Health Monitor®

Clinician Update

COPD Management

Illustration by Keith Negley

MODEL OF CARE

The GOLD Report: Key treatment UPDATES

The overarching message: Proactive management—meaning escalating therapy at the right time—is critical for improving outcomes.

The importance of managing the risk of exacerbation in chronic obstructive pulmonary disease (COPD) cannot be overstated. Research shows that even a single exacerbation can cause increased airway inflammation and lasting airflow impairment.[1,2] Each episode hastens lung function decline, and the more severe the exacerbation, the greater the loss of function. Exacerbations also increase the risk of death from COPD, and that risk rises with greater episode frequency.[3-5]

To reflect the increased risks for patients with uncontrolled COPD, guidelines published in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report, which is updated yearly, offer valuable evidence-based strategies for managing COPD at all levels of severity. For patients with signs of worsening disease, here are important pharmacotherapy recommendations in the Report:

1.
TREAT AGGRESSIVELY WITH TRIPLE THERAPY.

The GOLD Report includes a table with interventions that have reduced death rates among specific populations based on patient characteristics and disease severity[6]—and triple therapy is the only drug treatment listed as reducing mortality in symptomatic

Continued on next page ►

COPD patients with a history of frequent or severe exacerbations. (See Table 1 for the GOLD recommendations.)

Along with improving outcomes, drug delivery of triple therapy has advanced: "LABAs, LAMAs and ICS have been administered concomitantly for the last 10 years," says Antonio Anzueto, MD, professor of medicine at the University of Texas San Antonio and Section Chief of Pulmonology for the South Texas Veterans Healthcare System. But over the past 7 years, he notes, the FDA's approval of single-inhaler LABA/LAMA/ICS combinations has allowed patients to take the three agents in a single draw, markedly increasing patient satisfaction and convenience.

But aside from convenience, "the efficacy of giving these three medications together is better," Dr. Anzueto says. "There's a synergistic effect when the medications are given at once."

The 2024 GOLD Report highlights studies showing that LABA/LAMA/ICS triple therapy significantly reduces the risk of moderate-to-severe exacerbations, which is crucial to avoid hospitalizations and improve outcomes. The 2024 GOLD Report also notes that clinical trials showed a nonsignificant trend for lower mortality (assessed as a safety outcome) with triple therapy vs. non-ICS-based therapies. These results were observational and therefore should be interpreted with caution.[6-9]

2. KNOW WHEN TO ESCALATE.

Symptom burden and the history of exacerbations should drive treatment decisions, says MeiLan Han, MD, MS, Professor of Medicine and Chief of the Division of Pulmonary and Critical Care at the University of Michigan. She and Dr. Anzueto, both members of the GOLD Science Committee that helped develop the recent guidelines, recommend escalating to triple therapy in the following cases:[6]

- **If symptoms persist** despite maximal dual-inhaled therapy.
- **After a COPD-related hospitalization,** start triple therapy "as soon as possible," urges Dr. Anzueto, to reduce the risk of a future episode.

In addition, Drs. Anzueto and Han suggest considering triple therapy if a patient has:

- An **eosinophil count ≥300** but no recent exacerbation.
- **Persistent asthma-like symptoms** such as dyspnea, cough or congestion regardless of exacerbation history or eosinophil count. "However, I usually won't try steroids if the eosinophils are less than 100," adds Dr. Han, citing the potential for adverse effects.

Table 1. Initiating triple therapy[6*]

FACTORS TO CONSIDER WHEN ADDING ICS TO LONG-ACTING BRONCHODILATORS

STRONGLY FAVORS USE	• History of hospitalization(s) for exacerbations of COPD • ≥2 moderate outpatient exacerbations of COPD per year • Blood eosinophils ≥300 cells/µL • History of, or concomitant, asthma
FAVORS USE	• One moderate outpatient exacerbation of COPD per year • Blood eosinophils ≥100 to <300 cells/µL
AGAINST USE	• Repeated pneumonia events • Blood eosinophils <100 cells/µL • History of mycobacterial infection

ICS = inhaled corticosteroids.
*Single-inhaler therapy may be more convenient and effective than multiple inhalers.
Source: 2024 GOLD Report. For complete recommendations, visit *goldcopd.org*.

One caveat: Avoid triple therapy in patients who cannot tolerate ICS, are at increased risk of pneumonia or have been hospitalized for bronchiectasis or other serious infections, as ICS can increase the risk of infection or exacerbate an existing infection, note Drs. Anzueto and Han.

3. EDUCATE PATIENTS ON SIGNS OF EXACERBATION.

Patients often under-report a worsening of their disease simply because they don't recognize it, so they need help understanding what an exacerbation looks and feels like, says Dr. Anzueto. "Patients generally cannot accurately determine when symptoms are very severe and when they can evolve into something else," he says. "Some patients visit the emergency room to treat a breathing problem and still are not aware that they are having an exacerbation."

Another problem: "Patients will limit activity to reduce symptoms rather than report them," says Dr. Han. "Some patients may try to self-treat their symptoms by increasing their SABA [short-acting beta agonist] without calling us first. What's more, some physicians may not adequately educate patients on when to call." Therefore, make sure you or your staff educate patients at every visit on the potential warning signs of an exacerbation, Dr. Anzueto says. Advise them to call you immediately if they notice changes in symptoms or routines, such as:

- Getting short of breath more often or with less exertion
- Coughing more frequently
- More congestion
- Feeling more symptoms during allergy season in the late winter and spring

Also, consider working with patients on an exacerbation management plan, which could help shorten an episode and reduce the risk of hospitalization.[10-12] (For examples, visit *copdfoundation.org* and *lung.org*). Devising a personalized plan based on the patient's individual characteristics and preferences will help them recognize an early potential warning sign, properly treat a symptom before it worsens and know when to call for help, Dr. Han notes.

