alone in patients 12 years of age and older with mild asthma uncontrolled despite treatment with a SABA with or without low-dose inhaled glucocorticoid or leukotriene receptor antagonist.[8] The combination regimen was superior to albuterol alone for the outcome of first severe asthma exacerbation (hazard ratio [HR] 0.53; 95% CI, 0.39 to 0.73; P<0.001).[8] The trial was stopped early due to significant reduction in the risk of severe exacerbations with combination therapy.

Recommendations:
- No changes to the PDL are recommended based on the review of the clinical evidence.
- Evaluate costs in executive session.

Summary of Prior Reviews and Current Policy
- The inhaled therapies for asthma and COPD are comprised of 5 classes: SABAs, LABAs, SAMAs, LAMAs, and ICS. For ease of administration, these drug classes are combined into single combination inhalers in the following iterations: ICS/LABA, LAMA/LABA, and LAMA/LABA/ICS.
- Previous reviews have found low- to moderate-quality evidence of no within-class differences in efficacy or harms for long-acting products (i.e., LABAs, LAMAs or ICS) for patients with asthma or COPD.
- This class was last reviewed in June of 2024 and no changes were made to the PDL based on a review of the evidence.
- After evaluation of costs in executive session, beclomethasone dipropionate HFA (QVAR RediHaler) and mometasone HFA (ASMANEX) were made preferred on the PDL and fluticasone propionate HFA was made non-preferred.
- A complete list of preferred and nonpreferred products is available in **Appendix 1**.
- Specific prior authorization requirements are outlined in **Appendix 6** for the following:
    - Non-preferred ICS inhalers
    - Non-preferred LABA inhalers
    - Non-preferred LAMA/LABA and LAMA/LABA/ICS inhalers

- There were over 2,000 claims for inhalers for asthma and COPD, costing almost $200,000, in quarter 4 of 2025 (September 1 to December 31).

Methods:
A Medline literature search for new systematic reviews and RCTs assessing clinically relevant outcomes to active controls, or placebo if needed, was conducted. A summary of the clinical trials is available in **Appendix 2** with abstracts presented in **Appendix 3**. The Medline search strategy used for this literature scan is available in **Appendix 4**, which includes dates, search terms and limits used. The OHSU Drug Effectiveness Review Project, Agency for Healthcare Research and Quality (AHRQ), National Institute for Health and Clinical Excellence (NICE), Department of Veterans Affairs, the Scottish Intercollegiate Guidelines Network (SIGN), and the Canada's Drug Agency (CDA-AMA) resources were manually searched for high quality and relevant systematic reviews. When necessary, systematic reviews are critically appraised for quality using the AMSTAR tool and clinical practice guidelines using the AGREE tool. The FDA website was searched for new drug approvals, indications, and pertinent safety alerts.

The primary focus of the evidence is on high quality systematic reviews and evidence-based guidelines. Randomized controlled trials will be emphasized if evidence is lacking or insufficient from those preferred sources.

New Systematic Reviews:

Zhu – Umeclidinium/Vilanterol for COPD
A systematic review and meta-analysis evaluated the efficacy of combination UMEC/VI and UMEC/VI/FF therapies compared to other active treatments or placebo in people with COPD.[1] Literature was searched up till June 30, 2024. Fifteen RCTs (n=31,184) met inclusion criteria. Individuals 18 years or older, average age of 64 years, with mild to moderate COPD were included. Trials lasted 8-52 weeks in duration. Eleven of the 15 RCTs evaluated UMEC/VI dual therapy effectiveness compared to other therapies, with the remaining 4 studies evaluating triple therapy.[1] Active treatment comparisons included: tiotropium, salmeterol, tiotropium/olodaterol, budesonide formoterol, salmeterol/fluticasone propionate, tiotropium/indacaterol, indacaterol/glycopyrrolate, glycopyrrolate/formoterol fumarate and fluticasone furoate/vilanterol. Evaluation of risk of bias by the authors determined that a majority of the studies had low risk.

Lung function, as measure by FEV_1, was significantly improve, compared to active treatment described above, with UMEC/VI (OR 1.98; 95% CI, 1.70 to 2.30) and transitional dyspnea index [TDI] values (OR 1.97; 95% CI, 1.72 to 2.26).[1] Quality of life scores, measured by St. George's Respiratory Questionnaire Total Score (SGRQTS), were reduced (OR 1.99; 95% CI, 1.71 to 2.32).[1] Triple therapy with UMEC/VI/FF also improved FEV_1 (OR, 1.93; 95% CI, 1.73 to 2.15) and TDI (OR 2.37; 95% CI, 2.15 to 2.61) with reduced SGRQ total scores (OR 1.83; 95% CI, 1.63 to 2.05).[1] Both treatments were well tolerated and associated with fewer adverse events compared to active treatment (described above). Overall, combination therapy with UMEC/VI and UMEC/VI/FF are effective treatment options for patients with COPD.[1]

Cochrane – Inhaled Corticosteroids with LABAs and LAMAs for COPD
A systematic review and meta-analysis evaluated the efficacy of adding an ICS to LAMA/LABA (triple therapy) for the treatment of COPD.[2] A total of 4 studies (n= 15,412) met inclusion criteria. Females represented 28% to 40% of the enrolled populations with the average age of all participants of 64.4 to 65.3 years. All participants had symptomatic air flow restriction (severe to very severe airflow limitation) with FEV_1 of <50% predicted.[2] Most participants had one or more moderate to severe COPD exacerbations in the last 12 months. Study duration was 24 weeks to 52 weeks.[2] The risk of bias was determined to be low in the

majority of studies. The primary outcomes were acute COPD exacerbations, respiratory health related quality of life, frequency of pneumonia and adverse events.

There was low-quality evidence that triple therapy (ICS/LAMA/LABA) reduced moderate-to-severe COPD exacerbations compared to LAMA/LABA inhalers (RR 0.74; 95% CI, 0.67 to 0.81; n=15,397).[2] Patients that had high blood eosinophil counts (150 -200 eosinophils/µL) may benefit more from triple therapy by a reduction in exacerbations (RR 0.67; 95% CI, 0.60 to 0.75) compared to those with low blood eosinophil counts (RR 0.87; 95% CI, 0.81 to 0.93); however, results were based on observational data.[2] Severe COPD exacerbations with triple therapy may be reduced more than LAMA/LABA therapy based on low-quality evidence (RR 0.75; 95% CI, 0.67 to 0.84).[2]

Quality of life was improved with triple therapy, as measured by a change of at least 4 points (which is the minimal clinically important difference [MCID]) in the SGRQ score (OR 1.35; 95% CI, 1.26 to 1.45) (high-quality evidence).[2] There is moderate-quality evidence that triple therapy may reduce symptoms, as measured by the TD (OR 1.33; 95% CI, 1.13 to 1.57). Changes in trough FEV_1 favored triple therapy although evidence was of low quality (mean difference [MD] 38.68 mL; 95% CI, 22.58 to 54.77).[2] Neither changes in TDI or trough FEV_1 were considered clinically meaningful.

When triple therapy is compared to LAMA/LABA there was an increased risk of pneumonia, 3.3% versus 1.9% (OR 1.74; 95% CI, 1.39 to 2.18) based on moderate-quality evidence.[2] There was low-quality evidence that serious adverse events and all-cause mortality were similar between the groups.