4. HELP THEM WITH ADHERENCE.

The GOLD Report also offers insights on encouraging medication adherence, with an emphasis on inhaler technique and suitability. Not taking inhaled COPD agents as prescribed can translate to poor symptom control, diminished quality of life and increased risk of exacerbations and death.[6] Yet despite the crucial role inhalers play in COPD management, research suggests adherence to these medications is poor overall.[6] For example, in one data review of some 61,000 Medicare beneficiaries diagnosed with COPD, slightly more than half were not using their inhalers at baseline.[10] Strategies to help ensure better adherence:

Prescribe a single inhaler when possible. Drs. Anzueto and Han say that adherence to single-inhaler triple therapy in their practices has been

A KEY RISK CLASSIFICATION: GROUP E

Treatment recommendations in the 2024 Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report include evidence-based strategies for using both drug and nondrug interventions. As in previous years, the latest edition lists recommendations for escalating drug therapy after an exacerbation. One recent change: a new algorithm for classifying risk in treatment-naïve patients.[6]

The previous classifications of A, B, C or D—in which C and D distinguished high risk by the level of symptoms—has been streamlined to three groups: A, B and E. The revision was made to recognize the clinical relevance of exacerbations, independent of the level of symptoms, and to position escalation of therapy earlier in the course of treatment. A brief summary of the classifications:[6]

- **Group A:** This includes patients in the early, stable stages of COPD who start treatment with a single bronchodilator.
- **Group B:** These patients have a greater symptom burden and require dual therapy with two of the following: a long-acting beta agonist (LABA), long-acting muscarinic antagonist (LAMA) or inhaled corticosteroids (ICS).
- **Group E:** In patients who have had two or more moderate exacerbations over the previous 12 months, or at least one episode that required hospitalization or Emergency Department visit, consider triple therapy (LABA and LAMA plus ICS). (See Table 1 on opposite page for more considerations when initiating triple therapy.)

good overall. And data suggest that patients who are on single-inhaler triple therapy are twice as likely to adhere compared with patients who are taking multiple-inhaler therapy.[11]

Gauge the patient's capabilities before choosing a device, Dr. Anzueto advises. Research shows that more than two-thirds of patients make at least one error during inhaler use.[6] While no single inhaler has shown superiority in clinical trials, choosing the appropriate device for each patient is critical to ensuring adherence, Dr. Anzueto says. For example, he says, using a powder-containing disc inhaler requires ample inspiratory flow, so an aerosol-based inhaler may be more suitable for patients with weak inhalation. In addition, patient preference, cognition, dexterity and strength also need to be considered when choosing an inhaler.[6]

Provide hands-on learning. Have your office staff coach patients on how to use the prescribed inhaler during the visit, Dr. Han suggests. Also have patients practice on a handheld simulated inhaler to help them learn to control their inspiratory flow before they use a real inhaler.

Refer them to educational resources and pulmonary rehab. "With the increase in virtual care, I do my best to coach patients via video chat, refer them to videos or ask them to have their pharmacist show them when they pick up their prescription," says Dr. Han. She also notes that the COPD Foundation posts instructional videos via its app (available at *copdfoundation.org*). Pulmonary rehabilitation programs also provide education on correct inhaler use. (For more on improving inhaler technique, see p. 17.)

Help them with medication access. Single-inhaler triple therapies are on some but not all payer formularies, notes Dr. Han. To head off problems, find out whether the patient's insurance covers the therapy before prescribing it. Also, find out if the insurer requires a copay. If the cost poses a burden, "the patient might get frustrated and decide not to take the medication," says Dr. Anzueto, so refer them to drug manufacturer websites for assistance programs, coupons and discount cards.

The bottom line: Treating COPD aggressively after an exacerbation, with the goal of preventing future episodes and disease progression, is crucial to helping patients live longer and improve their quality of life. "The risk of future hospitalization for COPD is greater for a patient who has been hospitalized," says Dr. Anzueto. "Treating aggressively after hospitalization will reduce that risk." ●

–by Pete Kelly

References

1. Blagev DP, et al. Stability of frequency of severe chronic obstructive pulmonary disease exacerbations and health care utilization in clinical populations. *Chronic Obstr Pulm Dis*. 2018;5(3):208-220.
2. Wedzicha JA, et al. COPD exacerbations: defining their cause and prevention. *Lancet*. 2007;370:786-796.
3. Dransfield MT, et al. Acute exacerbations and lung function loss in smokers with and without chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2017;195(3):324-330.
4. Halpin DMG, et al. Effect of a single exacerbation on decline in lung function in COPD. *Respir Med*. 2017;128:85-91.
5. Rothnie KJ. Natural history of chronic obstructive pulmonary disease in a general practice-based population with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med*. 2018;198(4):464-471.
6. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for Prevention, Diagnosis and Management of COPD: 2024 Report. Available at *goldcopd.org*.
7. Alcazar-Navarrete B, et al. Clinical characteristics, treatment persistence, and outcomes among patients with COPD treated with single- or multiple-inhaler triple therapy: A retrospective analysis in Spain. *Chest*. 2022;162(5):1017-1029.
8. Rabe KF. Triple inhaled therapy at two glucocorticoid doses in moderate-to-very-severe COPD. *N Engl J Med*. 2020;383:35-48.
9. Lipson DA, et al. Once-daily single inhaler versus dual therapy in patients with COPD. *N Engl J Med*. 2018;378(18):1671-1680.
10. Bengtson LGS, et al. Development and validation of a drug adherence index for COPD. *J Manag Care Spec Pharm*. 2021;27(2):198-209.
11. Mannino D, et al. Adherence and persistence to a once-daily single-inhaler versus multiple-inhaler triple therapy among patients with chronic obstructive pulmonary disease in the USA: a real-world study. *Respir Med*. 2022;197:106807.
12. Lenferink A, et al. Exacerbation action plans for patients with COPD and comorbidities: a randomized controlled trial. *Eur Respir J*. 2019;54:1802134.

PRACTICE PEARLS

Evidence-based guidelines for smoking cessation

For many patients who use tobacco, combining cessation agents with counseling is the key to quitting. These expert guidelines can help you implement a treatment plan tailored to their needs.