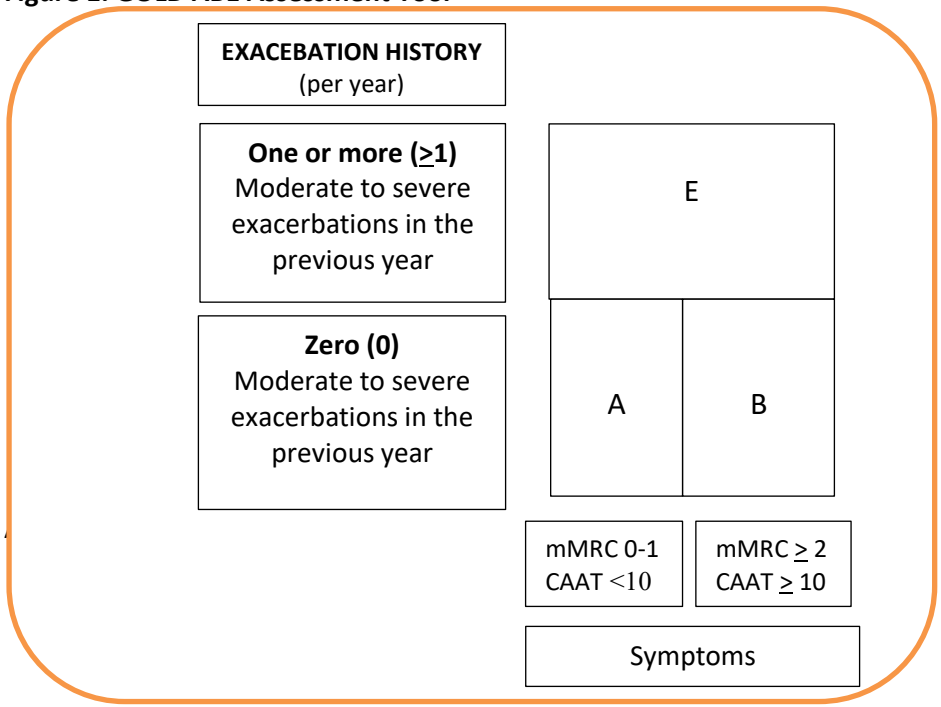
After review, 6 systematic reviews were excluded due to poor quality, wrong study design of included trials (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical).[9–15]

New Guidelines:
High Quality Guidelines:

<u>GOLD Guidelines – Global Initiative for Chronic Obstructive Lung Disease</u>
In 2026, GOLD published their annual update of guidance for management of COPD.[3] The evidence was graded as A (high-quality evidence from RCTs without significant limitations), B (from RCTs with limitations), C (non-randomized trials and observational studies), and D (panel consensus). Important updates related to management and pharmacotherapy include: new definitions of GOLD A, B and E categories, revised management cycle and treatment algorithm to emphasize the distinction between initial pharmacotherapy and follow-up treatment, use of biologic therapy, and management of COPD exacerbations. For a full description of all the 2026 updates consult the GOLD report.[3]

One clarifications made in the 2026 recommendations are to the GOLD ABE Assessment Tool (**Figure 1**).[3] The recommendations are that the categories be adjusted to emphasize the importance that moderate to severe exacerbations play in predicting subsequent events.[3] If exacerbations are more frequent or severe, the risk of additional exacerbations is even higher.[3] The threshold has been reduced so that even one moderate exacerbation may be cause for treatment escalation.

Figure 1. GOLD ABE Assessment Tool[3]



The guideline also updated its management of COPD recommendations.[3] Patients who smoke are strongly encouraged to quit (Evidence A).[3] Guideline recommended vaccines for people with COPD are: COVID-19 vaccination, influenza, pneumococcal, and RSV (Evidence B for all but RSV which has Evidence level A).[3] Tetanus, diphtheria, and acellular pertussis vaccine (Tdap) vaccination and the shingles vaccine are also recommended (Evidence B). In additional to pharmacotherapy interventions, non-pharmacological measures should be considered (i.e., pulmonary rehabilitation, exercise training, COPD education) which has been shown to improve exercise capacity and quality of life in patients with COPD.[3] Long-term oxygen therapy may improve survival in patients with severe resting chronic hypoxemia, but otherwise should not be prescribed for patients with stable COPD and those with resting or exercise-induced moderate desaturation.[3] Surgical or bronchoscopic interventions may be beneficial in select patients with advanced emphysema refractory to optimized medical care.

Pharmacological Maintenance Treatment of COPD:[3]

- Initial pharmacotherapy should be selected based on the severity of symptoms, exacerbation risk, adverse reactions, patient comorbidities, drug availability, cost and the patient's preference and ability to use drug delivery devices (**Table 1**).[3]
- Attainment and barriers to treatment goals should be reviewed at intervals dependent upon disease severity.
- LABA + LAMA + ICS is the only pharmacotherapy with evidence of a mortality reduction in COPD patients with symptoms and history of frequent and/or severe exacerbations.

Table 1. Pharmacological Management for the Treatment of COPD[3]

Initial Treatment		
Group	**Treatment**	**Notes**
E	LABA + LAMA*	Consider LABA + LAMA + ICS if blood eos ≥ 300 cells/µL
A	Bronchodilator (no specific treatment recommended)	Short or long-acting bronchodilators, but long-acting are preferred
B	LABA + LAMA*	Combination with LABA + LAMA is the preferred therapy If combination therapy is not appropriate then there is no comparative evidence suggesting one class of long-acting bronchodilator over another (LABA or LAMA) Treat comorbidities if present
Follow-up Treatment if Dyspnea or Exacerbation		
Symptom	**Treatment**	**Notes**
Persistent dyspnea	LABA or LAMA ↓ LABA + LAMA	• Consider switching inhaler device or molecules • Implement or escalate non-pharmacological treatment(s) • Consider adding ensifentrine • Evaluate for other causes of dyspnea and treat if indicated
One or more moderate or severe exacerbation	LABA or LAMA ↓ LABA + LAMA – if blood eos < 300 cells/µL **OR** LABA + LAMA + ICS – if blood eos ≥ 300 cells/µL	• If patient continues to have symptoms move to next row
Ongoing symptoms and taking LABA + LAMA therapy	LABA + LAMA + ICS – if blood eos ≥ 100 cells/µL **OR** - If blood eos < 100 cells/µL > Roflumilast **OR** Azithromycin	• Roflumilast is preferred if FEV_1 < 50% & chronic bronchitis • Azithromycin preferentially in former smokers
Ongoing symptoms and taking LABA + LAMA + ICS therapy	Roflumilast **OR** Azithromycin	• Roflumilast is preferred if FEV_1 < 50% & chronic bronchitis • Azithromycin preferentially in former smokers
Ongoing symptoms and taking LABA + LAMA + ICS therapy **AND** Two moderate or one severe exacerbation **AND** blood eos ≥ 300 cells/µL	Biologic Therapy	• Dupilumab (with chronic bronchitis) • Mepolizumab (with or without chronic bronchitis)
Patients taking LABA + ICS		
LABA + ICS and no relevant exacerbation history	Consider changing to LABA + LAMA	• NA

LABA + ICS with no relevant exacerbation history and high symptoms	Consider LABA + LAMA + ICS	• If the patient has no current exacerbations and previous positive response to treatment and low symptoms then continue LABA + ICS treatment
LABA + ICS and current exacerbations with blood eos < 100 cells/µL	Consider changing to LABA + LAMA	• Blood eosinophils dictate best treatment path
LABA + ICS and current exacerbations with blood eos ≥ 100 cells/µL	Consider escalating to LABA + LAMA + ICS	• NA

Key: * Single combination inhaler may be more convenient and improve adherence to treatment
Abbreviations: eos = eosinophil count; FEV_1 = forced expiratory volume in 1 second; ICS = inhaled corticosteroid; LABA = long-acting beta-agonist; LAMA = long-acting muscarinic receptor antagonist; NA = not applicable.