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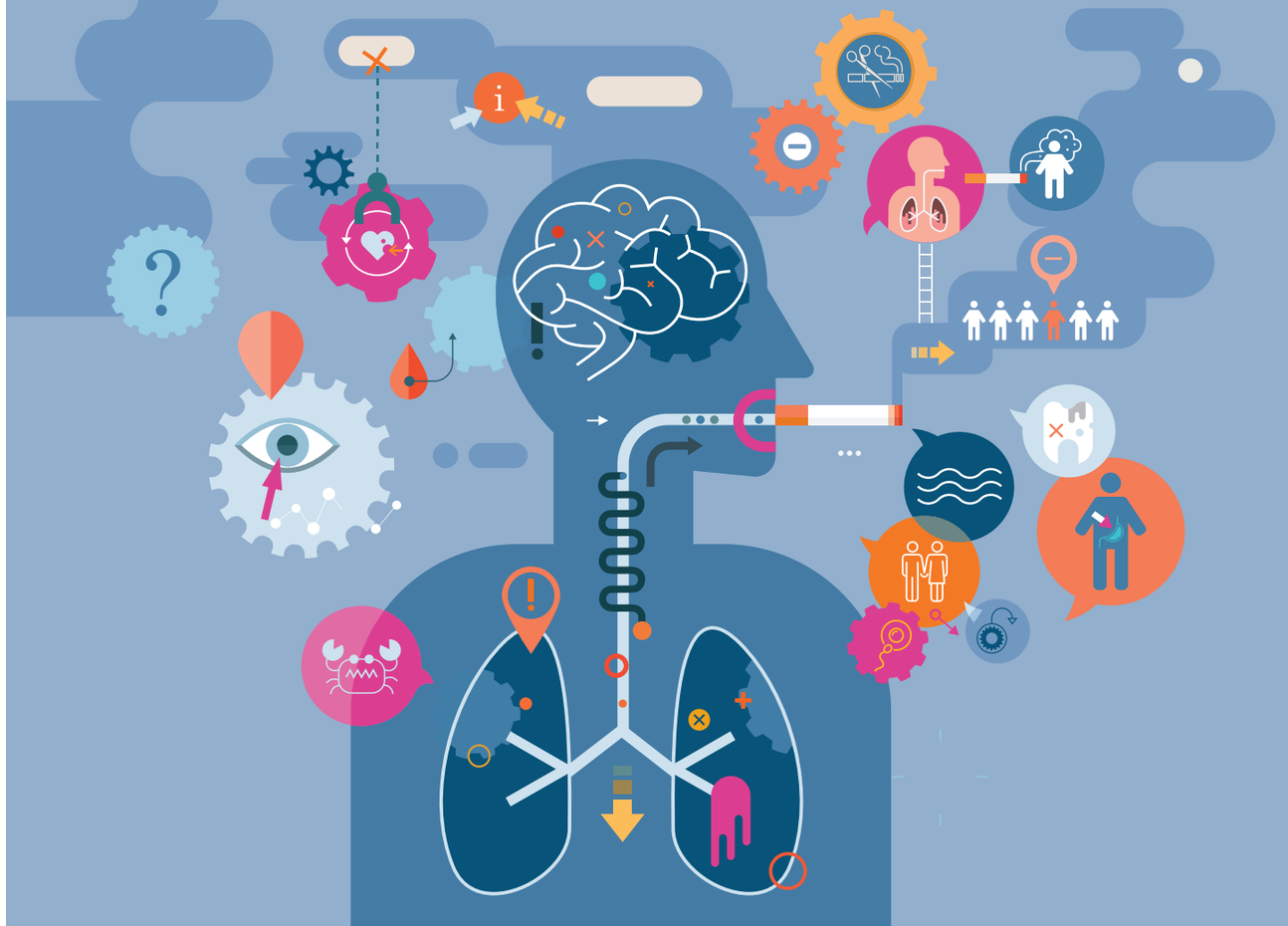


According to the CDC, an estimated 28 million adults in the United States smoke cigarettes—yet almost 70% say they want to quit, about half try to quit in any given year, but less than 10% are able to do it.[1]

What's especially surprising: Only 1 in 3 smokers received smoking cessation assistance during their cardiology visit, according to a study in the *Journal of the American Heart Association*. While the reasons are unclear, a lack of time during office visits and the assumption that the primary care provider should discuss smoking cessation may be factors.[2,3] For some healthcare professionals, ambivalence may even play a part.[4]

Pulmonologist Panagis Galiatsatos, MD, MHS, Director of the Tobacco Treatment Clinic and Associate Professor at Johns Hopkins School of Medicine, can understand why physicians may not broach the topic, explaining, "If patients are still smoking in 2024 and they're an adult, you've got to think of them as the most refractory case." That can feel daunting for a clinician to attempt to take on.

But healthcare professionals can have a positive impact on their patients' ability to quit. Here are counseling strategies proven to work.

Be anti-smok*ing*, not anti-smok*er*

Using a nonjudgmental tone is important for helping patients to open up and in some cases disclose their smoking status in the first place. Reminds Dr. Galiatsatos, "This is a population that's been stigmatized and shamed." How he suggests thinking of it: "Tobacco is a legal product that has been placed in society and is used oftentimes in the most disadvantaged neighborhoods. Don't fault the person for what society has been allowing for hundreds of years," he says. Instead, look at smoking as requiring treatment, "like any other disease deserves," advises Dr. Galiatsatos, and take care to use understanding language that recognizes how difficult it is to quit.

Advise mindfulness

Dr. Galiatsatos encourages mindfulness when counseling a patient who smokes, having them question the reason they're doing it at the time (e.g., always after a meal or when stressed). Understanding why they reach for tobacco can help them get to the root cause. "That's key because they'll be living the same life as they did before—but without cigarettes as a coping mechanism," he explains. The more they call on mindfulness, he says, "the more they can deliberately pull away from the subconscious act of smoking. Ultimately, the goal is no longer simply to quit, but to learn to *stay* quit." Each time they're able to delay or say no to a cigarette, the stronger their ability to abstain in other situations.