If a patient has asthma and COPD, they should be considered different diseases and pharmacotherapy should primarily follow asthma guidelines.[3] The use of ICS with long-acting bronchodilators in patients with COPD should be considered in patients with history of hospitalization for COPD exacerbations, 2 or more moderate exacerbations of COPD per year, blood eosinophils of 300 cells/µL or higher, or history of asthma, as these characteristics strongly favor ICS use. For patients with 1 or more moderate exacerbation of COPD annually or blood eosinophils 100 to <300 cells/µL, the use of ICS is favored. For patients with repeat pneumonia, blood eosinophils < 100 cells/µL, or history of mycobacterial infection, the use of ICS is not recommended.[3] De-escalation of ICS is recommended for patients that develop pneumonia or other adverse reactions.[3]

The GOLD guidelines also offer recommendations for the management of COPD exacerbations. Recommendations include:
- Initiation of SABAs with or without short-acting anticholinergics as the initial bronchodilators to treat an acute exacerbation (Evidence C).[3]
- Systemic corticosteroids for 5 days can be considered to improve lung function (FEV_1), oxygenation, and shorten recovery time and hospitalization time (Evidence A).[3]
- Antibiotics are recommended in patients with purulent sputum, prior positive sputum bacteria culture, or requiring mechanical ventilation (invasive or noninvasive) (Evidence A). When given for 5 days they have been shown to shorten recovery time, reduce risk of relapse, reduce treatment failure, and shorten hospitalizations (Evidence B).[3]
- Consider appropriate regimens to decrease frequency of COPD exacerbations

<u>SIGN Guidelines – Asthma: Diagnosing, Monitoring and Chronic Asthma Management (SIGN 245)</u>
A collaboration between the BTS, NICE and SIGN published recommendations for the management of chronic asthma in 2024, with a minor update in November 2025.[4] The guideline includes diagnosis and assessment of asthma in adults and children, pharmacological treatment, and monitoring. This review will focus on recommendations for pharmacotherapy in asthma.

Assessment of uncontrolled asthma should be done prior to initiating medications or adjusting asthma medications.[5] Adherence, inhaler technique, alternative diagnoses or comorbidities, smoking, and occupation exposure, psychosocial factors, seasonal factors and environmental factors should be considered. Determine fractional exhale nitric oxide (FeNO) level if possible.[4] If levels are high, there may be adherence issues or need for an increased dose of corticosteroid. Recommendations for asthma medication management in those 12 and older are included in **Table 3,** for those 5 to 11 years in **Table 4** and for

those under 5 in **Table 5.** Response to treatment should be reviewed 8-12 weeks after starting or adjusting treatment.[4] If considering step-down treatment for people aged 12 and over who are using low-dose maintenance ICS plus a SABA as needed or low-dose MART (maintenance and reliever therapy), step down to low-dose ICS/formoterol combination inhaler as needed (as-needed anti-inflammatory reliever [AIR] therapy).[4] The use of MART allows for individuals to use the same inhaler for maintenance and rescue therapy because it contains an ICS and a fast-acting beta-agonist, such as formoterol. Anti-inflammatory Reliever therapy, known as AIR therapy, uses a single inhaler containing a fast-acting bronchodilator, such as formoterol, and an ICS to use as needed, in place of traditional SABA therapy.

Table 3. SIGN Pharmacotherapy Recommendations for Asthma Management in People Aged 12 and Over[4]

Recommendation
Do not prescribe a SABA to people of any age with asthma without a concomitant prescription of an ICS.
Initial Management
Offer low-dose ICS/formoterol combination inhaler for as needed symptom relief (AIR therapy).*
Highly symptomatic patients or those with severe exacerbations: start with low-dose MART therapy in addition to treating acute symptoms. Consider step-down therapy to AIR therapy.
Offer low-dose MART to people aged 12 and over with asthma that is not controlled with an as needed low-dose ICS/formoterol combination inhaler.
Offer moderate-dose MART to people aged 12 and over with asthma that is not controlled on low-dose MART.
For people not controlled on moderate-dose MART despite good adherence, check the FeNO level and blood eosinophil count if available. If neither level is raised, consider trial of LTRA or LAMA.
Uncontrolled Asthma
If using a SABA only, change treatment to low-dose ICS/formoterol combination inhaler used as needed (as-needed AIR therapy).
Consider changing treatment to low-dose MART for people with asthma that is not controlled on: • Regular low-dose ICS plus SABA as needed • Regular low-dose ICS/LABA combination inhaler plus SABA as needed • Regular low-dose ICS and supplementary therapy (LTRA) plus SABA as needed • Regular low-dose ICS/LABA combination inhaler and supplementary therapy (LTRA) plus SABA as needed
Consider changing treatment to moderate-dose MART for people with asthma that is not controlled on: • Regular moderate-dose ICS plus SABA as needed • Regular moderate-dose ICS/LABA combination inhaler plus SABA as needed • Regular moderate-dose ICS and supplementary therapy (LTRA or LAMA, or both) plus SABA as needed • Regular moderate-dose ICS/LABA combination inhaler and supplementary therapy (LTRA or LAMA, or both) plus SABA as needed
When changing from low- or moderate-dose ICS (or ICS/LABA combination inhaler) plus supplementary therapy to MART, consider whether to stop or continue the supplementary therapy based on the degree of benefit achieved when first introduced.
Key: * Only certain budesonide/formoterol inhalers are approved for as-needed AIR therapy in mild asthma Abbreviations: AIR – anti-inflammatory reliever; FeNO – fractional exhaled nitric oxide (FeNO); ICS – inhaled corticosteroid; LABA – long-acting beta-agonist; LAMA – long-acting muscarinic receptor antagonist; LTRA – leukotriene receptor antagonist; MART – maintenance and reliever therapy; SABA – short-acting beta-agonist.

Table 4. SIGN Pharmacotherapy Recommendations for Asthma Management in People Aged 5 to 11 years[4]

Recommendation
Initial Management
Offer a twice-daily pediatric low-dose ICS with SABA as needed.
Consider pediatric low-dose MART for children with asthma that is not controlled on low-dose ICS plus SABA as needed, as long as they are assessed to have the ability to manage a MART regimen*.
Uncontrolled Asthma Management
Consider increasing to pediatric moderate-dose MART if asthma is not controlled on pediatric low-dose MART.
Consider adding a LTRA to twice daily pediatric low-dose ICS plus SABA as needed when a child has uncontrolled asthma and is assessed as unable to manage the MART regimen.
Offer a twice daily pediatric low-dose ICS/LABA combination inhaler plus SABA as needed to children assessed as unable to manage the MART regimen if their asthma is not controlled on pediatric low-dose ICS plus SABA as needed (with or without a LTRA depending on previous response).
Offer a twice daily pediatric moderate-dose ICS/LABA inhaler plus SABA as needed to children with asthma that is not controlled on pediatric low-dose ICS/LABA plus SABA as needed (with or without an LTRA depending on previous response).
Key: * only one budesonide/formoterol dry powder inhaler (100 micrograms/6 micrograms per inhalation) is licensed for MART in children aged 6 to 11 years. Abbreviations: ICS – inhaled corticosteroid; LABA – long-acting beta-agonist; LAMA – long-acting muscarinic receptor antagonist; LTRA – leukotriene receptor antagonist; MART – maintenance and reliever therapy; SABA – short-acting beta-agonist.

Table 5. SIGN Pharmacotherapy Recommendations for Asthma Management in Children under 5 years[4]

Recommendation
Newly Suspected Asthma, Confirmed Asthma, or Uncontrolled on Current Treatment
Consider an 8 to 12 week trial of twice-daily pediatric ICS as maintenance therapy (with SABA for reliever therapy) in children under 5 with suspected asthma and: • symptoms at presentation that indicate the need for maintenance therapy (for example, interval symptoms in children with another atopic disorder), **or** • severe acute episodes of difficulty breathing and wheeze (for example, requiring hospital admission, or needing 2 or more courses of oral corticosteroids)
If symptoms resolve during the trial period, but then recur by the 3-month review or the child has an acute episode requiring systemic corticosteroids or hospitalization: • restart regular ICS (begin at a pediatric low dose and titrate up to a pediatric moderate dose if needed) with SABA as needed and consider a further trial without treatment after reviewing the child within 12 months
If suspected asthma is uncontrolled in children under 5 on a pediatric moderate dose of ICS as maintenance therapy (with SABA as needed), consider a LTRA in addition to the ICS. Give the LTRA for a trial period of 8 to 12 weeks (unless there are side effects), then stop it if it is ineffective.
If suspected asthma is uncontrolled in children under 5 on a pediatric moderate dose of ICS as maintenance therapy and a trial of an LTRA has been unsuccessful or not tolerated, stop the LTRA and refer the child to a specialist in asthma care for further investigation and management.
Abbreviations: ICS – inhaled corticosteroid; LTRA – leukotriene receptor antagonist; SABA – short-acting beta-agonist.

In April 2025, a reminder was issued of the risk of severe asthma attacks and increased mortality with the overuse of SABA with or without an ICS.[4]

GINA – Global Strategy for Asthma Management and Prevention

In 2025, GINA updated asthma diagnosis and management guidance for adults and children.[5] The focus of this update will be on pharmacotherapy recommendations for asthma.

The goal of asthma management is to control symptoms, prevent exacerbations, airway damage and medication side-effects. Pharmacotherapy recommendations are presented in **Table 6**.[5]

Table 6. GINA General Asthma Pharmacotherapy Recommendations[5]

Recommendation	Notes
1. Makes sure every patient has an ICS (or combination that contains an ICS)	- This recommendation applies even if symptoms are infrequent. - ICS medication should be started as soon as possible after diagnosis. - Any patient can have a severe exacerbation, even if asthma is mild. - ICS products decrease risk of asthma hospitalization and death. - Early ICS treatment with low-dose ICS is associated with better lung function. - Patients who have a severe exacerbation when not using an ICS have worse long-term lung function compared to those that use an ICS.
2. Every patient needs a reliever inhaler containing a rapid-acting bronchodilator to use for symptom management	- Options include ICS-formoterol, ICS-SABA or SABA. - Low-dose ICS-formoterol is the preferred option in adolescents and adults compared to regimens containing SABAs.
3. Treatment containing only as-needed SABAs are not recommended.	- The use of SABA-only treatments has been shown to increase risk of exacerbations, worsen lung function and increase risk of death due to asthma.
Abbreviations: ICS = inhaled corticosteroid; SABA= Short-acting beta-agonist	

Specific, step-based treatment recommendations are included below in **Table 7**. The table refers to anti-inflammatory reliever (AIR) therapy, which is the use of ICS-formoterol combination inhaler as needed for asthma symptoms.[5] The table also describes the use of maintenance-and-reliever therapy (MART), which is the combination ICS-formoterol is taken as a daily maintenance treatment and an extra dose is used of the same medication when there are asthma symptoms. Once good asthma control has been achieved and maintained for 2-3 months, consider stepping down therapy to the lowest treatment dose to control both symptoms and exacerbations.[5] In adults and adolescents with severe asthma, assessment for asthma inflammatory phenotype and sputum eosinophil count is recommended, if available, to guide treatment. Maintenance oral corticosteroids should only be used as a last resort.[5]

Table 7. Pharmacotherapy Recommendations by GINA for Adults and Adolescents 12 Years and Older[5]

Track 1 – Preferred Controller and Reliever Therapy				
Step 1–2	**Step 3**	**Step 4**	**Step 5**	
AIR-only: low-dose ICS-formoterol as needed	MART with low-dose maintenance ICS-formoterol	MART with medium-dose maintenance ICS-formoterol	Add-on LAMA. Refer for assessment of phenotype. Consider high-dose maintenance ICS-formoterol. Consider biologics: anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP*	
Reliever therapy for all steps: As-needed low-dose ICS-formoterol				
Track 2 – Alternative Controller and Reliever				
Step 1	**Step 2**	**Step 3**	**Step 4**	**Step 5**
Reliever only; if SABA used, take ICS with each dose	Low-dose maintenance ICS	Low-dose maintenance ICS–LABA	Medium-dose maintenance ICS–LABA.	Add-on LAMA. Refer for phenotype assessment. Consider biologics: anti-IgE, anti-IL5/5R, anti-IL4Rα, anti-TSLP*
Reliever therapy for all steps: As-needed ICS–SABA or as-needed SABA				

Abbreviations: AIR = Anti-inflammatory reliever; ICS = Inhaled corticosteroids; IL = interleukin; LABA = Long-acting beta2-agonist; LAMA = Long-acting muscarinic antagonist; LTRA leukotriene receptor antagonist; MART = maintenance-and-reliever therapy with ICS-formoterol; SABA= Short-acting beta2-agonist; TSLP = Thymic stromal lymphopoietin.
Key: * Anti-IgE (anti-immunoglobulin E) like omalizumab for severe allergic asthma; Anti-IL5/5R (anti-interleukin 5 or anti-interleukin 5 receptor alpha for severe eosinophilic asthma) like reslizumab, mepolizumab, benralizumab; Anti-IL4Rα (anti-interleukin 4 receptor alpha) like dupilumab for severe eosinophilic asthma/asthma Type 2 airway inflammation or for patients requiring maintenance oral corticosteroids; anti-TSLP (anti-thymic stromal lymphopoietin) like tezepelumab.

Treatment recommendations for children 6-11 years with asthma are described in **Table 8**.[5]

Table 8. Pharmacotherapy Recommendations by GINA for Children 6-11 years[5]

Preferred Controller				
Step 1	**Step 2**	**Step 3**	**Step 4**	**Step 5**
Low-dose ICS taken whenever SABA taken	Daily low-dose inhaled corticosteroid (ICS)	Low-dose ICS-LABA OR medium-dose ICS OR very-low-dose ICS-formoterol maintenance and reliever (MART)	Medium-dose ICS-LABA OR low-dose ICS-formoterol MART OR refer for expert advice	Refer for phenotypic assessment ± higher-dose ICS-LABA or add-on therapy (e.g., LAMA, anti-IgE, anti-IL4Rα, anti-IL5)
Other Controller Options				
Step 1	**Step 2**	**Step 3**	**Step 4**	**Step 5**
Low-dose ICS taken whenever SABA taken	Daily LTRA OR low-dose ICS whenever SABA taken	Low-dose ICS + LTRA	Add tiotropium OR add LTRA	As last resort, consider low-dose OCS but monitor for side effects
Reliever therapy for all steps: As-needed SABA (or ICS-formoterol reliever in MART Steps 3 and 4)				
Abbreviations: anti-IgE = anti-immunoglobulin E; anti-IL4Rα = anti-interleukin 4 receptor alpha; anti-IL5 = anti-interleukin 5; ICS = Inhaled corticosteroids; Ig = immunoglobulin; LABA = Long-acting beta2-agonist; LAMA = Long acting muscarinic antagonist; LTRA = Leukotriene receptor antagonist; MART = maintenance-and-reliever therapy with ICS-formoterol; OCS = oral corticosteroid; SABA= Short-acting beta2-agonist.				