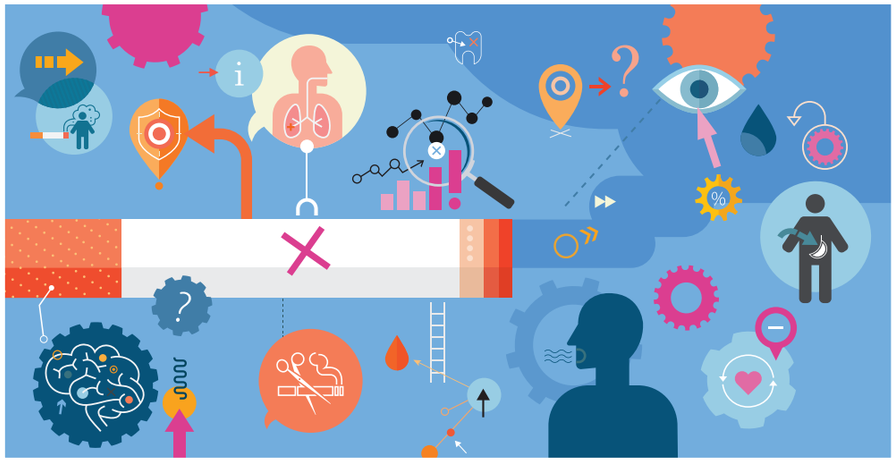
Offer pharmacotherapy

When combined with counseling, medication can increase quit rates, but many patients are not offered this option. To assist clinicians, a multidisciplinary panel of experts, including Dr. Galiatsatos, created the American Thoracic Society's 2020 clinical guideline on initiating pharmacotherapy in tobacco-dependent adults.[5] "These are guidelines, not rules," stresses Dr. Galiatsatos. "You should make the best decision for each patient." General recommendations:

Treat beyond 12 weeks.

The guideline panel concluded that extending the duration past the typical 12-week period used in clinical trials resulted in better outcomes with similar rates of adverse events as the shorter timeline.[6-9] While studies are usually done on a 12-week basis, that time period is often chosen because "that's how long the research grants lasted," says Dr. Galiatsatos, adding that a realistic timeframe for achieving the goal is longer, as with many medical treatments. "You wouldn't start a patient on a blood pressure medicine and say, 'You've got 3 months to reach blood pressure goals.' " Instead, extend treatment as necessary, provided the patient isn't having side effects. Even with the help of medication, "I've had patients take a total of 2 years to ultimately stop," Dr. Galiatsatos says.

> "I tell the patient, 'I'm not asking you to become a nonsmoker overnight. Just start the medication and come back in 4 weeks.' "
>
> —PANAGIS GALIATSATOS, MD, MHS



Favor use of varenicline.

The guideline panel strongly recommends varenicline in multiple instances based on analysis of published research. Factors to keep in mind:

- ***It's more effective than bupropion and the nicotine patch.*** When analyzing varenicline and the nicotine patch head-to-head, the panel concluded that varenicline is preferred because it leads to longer periods of abstinence and may be better at reducing the risk of relapse.[10,11]

Varenicline is also recommended over bupropion, even though both work on the same neurotransmitter. While they each target dopamine to blunt the rewarding effects of smoking, varenicline goes one step further to block the nicotine receptors, says Dr. Galiatsatos. Some patients report feeling nauseated when they smoke while taking it because, he says, "the nicotine has to find other places to go." It's this extra step that makes it the more effective choice in achieving smoking abstinence and is recommended by the panel, despite its generally higher cost.

The expert panel also made two additional recommendations for varenicline labeled as "conditional," meaning there was not enough clinical data to garner a unanimous "strong" recommendation:

1) Varenicline may be used rather than electronic cigarettes. Although the panel was united in varenicline being the preferred intervention, the recommendation was left in question because the panel could not find any studies directly comparing the two.

2) Varenicline may be used in combination with a nicotine patch rather than using varenicline alone. However, there is some evidence that combining them may increase the risk of side effects such as insomnia, abnormal dreams and headache, so use caution when doing so.[12,13]

- ***It can be used in patients who have a psychiatric condition.*** Because of early black-box warnings—which have since been removed—varenicline has had limited use in patients with psychiatric disorders. But experts say it's time to reconsider the agent's role in this patient population. After reviewing two large randomized controlled trials that compared varenicline with a nicotine patch among participants with mental illness,[14,15] the panel concluded that varenicline was associated with a higher likelihood of cessation at 6 months without evidence of an increase in serious adverse events.

This is important, as smoking is particularly common among people with mental health disorders. According to the National Institute on Drug Abuse, some estimates put the prevalence of smoking among people with schizophrenia as high as 70% to 85% and for those with bipolar disorder at 50% to 70%.[16] With smoking as the leading cause of preventable death in all people, having varenicline as an option can be a game-changer for patients with psychiatric conditions, says Dr. Galiatsatos: "Working on these guidelines, we had a psychologist who stood up and said, 'This is going to save my patients' lives.' "

- ***It can work as a form of "pretreatment."*** The panel suggests using varenicline as a pretreatment—that is, prescribing it before a patient has indicated readiness to quit—because even those who are reluctant have higher success rates while taking it.[17,18] If you

wait until the patient tells you they're ready to quit, Dr. Galiatsatos says, "You're delaying medical care for the patient."

Of course, pharmacotherapy should be presented as an option in a collaborative manner. "I tell the patient, 'I'm not asking you to become a nonsmoker overnight. Just start the medication and come back in 4 weeks,' " he says. After seeing how the medication can help curb their desire to smoke, they may be more willing to make the lifestyle changes that can support cessation.

If a patient isn't ready to start medication, Dr. Galiatsatos says to respect that decision—but let them know you'll be following up at the next visit to see if they've become more open to the idea.

Explain how medication helps—and why it's only part of the treatment plan.

While smoking-cessation agents are a crucial piece of the puzzle, they should always be combined with behavioral interventions. The analogy that Dr. Galiatsatos gives: "Say you wanted to run but your knees hurt, so you stop after taking a few steps." He likens these medications to taking a pain reliever to help you push through the initial discomfort. "They simply lower cravings so you can say no over and over again." In the meantime, he says, the patient has to do the work of learning new ways of coping. He tells them that by building new habits, "you're building a new identity as a nonsmoker." ●

–by Beth Shapouri

References

1. **Centers for Disease Control and Prevention. Smoking Cessation: Fast Facts. Updated March 21, 2022. Available at *cdc.gov*.**
2. **Sardana M, et al. Provider-Level Variation in Smoking Cessation Assistance Provided in the Cardiology Clinics: Insights From the NCDR PINNACLE Registry. *J Am Heart Assoc.* 2019;8:e011307.**
3. **American Heart Association. "Who's helping smokers quit? Probably not their heart doctor, study says." Published June 28, 2019. Available at *heart.org.***
4. **Mooren K, et al. The attitudes of pulmonologists regarding smoking behavior of their patients with advanced COPD: a qualitative research. *Int J Chron Obstruct Pulmon Dis*. 2019;14:2673-2679.**
5. **Leone FT, et al. Initiating Pharmacologic Treatment in Tobacco-Dependent Adults. An Official American Thoracic Society Clinical Practice Guideline. *Am J Respir Crit Care Med.* 2020;202(2):e5-e31.**
6. **Schnoll RA, et al. Effectiveness of extended-duration transdermal nicotine therapy: a randomized trial. *Ann Intern Med*. 2010;152:144-151.**
7. **Hays JT, et al. Sustained-release bupropion for pharmacologic relapse prevention after smoking cessation: a randomized, controlled trial. *Ann Intern Med*. 2001;135:423-433.**
8. **Schlam TR, et al. Comparative effectiveness of intervention components for producing long-term abstinence from smoking: a factorial screening experiment. *Addiction*. 2016;111:142-155.**
9. **Evins AE, et al. Maintenance treatment with varenicline for smoking cessation in patients with schizophrenia and bipolar disorder: a randomized clinical trial. *JAMA*. 2014;311:145–154.**
10. **Aubin HJ, et al. Varenicline versus transdermal nicotine patch for smoking cessation: results from a randomised open-label trial. *Thorax*. 2008;63:717-724.**
11. **Baker TB et al. Effects of nicotine patch vs varenicline vs combination nicotine replacement therapy on smoking cessation at 26 weeks: a randomized clinical trial. *JAMA*. 2016;315:371-379.**
12. **Ramon JM, et al. Combining varenicline and nicotine patches: a randomized controlled trial study in smoking cessation. *BMC Med.* 2014;12:172.**
13. **Hajek P, et al. Is a combination of varenicline and nicotine patch more effective in helping smokers quit than varenicline alone? A randomised controlled trial. *BMC Med.* 2013;11:140.**
14. **Anthenelli RM, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. *Lancet*. 2016;387:2507-2520.**
15. **Rohsenow DJ, et al. Varenicline versus nicotine patch with brief advice for smokers with substance use disorders with or without depression: effects on smoking, substance use and depressive symptoms. *Addiction*. 2017;112:1808-1820.**
16. **National Institute on Drug Abuse. Do people with mental illness and substance use disorders use tobacco more often? Published February 24, 2023.**
17. **Baker CL, et al. A cost-effectiveness analysis of varenicline for smoking cessation using data from the EAGLES trial. *Clinicoecon Outcomes Res*. 2018;10:67-74.**
18. **Jackson KC II, et al. An employer-based cost-benefit analysis of a novel pharmacotherapy agent for smoking cessation. *J Occup Environ Med.* 2007;49:453-460.**

KRONOS—STUDY 2:

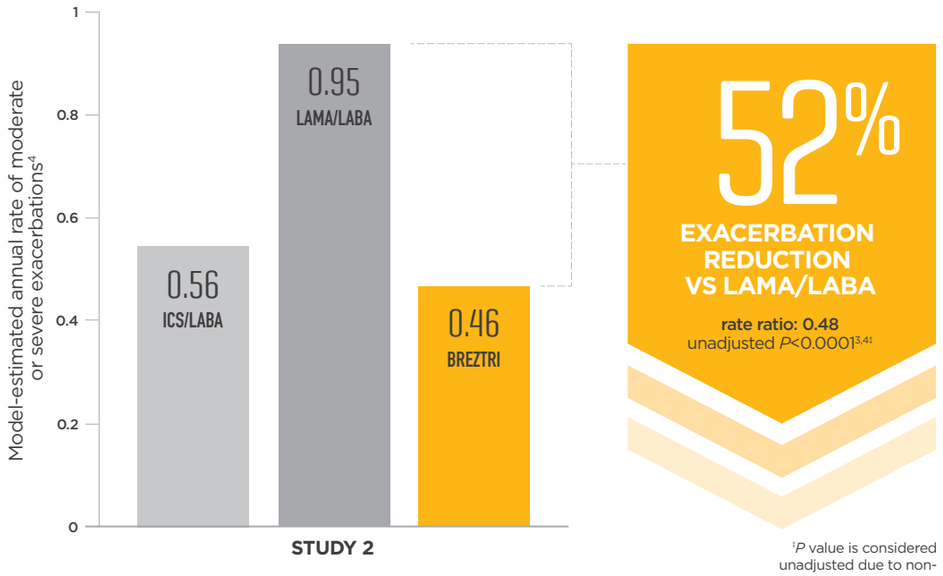
HOW WILL YOU HELP PROTECT YOUR PATIENTS FROM AN EXACERBATION?

For patients with COPD regardless of exacerbation history[3*]

In a 24-week study where the majority of patients did not have a history of exacerbations within the last year,[4]

BREZTRI was the ONLY triple therapy[†] vs LAMA/LABA to prevent moderate or severe exacerbations with a 52% reduction[3-5]

Secondary Endpoint: Rate of Moderate or Severe Exacerbations[3,4]



52% EXACERBATION REDUCTION VS LAMA/LABA

rate ratio: 0.48
unadjusted *P*<0.0001[3,4‡]

[‡]*P* value is considered unadjusted due to non-significant results higher in the testing hierarchy.

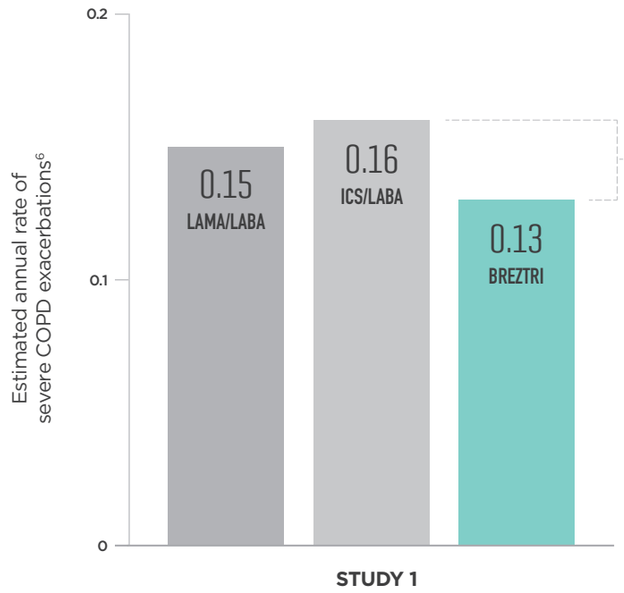
18% REDUCTION VS ICS/LABA
(rate ratio=0.82; *P*=0.2792)[3,4]

BREZTRI is not indicated for the relief of acute bronchospasm or for the treatment of asthma.