The pharmacotherapy recommendations for asthma treatment for those 5 years and younger by GINA are outlined in **Table 9**.[5] Updated acute exacerbation recommendations include a new oxygen saturation target of 94% or greater with supportive intravenous magnesium in severe cases (if the child is 2 or older).[5] Prompt use of SABA with a spacer (4-6 puffs or 2.5 mg by nebulizer every 20 minutes) is recommended as initial management.

Table 9. Pharmacotherapy Recommendations by GINA for Children 5 years and younger[5]

Preferred Controller			
Step 1	**Step 2**	**Step 3**	**Step 4**
Insufficient evidence for daily controller	Daily low-dose ICS	Double low-dose ICS	Continue controller & refer for specialist assessment
Other Controller Options (limited evidence, or less evidence for efficacy or safety)			
Step 1	**Step 2**	**Step 3**	**Step 4**
Consider intermittent short course ICS at onset of viral illness	Daily LTRA or intermittent short course ICS at onset of respiratory illness	Consider specialist referral	NA
Reliever therapy for all steps: As-needed SABA			
Consider the Steps Above For Children With:			
Infrequent acute wheezing episodes (e.g., viral-induced) and no interval asthma symptoms	Asthma symptoms not well controlled or ≥1 severe exacerbation in past year	Asthma not well controlled on low-dose ICS	Asthma not well controlled on double ICS
		Before stepping up, check for alternative diagnosis and inhaler skills, review adherence and exposures	
Abbreviations: ICS = Inhaled corticosteroids; LTRA = Leukotriene receptor antagonist; NA = not applicable			

VA/DOD – Primary Care Management of Asthma

The 2019 guidance on managing asthma was updated in 2025 by the VA/DOD. Evidence is current from May of 2024.[6] There were 14 new, reviewed or amended recommendations included in the guideline.

New pharmacotherapy recommendations include[6]:

- For individuals 12 years and older, ICS combined with rapid-onset LABA (e.g., formoterol) is suggested for control and relief. (Weak recommendation for treatment)
- For individuals with uncontrolled asthma on ICS and LABA who use SABA for relief, it is suggested that ICS and rapid-acting LABA as both for controller and reliever. (Weak recommendation for treatment)
- For individuals with asthma that are 12 years and older that are not controlled by medium and high dose ICS and LABA, it is suggested to add a LAMA. (Weak recommendation for treatment)
- For individuals with exercise-induced bronchoconstriction, the VA suggests pre-exertional SABA. (Weak recommendation for treatment)

In patients with confirmed asthma, the VA/DOD recommends starting or continuing therapy with an ICS and rapid-onset LABA as a reliever and to initiate asthma education and care management.[6] If the patient has more than mild symptoms, a ICS and rapid-onset LABA as controller and reliever is recommended. If the patient still has symptoms, verify adherence and proper inhaler technique and/or dose escalation. If the patient's symptoms are controlled, recommend reassessment in 3 months.[6] If symptoms are stable for 90 days or more, consider step-down therapy. If the patient continues to have symptoms with on ICS/rapid-onset LABA therapy, consider increasing to moderate dose ICS and rapid-onset LABA as controller and reliever. If a patient continues to have symptoms on moderate ICS/rapid-onset LABA therapy, add LAMA and consider specialist referral.[6]

New Formulations:

None identified.

New FDA Safety Alerts:

None identified.

References:

1. Zhu H, Lei J, Gao F, et al. Evaluation of comparative efficacy of Umeclidinium/Vilanterol versus other bronchodilators in the management of chronic obstructive pulmonary disease: a systematic review and meta-analysis of RCTs. *BMJ Pulmonary Medicine.* 2024;24(1):609.

2. van Geffen WH, Tan DJ, Walters JAE, Walters EH. Inhaled corticosteroids with combination inhaled long-acting beta2-agonists and long-acting muscarinic antagonists for chronic obstructive pulmonary disease. *Cochrane Database of Systematic Reviews*. 2023, Issue 12. Art. No.: CD011600. DOI: 10.1002/14651858.CD011600.pub3.

3. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. 2026 Report. Available at: https://goldcopd.org/wp-content/uploads/2026/01/GOLD-REPORT-2026-v1.3-8Dec2025_WMV2.pdf. Accessed March 3, 2026.

4. Scottish Intercollegiate Guideline Network. Asthma: diagnosis, monitoring and chronic asthma management (BTS, NICE, SIGN). A National Clinical Guideline - SIGN 245. November 2025. Available at: https://www.sign.ac.uk/media/2377/ng245-asthma-guideline-20251112.pdf. Accessed: March 9, 2026.

5. Global Initiative for Asthma. Global Strategy for Asthma Management and Prevention, 2025. Updated November 2025. Available from: www.ginasthma.org. Accessed March 16, 2025.

6. Department of Veterans Affairs/Department of Defense. VA/DOD Clinical practice guideline for the primary care management of asthma - Version 4.0. 2025. Available at: https://www.healthquality.va.gov/HEALTHQUALITY/guidelines/CD/asthma/Asthma-CPG_2025-Guideline_final_20250528.pdf. Accessed March 18, 2026.

7. Bareille P, Forth R, Imber V, et al. Once-daily fluticasone furoate/vilanterol vs once-daily fluticasone furoate in patients with asthma aged 5 to 17 years. *Annals of Allergy, Asthma and Immunology*. 2024;133(5):537-544.

8. LaForce C, Albers F, Danilewicz A, et al. As-needed albuterol–budesonide in mild asthma. *N Engl J Med*. 2025;393:113-124.

9. Thathera R, Garg A, Ahmed S, et al. Safety and efficacy of budesonide/glycopyrrolate/formoterol fumarate compared with glycopyrrolate/formoterol fumarate for the treatment of COPD: A systematic review and meta-analysis. *J of Am Pharm Assoc*. 2026;66 (1):1-9.

10. Bolner G, Yi R, Dall'Acqua JC, et al. Long-acting muscarinic antagonists as add-on treatment for asthma in children under age 12: a systematic review and meta-analysis. *Paediatric Resp Reviews*. 2026;57:3-10.

11. Braido F, Vlachaki I, Nilolaids G, et al. Single inhaler with beclomethasone, formoterol, and glycopyrronium versus triple therapies in adults with uncontrolled asthma: a systematic review and meta-analysis. *Scientific Reports*. 2025;15(1):4191.

12. Rayner D, Ferri D, Guyatt G, et al. Inhaled reliever therapies for asthma: a systematic review and meta-analysis. *JAMA*. 2025;333(2):143-152.