*Study 2: Patients (N=1902) were not required to have a history of moderate or severe exacerbations in the year prior to screening.
[†]Fixed-dose combination: ICS/LAMA/LABA.

ETHOS—STUDY 1*

SELECT SECONDARY ENDPOINT: ANNUAL RATE OF SEVERE COPD EXACERBATIONS[6]



20% EXACERBATION REDUCTION VS ICS/LABA

rate ratio: 0.80
95% CI: 0.66 to 0.97[5†]

[†]Controlling for multiple comparisons, results cannot be considered statistically significant.

16% reduction vs LAMA/LABA (rate ratio: 0.84; 95% CI: 0.69 to 1.03)[6]

BREZTRI is not indicated for the relief of acute bronchospasm or for the treatment of asthma.

*Study 1: Patients (N=8588) with ≥1 moderate or severe exacerbation(s) in the year prior to screening. Inclusive of a US patient population.

IMPORTANT SAFETY INFORMATION (continued)

- Oropharyngeal candidiasis has occurred in patients treated with orally inhaled drug products containing budesonide. Advise patients to rinse their mouths with water without swallowing after inhalation
- Lower respiratory tract infections, including pneumonia, have been reported following ICS. Physicians should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of pneumonia and exacerbations frequently overlap
- Due to possible immunosuppression, potential worsening of infections could occur. Use with caution. A more serious or fatal course of chickenpox or measles can occur in susceptible patients
- Particular care is needed for patients transferred from systemic corticosteroids to ICS because deaths due to adrenal insufficiency have occurred in patients during and after transfer. Taper patients slowly from systemic corticosteroids if transferring to BREZTRI
- Hypercorticism and adrenal suppression may occur with regular or very high dosage in susceptible individuals. If such changes occur, consider appropriate therapy
- Caution should be exercised when considering the coadministration of BREZTRI with long-term ketoconazole and other known strong CYP3A4 Inhibitors. Adverse effects related to increased systemic exposure to budesonide may occur
- If paradoxical bronchospasm occurs, discontinue BREZTRI immediately and institute alternative therapy
- Anaphylaxis and other hypersensitivity reactions (eg, angioedema, urticaria or rash) have been reported. Discontinue and consider alternative therapy

IMPORTANT SAFETY INFORMATION (continued)

- Use caution in patients with cardiovascular disorders, especially coronary insufficiency, as formoterol fumarate can produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, systolic or diastolic blood pressure, and also cardiac arrhythmias, such as supraventricular tachycardia and extrasystoles
- Decreases in bone mineral density have been observed with long-term administration of ICS. Assess initially and periodically thereafter in patients at high risk for decreased bone mineral content
- Glaucoma and cataracts may occur with long-term use of ICS. Worsening of narrow-angle glaucoma may occur, so use with caution. Consider referral to an ophthalmologist in patients who develop ocular symptoms or use BREZTRI long term. Instruct patients to contact a healthcare provider immediately if symptoms occur
- Worsening of urinary retention may occur. Use with caution in patients with prostatic hyperplasia or bladder-neck obstruction. Instruct patients to contact a healthcare provider immediately if symptoms occur

Please see additional Important Safety Information throughout and Brief Summary of Prescribing Information on adjacent pages.

BREZTRI AEROSPHERE®
(budesonide, glycopyrrolate, and formoterol fumarate) Inhalation Aerosol

STUDY DESIGNS

ETHOS[6]

Study 1 design: 52-week, Phase 3, randomized 1:1:1:1, double-blind, multicenter, parallel-group trial of 8588 patients with moderate to very severe COPD, comparing BREZTRI MDI 320/18/9.6 mcg (n=2157), BUD/GLY/FORM MDI 160/18/9.6 mcg (n=2137), GLY/FORM MDI 18/9.6 mcg (n=2143), and BUD/FORM MDI 320/9.6 mcg (n=2151), each administered BID. Patients were 40-80 years of age, smoking history of ≥10 pack-years, symptomatic COPD while receiving ≥2 inhaled maintenance therapies, and had a history of ≥1 moderate or severe exacerbation(s) in the previous year. The primary endpoint was the annual rate of moderate or severe COPD exacerbations, and secondary endpoints included the annual rate of severe COPD exacerbations and time to death (all cause). Moderate exacerbations were defined as those leading to treatment with systemic corticosteroids and/or antibiotics, and severe exacerbations as those resulting in hospitalization or death.

KRONOS[4]

Study 2 design: 24-week, Phase 3, randomized 2:2:1:1, double-blind, multicenter, parallel-group trial of 1902 patients with moderate to very severe COPD, comparing BREZTRI MDI 320/18/9.6 mcg (n=640), GLY/FORM MDI 18/9.6 mcg (n=627), BUD/FORM MDI 320/9.6 mcg (n=316), and open-label BUD/FORM DPI 400/12 mcg (n=319), each administered BID. Patients were 40-80 years of age, smoking history of ≥10 pack-years, symptomatic COPD while receiving ≥2 inhaled maintenance therapies with no requirement for a moderate or severe exacerbation(s) in the previous year. Primary endpoints were FEV_1 $AUC_{0\text{-}4}$ for BREZTRI vs BUD/FORM MDI and change from baseline in morning pre-dose trough FEV_1 for BREZTRI vs GLY/FORM MDI at Week 24. Secondary endpoints included the rate of moderate or severe COPD exacerbations. Moderate exacerbations were defined as those leading to treatment with systemic corticosteroids and/or antibiotics, and severe exacerbations as those resulting in hospitalization or death.