13. Rogliani P, Ritondo BL, Zerillo B, Cazzola M, Matera MG, Calzetta L. Adding a Second bronchodilator in COPD: a meta-analysis on the risk of specific cardiovascular serious adverse events of tiotropium/olodaterol fixed-dose combination. *COPD: Journal of Chronic Obstructive Pulmonary Disease*. 2020;17(2):215-223. doi:10.1080/15412555.2020.1749252

14. Zhai C, Wang F, Xu, et al. Umeclidinium plus vilanterol versus fluticasone propionate plus salmeterol for chronic obstructive pulmonary disease: a meta-analysis of randomized, controlled trials. *Postgraduate Med J.* 2024;100(1188):721-729.

15. Alsubheen S, Rodrigues M, Thorlund K. Effect of fixed-dose tiotropium/olodaterol combined therapy on exercise-related outcome measures in individuals with chronic obstructive pulmonary disease: a systematic review and meta-analysis. *Expert Review of Resp Med*. 2025;19(10):1081-1092.

Appendix 1: Current Preferred Drug List

Corticosteroids, Inhaled

Generic	Brand	Form	PDL
beclomethasone dipropionate	QVAR REDIHALER	HFA AEROBA	Y
budesonide	PULMICORT FLEXHALER	AER POW BA	Y
fluticasone furoate	ARNUITY ELLIPTA	BLST W/DEV	Y
fluticasone furoate	FLUTICASONE FUROATE	BLST W/DEV	Y
fluticasone propionate	FLUTICASONE PROPIONATE	BLST W/DEV	Y
mometasone furoate	ASMANEX	AER POW BA	Y
mometasone furoate	ASMANEX HFA	HFA AER AD	Y
budesonide	BUDESONIDE	AMPUL-NEB	N
budesonide	PULMICORT	AMPUL-NEB	N
ciclesonide	ALVESCO	HFA AER AD	N
fluticasone propionate	ARMONAIR DIGIHALER	AER PW BAS	N
fluticasone propionate	FLUTICASONE PROPIONATE HFA	AER W/ADAP	N

Corticosteroids/Beta-agonist Combination, Inhalers

Generic	Brand	Form	PDL
budesonide/formoterol fumarate	BREYNA	HFA AER AD	Y
budesonide/formoterol fumarate	BUDESONIDE-FORMOTEROL FUMARATE	HFA AER AD	Y
budesonide/formoterol fumarate	SYMBICORT	HFA AER AD	Y
fluticasone propion/salmeterol	AIRDUO RESPICLICK	AER POW BA	Y
fluticasone propion/salmeterol	FLUTICASONE-SALMETEROL	AER POW BA	Y
fluticasone propion/salmeterol	ADVAIR DISKUS	BLST W/DEV	Y
fluticasone propion/salmeterol	FLUTICASONE-SALMETEROL	BLST W/DEV	Y
fluticasone propion/salmeterol	WIXELA INHUB	BLST W/DEV	Y
fluticasone propion/salmeterol	ADVAIR HFA	HFA AER AD	Y
fluticasone propion/salmeterol	FLUTICASONE-SALMETEROL HFA	HFA AER AD	Y
mometasone/formoterol	DULERA	HFA AER AD	Y
albuterol sulfate/budesonide	AIRSUPRA	HFA AER AD	N
fluticasone propion/salmeterol	AIRDUO DIGIHALER	AER PW BAS	N
fluticasone/vilanterol	BREO ELLIPTA	BLST W/DEV	N
fluticasone/vilanterol	FLUTICASONE-VILANTEROL	BLST W/DEV	N

Beta-agonists, Inhaled Long-acting

Generic	Brand	Form	PDL
salmeterol xinafoate	SEREVENT DISKUS	BLST W/DEV	Y
arformoterol tartrate	ARFORMOTEROL TARTRATE	VIAL-NEB	N
arformoterol tartrate	BROVANA	VIAL-NEB	N

formoterol fumarate	FORMOTEROL FUMARATE	VIAL-NEB	N
formoterol fumarate	PERFOROMIST	VIAL-NEB	N
olodaterol HCl	STRIVERDI RESPIMAT	MIST INHAL	N

Beta-agonists, Inhaled Short-acting

Generic	Brand	Form	PDL
albuterol sulfate	ALBUTEROL SULFATE HFA	HFA AER AD	Y
albuterol sulfate	VENTOLIN HFA	HFA AER AD	Y
albuterol sulfate	ALBUTEROL SULFATE	VIAL-NEB	Y
albuterol	ALBUTEROL	AER REFILL	N
albuterol sulfate	PROAIR RESPICLICK	AER POW BA	N
albuterol sulfate	PROAIR DIGIHALER	AER PW BAS	N
levalbuterol HCl	LEVALBUTEROL CONCENTRATE	VIAL-NEB	N
levalbuterol HCl	LEVALBUTEROL HCL	VIAL-NEB	N
levalbuterol tartrate	LEVALBUTEROL TARTRATE HFA	HFA AER AD	N
levalbuterol tartrate	XOPENEX HFA	HFA AER AD	N

LAMA/LABA Combination, Inhalers

Generic	Brand	Form	PDL
tiotropium Br/olodaterol HCl	STIOLTO RESPIMAT	MIST INHAL	Y
umeclidinium brm/vilanterol tr	ANORO ELLIPTA	BLST W/DEV	Y
umeclidinium brm/vilanterol tr	UMECLIDINIUM-VILANTEROL	BLST W/DEV	Y
aclidinium brom/formoterol fum	DUAKLIR PRESSAIR	AER POW BA	N
budesonide/glycopyr/formoterol	BREZTRI AEROSPHERE	HFA AER AD	N
fluticasone/umeclidin/vilanter	TRELEGY ELLIPTA	BLST W/DEV	N
glycopyrrolate/formoterol fum	BEVESPI AEROSPHERE	HFA AER AD	N

Muscarinic Agonists, Inhaled

Generic	Brand	Form	PDL
ipratropium bromide	ATROVENT HFA	HFA AER AD	Y
ipratropium bromide	IPRATROPIUM BROMIDE	SOLUTION	Y
ipratropium/albuterol sulfate	IPRATROPIUM-ALBUTEROL	AMPUL-NEB	Y
ipratropium/albuterol sulfate	COMBIVENT RESPIMAT	MIST INHAL	Y
tiotropium bromide	SPIRIVA RESPIMAT	MIST INHAL	Y
umeclidinium bromide	INCRUSE ELLIPTA	BLST W/DEV	Y
aclidinium bromide	TUDORZA PRESSAIR	AER POW BA	N
revefenacin	YUPELRI	VIAL-NEB	N
tiotropium bromide	SPIRIVA HANDIHALER	CAP W/DEV	N
tiotropium bromide	TIOTROPIUM BROMIDE	CAP W/DEV	N

Appendix 2: New Comparative Clinical Trials

A total of 131 citations were manually reviewed from the initial literature search. After further review, 129 citations were excluded because of wrong study design (e.g., observational), comparator (e.g., no control or placebo-controlled), or outcome studied (e.g., non-clinical). The remaining 2 trials are summarized in the table below. Full abstracts are included in **Appendix 3**.

Table 10. Description of Randomized Comparative Clinical Trials.