References

1. Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease (2024 report). Accessed January 3, 2024. https://goldcopd.org/2024-gold-report/ **2.** Data on File, US-69687, AZPLP. **3.** BREZTRI AEROSPHERE [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2022. **4.** Ferguson GT, Rabe KF, Martinez FJ, et al. Triple therapy with budesonide/glycopyrrolate/formoterol fumarate with co-suspension delivery technology versus dual therapies in chronic obstructive pulmonary disease (KRONOS): a double-blind, parallel-group, multicentre, phase 3 randomised controlled trial [article and supplementary appendix]. *Lancet Respir Med*. 2018;6(10):747-758. **5.** Trelegy (fluticasone furoate, umeclidinium, and vilanterol inhalation powder) [package insert]. GSK group of companies, 2022. **6.** Rabe KF, Martinez FJ, Ferguson GT,et al; ETHOS Investigators. Triple inhaled therapy at two glucocorticoid doses in moderate-to-very-severe COPD [article and supplementary appendix]. *N Engl J Med*. 2020;383(1):35-48.

Abbreviations

$AUC_{0\text{-}4}$=area under the curve from 0-4 hours, **BID**=twice daily, **BUD**=budesonide, **CI**=confidence interval, **COPD**=chronic obstructive pulmonary disease, **DPI**=dry powder inhaler, **ED**=emergency department, **FEV_1**=forced expiratory volume in 1 second, **FORM**=formoterol fumarate, **GLY**=glycopyrrolate, **ICS**=inhaled corticosteroid, **LABA**=long-acting $beta_2$-adrenergic agonist, **LAMA**=long-acting muscarinic antagonist, **MDI**=metered dose inhaler.

IMPORTANT SAFETY INFORMATION (continued)

- Use caution in patients with convulsive disorders, thyrotoxicosis, diabetes mellitus, and ketoacidosis or unusually responsive to sympathomimetic amines
- Be alert to hypokalemia or hyperglycemia
- Most common adverse reactions in a 52-week trial (incidence ≥ 2%) were upper respiratory tract infection (5.7%), pneumonia (4.6%), back pain (3.1%), oral candidiasis (3.0%), influenza (2.9%), muscle spasms (2.8%), urinary tract infection (2.7%), cough (2.7%), sinusitis (2.6%), and diarrhea (2.1%). In a 24-week trial, adverse reactions (incidence ≥ 2%) were dysphonia (3.3%) and muscle spasms (3.3%)
- BREZTRI should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors and tricyclic antidepressants, as these may potentiate the effect of formoterol fumarate on the cardiovascular system
- BREZTRI should be administered with caution to patients being treated with:
  - Strong cytochrome P450 3A4 inhibitors (may cause systemic corticosteroid effects)
  - Adrenergic drugs (may potentiate effects of formoterol fumarate)
  - Xanthine derivatives, steroids, or non-potassium sparing diuretics (may potentiate hypokalemia and/or ECG changes)
  - Beta-blockers (may block bronchodilatory effects of beta-agonists and produce severe bronchospasm)
  - Anticholinergic-containing drugs (may interact additively). Avoid use with BREZTRI
- Use BREZTRI with caution in patients with hepatic impairment, as budesonide and formoterol fumarate systemic exposure may increase. Patients with severe hepatic disease should be closely monitored

Please see additional Important Safety Information throughout and Brief Summary of Prescribing Information on adjacent pages.

You are encouraged to report the negative side effects of prescription drugs to the FDA. Visit www.FDA.gov/medwatch or call 1-800-FDA-1088.

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BREZTRI AEROSPHERE® (budesonide, glycopyrrolate, and formoterol fumarate) Inhalation Aerosol

BREZTRI AEROSPHERE®
(budesonide, glycopyrrolate, and formoterol fumarate) inhalation aerosol, for oral inhalation use

BRIEF SUMMARY of PRESCRIBING INFORMATION
For full Prescribing Information, see package insert.

INDICATIONS AND USAGE
BREZTRI AEROSPHERE is indicated for the maintenance treatment of patients with chronic obstructive pulmonary disease (COPD).

Limitations of Use:
BREZTRI AEROSPHERE is not indicated for the relief of acute bronchospasm or for the treatment of asthma *[see Warnings and Precautions (5.1, 5.2) in the full Prescribing Information]*.

CONTRAINDICATIONS
BREZTRI AEROSPHERE is contraindicated in patients who have demonstrated hypersensitivity to budesonide, glycopyrrolate, formoterol, or any of the excipients *[see Warnings and Precautions (5.11) and Description (11) in the full Prescribing Information]*.

WARNINGS AND PRECAUTIONS

Serious Asthma-Related Events – Hospitalizations, Intubations, Death
The safety and efficacy of BREZTRI AEROSPHERE in patients with asthma have not been established. BREZTRI AEROSPHERE is not indicated for the treatment of asthma.

Use of long-acting $beta_2$-adrenergic agonists (LABA) as monotherapy [without inhaled corticosteroid (ICS)] for asthma is associated with an increased risk of asthma-related death. Available data from controlled clinical trials also suggest that use of LABA as monotherapy increases the risk of asthma-related hospitalization in pediatric and adolescent patients. These findings are considered a class effect of LABA monotherapy. When a LABA is used in fixed-dose combination with ICS, data from large clinical trials do not show a significant increase in the risk of serious asthma-related events (hospitalizations, intubations, death) compared with ICS alone.

Available data do not suggest an increased risk of death with use of LABA in patients with COPD.

Deterioration of Disease and Acute Episodes
BREZTRI AEROSPHERE should not be initiated in patients with acutely deteriorating COPD, which may be a life-threatening condition. BREZTRI AEROSPHERE has not been studied in patients with acutely deteriorating COPD. The use of BREZTRI AEROSPHERE in this setting is not appropriate.

BREZTRI AEROSPHERE should not be used for the relief of acute symptoms, i.e., as rescue therapy for the treatment of acute episodes of bronchospasm. BREZTRI AEROSPHERE has not been studied in the relief of acute symptoms and extra doses should not be used for that purpose. Acute symptoms should be treated with an inhaled short-acting $beta_2$-agonist.