Study	Comparison	Population	Primary Outcome	Results	Notes/Limitations
Bareille, et al[7] DB, Phase 3, RCT	Fluticasone furoate (FF)/vilanterol (VI) (50/25 µg once daily for children and 100/25 µg once daily for adolescents) Versus Fluticasone furoate (FF) (50 µg once daily in children and 100 µg once daily in adolescents) Treatment duration: 24-week	Participants 5-17 years with 6 months or more asthma history that was uncontrolled on ICS monotherapy N = 902	Week 12 weighted mean FEV_1; 0-4 hours in those 5-17 years (US requirement) and change from baseline pre-dose morning peak expiratory flow (change AM PEF) averaged over weeks 1-12 in participants 5-11 years (European regulatory requirements)	Weighted mean FEV_1 (0-4 hours) FF/VI: 0.406 L FF: 0.323 L TD 0.083 L (95% CI, 0.037 to 0.129); P<0.001 Change AM PEF: FF/VI: 12.0 L FF: 8.8 L TD 3.2 L/min (95% CI, -2.0 to 8.4); P = 0.228	- Patients had a 4-week open-label run in period with fluticasone propionate (100 µg twice daily) - Baseline FEV_1 2.04 L - Most patients had asthma more than 1 and less than 10 years - Changes in FEV_1 were clinically (increase of 10% or more) and statistically significant - No new safety concerns
LaForce, et al[8] BATURA DB, Phase 3b, RCT	Albuterol 180 µg + budesonide 160 µg as needed Vs. Albuterol 180 µg as needed Treatment duration: up to 52 weeks	Participants 12 years and older with mild asthma that was uncontrolled despite treatment with a SABA with or without low-dose inhaled glucocorticoid or leukotriene receptor antagonist N = 2516	First severe asthma exacerbation (assessed in a time-to-event analysis)	Severe asthma exacerbation: Albuterol/budesonide: 62 (5.1%) Albuterol: 110 (9.1%) HR 0.53 (95% CI, 0.39 to 0.73) P<0.001	- Mean age was 42.7 years, 68% female, White 70% - Adverse events were similar between groups - Trial stopped early due to significantly lower risk of severe exacerbations with combination treatment

Abbreviations: CI = confidence interval; DB = double blind; FEV_1 = forced expiratory flow volume in 1 second; HR = hazard ratio; ICS = inhaled corticosteroid; PEF = peak expiratory flow; RCT = randomized clinical trial; SABA = short-acting beta agonist; TD = treatment difference.

Appendix 3: Abstracts of Comparative Clinical Trials

Once-daily fluticasone furoate/vilanterol vs once-daily fluticasone furoate in patients with asthma aged 5 to 17 years

Bareille P, Forth R, Imber V, et al

Background: Limited data exist comparing inhaled corticosteroid (ICS) plus adjunctive therapy vs ICS alone in pediatric asthma patients.

Objective: To evaluate the efficacy and safety of fluticasone furoate/vilanterol (FF/VI) vs FF in children and adolescents with asthma.

Methods: This phase 3, randomized, double-blind, multicenter study (NCT03248128) included participants aged 5 to 17 years with six months or more asthma history uncontrolled on ICS monotherapy. Participants received 4-week open-label fluticasone propionate(100 µg) twice daily before 1:1 randomization to 24-week double-blind FF (50 µg:100 µg) or FF/VI (50/25 µg:100/25 µg) once daily. Two populations with different primary endpoints were analyzed to meet United States (week 12 weighted mean forced expiratory volume in 1 second [FEV_1; 0-4 hours]; participants aged 5–17 years) and European (change from baseline pre-dose morning peak expiratory flow[ΔAM PEF] averaged over weeks 1-12; participants aged 5-11 years) regulatory requirements.

Results: Overall, 902 participants, including 673 children aged 5 to 11 years, were randomized and treated. In participants aged 5 to 17, week 12 weighted mean FEV_1(0-4 hours) was greater with FF/VI vs FF (difference: 0.083 L; $P < .001$). In participants aged 5 to 11, ΔAM PEF over weeks 1 to 12 showed numerical improvement with FF/VI vs FF but was not statistically significant (difference: 3.2 L/min; $P = .228$). No drug-related serious adverse events or deaths were reported.

Conclusion: FF/VI significantly improved weighted mean FEV_1 (0-4 hours; participants aged 5-17 years), but not ΔAM PEF (participants aged 5-11 years) vs FF. No new safety concerns were apparent.

As-Needed Albuterol–Budesonide in Mild Asthma

Craig LaForce, M.D., Frank Albers, M.D., PhD, Anna Danilewicz, B.Sc., et al

As-needed use of albuterol–budesonide has been shown to result in a significantly lower risk of severe asthma exacerbation than as-needed use of albuterol alone among patients with moderate-to-severe asthma. Data on albuterol–budesonide in mild asthma are needed.

We conducted a fully virtual, decentralized, phase 3b, multicenter, double-blind, event-driven trial involving persons 12 years of age or older with disease that was uncontrolled despite treatment for mild asthma with a short-acting β_2-agonist (SABA) with or without a low-dose inhaled glucocorticoid or leukotriene-receptor antagonist. Participants were randomly assigned in a 1:1 ratio to a fixed-dose combination of 180 µg of albuterol and 160 µg of budesonide (with each dose consisting of two inhaler actuations of 90 µg and 80 µg, respectively) or 180 µg of albuterol (with each dose consisting of two inhaler actuations of 90 µg) on an as-needed basis for up to 52 weeks. The primary end point was the first severe asthma exacerbation, assessed in a time-to-event analysis, in the on-treatment efficacy population, and the key secondary end point was the first severe exacerbation in the intention-to-treat population. Secondary end points included the annualized rate of severe asthma exacerbations and exposure to systemic glucocorticoids.

A total of 2516 participants underwent randomization; 1797 (71.4%) completed the trial. Of 2421 participants in the full analysis population (1209 assigned to the albuterol–budesonide group and 1212 to the albuterol group), 97.2% were 18 years of age or older; 74.4% used a SABA alone at baseline. The trial was stopped for efficacy at a prespecified interim analysis. A severe exacerbation occurred in 5.1% of the participants in the albuterol–budesonide group and in 9.1% of those in the albuterol group in the on-treatment efficacy population (hazard ratio, 0.53; 95% confidence interval [CI], 0.39 to 0.73) and in 5.3% and 9.4%, respectively, in the intention-to-treat population (hazard ratio, 0.54; 95% CI, 0.40 to 0.73) (P<0.001 for both comparisons). The annualized rate of severe asthma exacerbations was lower with albuterol–budesonide than with albuterol (0.15 vs. 0.32; rate

ratio, 0.47; 95% CI, 0.34 to 0.64), as was the mean annualized total dose of systemic glucocorticoids (23.2 vs. 61.9 mg per year). Adverse events were similar in the two treatment groups.

As-needed use of albuterol–budesonide resulted in a lower risk of a severe asthma exacerbation than as-needed use of albuterol alone among participants with disease that was uncontrolled despite treatment for mild asthma.

Appendix 4: Medline Search Strategy

Database(s): **Ovid MEDLINE(R) ALL** 1946 to February 23, 2026

Search Strategy:

#	Searches	Results
1	Tiotropium Bromide/ or tiotropium.mp.	2117
2	umeclidinium.mp.	452
3	aclidinium.mp.	269
4	budesonide.mp. or Budesonide/	8039
5	Glycopyrrolate/ or glycopyrrolate.mp.	1914
6	olodaterol.mp.	284
7	vilanterol.mp.	660
8	Formoterol Fumarate/ or formoterol.mp.	3334
9	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8	13951
10	limit 9 to (english language and humans and yr="2024 -Current")	626
11	limit 10 to (clinical trial, phase iii or guideline or meta analysis or practice guideline or "systematic review")	76

Database(s): **Ovid MEDLINE(R) ALL** 1946 to March 03, 2026

Search Strategy:

#	Searches	Results
1	ipratropium.mp. or Ipratropium/	2776
2	revefenacin.mp.	53

3	mometasone.mp.	1559
4	Albuterol/ or albuterol.mp.	11569
5	Salmeterol Xinafoate/ or salmeterol.mp.	3290
6	vilanterol.mp.	659
7	aformoterol.mp.	1
8	olodaterol.mp.	284
9	levalbuterol.mp. or Levalbuterol/	176
10	fluticasone.mp. or Fluticasone/	5536
11	beclomethasone dipropionate.mp. or Beclomethasone/	3615
12	budesonide.mp. or Budesonide/	8043
13	ciclesonide.mp.	511
14	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13	29345
15	limit 14 to (english language and humans and yr="2023 -Current")	1281
16	limit 15 to yr="2023 -Current"	1281
17	limit 16 to (clinical trial, phase iii or guideline or meta-analysis or practice guideline or "systematic review")	131

Appendix 5: Key Inclusion Criteria

Population	Patients with asthma or COPD
Intervention	Inhalers used to treat asthma and/or COPD (e.g., ICS, LABA, LAMA, SABA, muscarinic agonists, ICS/LABA, ICS/LABA/LAMA, LABA/LAMA)
Comparator	Placebo or active treatment
Outcomes	Change in exacerbations, lung function, hospitalizations, mortality
Setting	Outpatient

Long-acting Beta-agonists (LABA)

Goals:
- To optimize the safe and effective use of LABA therapy in patients with asthma and chronic obstructive pulmonary disease (COPD).

Length of Authorization:
- Up to 12 months

Requires PA:
- Non-preferred LABA products

Covered Alternatives:
- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 Code	
2. Has the patient tried and failed, have contraindications or documented inability to use the preferred products?	**Yes:** Go to #3	**No:** Deny; Medical appropriateness. Inform prescriber of preferred LABA therapies.
3. Does the patient have a diagnosis of asthma or reactive airway disease?	**Yes:** Go to #5	**No:** Go to #4
4. Does the patient have a diagnosis of COPD, mucopurulent chronic bronchitis and/or emphysema?	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny; medical appropriateness. Need a supporting diagnosis. If prescriber believes diagnosis is appropriate, inform prescriber of the appeals process for Medical Director Review.

Approval Criteria		
5. Does the patient have an active prescription for an inhaled corticosteroid (ICS) or an alternative asthma controller medication?	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny; medical appropriateness

P&T/DUR Review: *6/26 (KS), 2/24 (DM); 10/23 (SF); 10/22 (KS), 10/20, 5/19; 1/18; 9/16; 9/15); 5/12; 9/09; 5/09*
Implementation: *3/1/18; 10/9/15; 8/12; 1/10*

Long-acting Muscarinic Antagonist/Long-acting Beta-agonist (LAMA/LABA) and LAMA/LABA/Inhaled Corticosteroid (LAMA/LABA/ICS) Combinations

Goals:
- To optimize the safe and effective use of LAMA/LABA/ICS therapy in patients with asthma and chronic obstructive pulmonary disease (COPD).
- Step-therapy required prior to coverage:
  - Asthma and COPD: short-acting bronchodilator and previous trial of two drug combination therapy (ICS/LABA, LABA/LAMA or ICS/LAMA). Preferred monotherapy inhaler LAMA and LABA products do NOT require prior authorization.

Length of Authorization:
- Up to 12 months

Requires PA:
- All non-preferred LAMA/LABA and LAMA/LABA/ICS products

Covered Alternatives:
- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria	
1. What diagnosis is being treated?	Record ICD10 Code

Approval Criteria		
2. Has the patient tried and failed, have contraindications or documented inability to use the preferred products?	**Yes:** Go to #3	**No:** Deny; Medical appropriateness. Inform prescriber of preferred product in class.
3. Does the patient have a diagnosis of asthma or reactive airway disease without COPD?	**Yes:** Go to #8	**No:** Go to #4
4. Does the patient have a diagnosis of COPD, mucopurulent chronic bronchitis and/or emphysema?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness. Need a supporting diagnosis. If prescriber believes diagnosis is appropriate, inform prescriber of the appeals process for Medical Director Review.
5. Is the request for a LAMA/LABA combination product?	**Yes:** Approve for up to 12 months. Stop coverage of all other LAMA and LABA inhalers or scheduled SAMA/SABA inhalers (PRN SABA or SAMA permitted).	**No:** Go to #6
6. Is the request for a 3 drug ICS/LABA/LAMA combination product and is there a documented trial of a LAMA and LABA, or ICS and LABA or ICS and LAMA?	**Yes:** Go to #7	**No:** Pass to RPh. Deny; medical appropriateness.
7. Is there documentation that the prescriber is willing to stop coverage of all other LAMA, LABA, and ICS inhaler combination products?	**Yes:** Approve for up to 12 months. Stop coverage of all other LAMA, LABA and ICS inhalers.	**No:** Pass to RPh. Deny; medical appropriateness.
8. Does the patient have an active prescription for an on-demand short-acting acting beta-agonist (SABA) and/or for ICS-formoterol?	**Yes:** Go to #9	**No:** Pass to RPh. Deny; medical appropriateness.

Approval Criteria		
9. Is the request for Trelegy Ellipta (ICS/LAMA/LABA) combination product and is there a documented trial of an ICS/LABA?	**Yes:** Approve for up to 12 months. Stop coverage of all other LAMA, LABA and ICS inhalers (with the exception of ICS-formoterol which may be continued)	**No:** Pass to RPh. Deny; medical appropriateness.

P&T Review: *6/26 (KS),2/24 (DM); 10/23(SF); 10/22(KS), 10/21; 12/20, 10/20, 5/19; 1/18; 9/16; 11/15; 9/15; 11/14; 11/13; 5/12; 9/09; 2/06*
Implementation: *4/1/24; 1/1/21; 3/1/18; 10/13/16; 1/1/16; 1/15; 1/14; 9/12; 1/10*

Inhaled Corticosteroids (ICS)

Goals:
- To optimize the safe and effective use of ICS therapy in patients with asthma and chronic obstructive pulmonary disease (COPD).

Length of Authorization:
- Up to 12 months

Requires PA:
- Non-preferred ICS products

Covered Alternatives:
- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 Code	
2. Has the patient tried and failed, have contraindications or documented inability to use the preferred products?	**Yes:** Go to #3	**No:** Deny; Medical appropriateness. Inform prescriber of preferred alternatives in class.

Approval Criteria		
3. Is the request for treatment of asthma or reactive airway disease?	**Yes:** Go to #6	**No:** Go to #4
4. Is the request for treatment of COPD, mucopurulent chronic bronchitis and/or emphysema?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness. Need a supporting diagnosis. If prescriber believes diagnosis is appropriate, inform prescriber of the appeals process for Medical Director Review.
5. Does the patient have an active prescription for an inhaled long-acting bronchodilator (anticholinergic or beta-agonist)?	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny; medical appropriateness.
6. Does the patient have an active prescription for an on-demand short-acting beta-agonist (SABA) or an alternative rescue medication for acute asthma exacerbations?	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny; medical appropriateness

P&T/DUR Review: *6/26 (KS), 2/24 (DM); 10/23 (SF); 10/22(KS), 10/20, 5/19, 1/18; 9/16; 9/15*
Implementation: *3/1/18; 10/13/16; 10/9/15*