When beginning treatment with BREZTRI AEROSPHERE, patients who have been taking inhaled, short-acting $beta_2$-agonists on a regular basis (e.g., four times a day) should be instructed to discontinue the regular use of these drugs and use them only for symptomatic relief of acute respiratory symptoms. When prescribing BREZTRI AEROSPHERE, the healthcare provider should also prescribe an inhaled, short-acting $beta_2$-agonist and instruct the patient on how it should be used. Increasing inhaled $beta_2$-agonist use is a signal of deteriorating disease for which prompt medical attention is indicated.

COPD may deteriorate acutely over a period of hours or chronically over several days or longer. If BREZTRI AEROSPHERE no longer controls symptoms, or the patient's inhaled, short-acting $beta_2$-agonist becomes less effective or the patient needs more inhalations of short-acting $beta_2$-agonist than usual, these may be markers of deterioration of disease. In this setting, re-evaluate the patient and the COPD treatment regimen at once. The daily dosage of BREZTRI AEROSPHERE should not be increased beyond the recommended dose.

Avoid Excessive Use of BREZTRI AEROSPHERE and Avoid Use with other Long-Acting $Beta_2$-Agonists
As with other inhaled drugs containing $beta_2$-adrenergic agents, BREZTRI AEROSPHERE should not be used more often than recommended, at higher doses than recommended, or in conjunction with other medications containing LABA, as an overdose may result. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs.

Patients using BREZTRI AEROSPHERE should not use another medicine containing a LABA (e.g., salmeterol, formoterol fumarate, arformoterol tartrate, indacaterol) for any reason *[see Drug Interactions (7.1) in the full Prescribing Information]*.

Oropharyngeal Candidiasis
BREZTRI AEROSPHERE contains budesonide, an ICS. Localized infections of the mouth and pharynx with *Candida albicans* have occurred in subjects treated with orally inhaled drug products containing budesonide. When such an infection develops, it should be treated with appropriate local or systemic (i.e., oral) antifungal therapy while treatment with BREZTRI AEROSPHERE continues. In some cases, therapy with BREZTRI AEROSPHERE may need to be interrupted. Advise the patient to rinse his/her mouth with water without swallowing following administration of BREZTRI AEROSPHERE to help reduce the risk of oropharyngeal candidiasis.

Pneumonia
Lower respiratory tract infections, including pneumonia, have been reported following the inhaled administration of corticosteroids. Physicians should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of pneumonia and exacerbations frequently overlap.

In a 52-week trial of subjects with COPD (n = 8,529), the incidence of confirmed pneumonia was 4.2% for BREZTRI AEROSPHERE 320 mcg/18 mcg/9.6 mcg (n = 2144), 3.5% for budesonide, glycopyrrolate and formoterol fumarate [BGF MDI 160 mcg/18 mcg/9.6 mcg] (n = 2124), 2.3% for GFF MDI 18 mcg/9.6 mcg (n = 2125) and 4.5% for BFF MDI 320 mcg/9.6 mcg (n = 2136).

Fatal cases of pneumonia occurred in 2 subjects receiving BGF MDI 160 mcg/18 mcg/9.6 mcg, 3 subjects receiving GFF MDI 18 mcg/9.6 mcg, and no subjects receiving BREZTRI AEROSPHERE 320 mcg/18 mcg/9.6 mcg.

In a 24-week trial of subjects with COPD (n = 1,896), the incidence of confirmed pneumonia was 1.9% for BREZTRI AEROSPHERE 320 mcg/18 mcg/9.6 mcg (n = 639), 1.6% for glycopyrrolate and formoterol fumarate [GFF MDI 18 mcg/9.6 mcg] (n = 625) and 1.9% for budesonide and formoterol fumarate [BFF MDI 320 mcg/9.6 mcg] (n = 320). There were no fatal cases of pneumonia in the study.

Immunosuppression and Risk of Infections
Patients who are using drugs that suppress the immune system are more susceptible to infection than healthy individuals. Chicken pox and measles, for example, can have a more serious or even fatal course in susceptible children or adults using corticosteroids. In such children or adults who have not had these diseases or been properly immunized, particular care should be taken to avoid exposure. How the dose, route, and duration of corticosteroid administration affects the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior corticosteroid treatment to the risk is also not known. If a patient is exposed to chickenpox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated (see the Prescribing Information for VZIG and IG). If chicken pox develops, treatment with antiviral agents may be considered.

ICS should be used with caution, if at all, in patients with active or quiescent tuberculosis infections of the respiratory tract; untreated systemic fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex.

Transferring Patients from Systemic Corticosteroid Therapy
HPA Suppression/Adrenal Insufficiency
Particular care is needed for patients who have been transferred from systemically active corticosteroids to ICS because deaths due to adrenal insufficiency have occurred in patients during and after transfer from systemic corticosteroids to less systemically available ICS. After withdrawal from systemic corticosteroids, a number of months are required for recovery of hypothalamic-pituitary-adrenal (HPA) function.

Patients who have been previously maintained on 20 mg or more per day of prednisone (or its equivalent) may be most susceptible, particularly when their systemic corticosteroids have been almost completely withdrawn. During this period of HPA suppression, patients may exhibit signs and symptoms of adrenal insufficiency when exposed to trauma, surgery, or infection (particularly gastroenteritis) or other conditions associated with severe electrolyte loss. Although BREZTRI AEROSPHERE may provide control of COPD symptoms during these episodes, in recommended doses it supplies less than normal physiological amounts of glucocorticoid systemically and does not provide the mineralocorticoid activity that is necessary for coping with these emergencies.

During periods of stress, or a severe COPD exacerbation, patients who have been withdrawn from systemic corticosteroids should be instructed to resume oral corticosteroids (in large doses) immediately and to contact their healthcare practitioner for further instruction. These patients should also be instructed to carry a warning card indicating that they may need supplementary systemic corticosteroids during periods of stress, or a severe COPD exacerbation.

Patients requiring oral corticosteroids should be weaned slowly from systemic corticosteroid use after transferring to BREZTRI AEROSPHERE. Prednisone reduction can be accomplished by reducing the daily prednisone dose by 2.5 mg on a weekly basis during therapy with BREZTRI AEROSPHERE. Lung function (forced expiratory volume in 1 second [FEV_1] or morning peak expiratory flow [PEF]), beta-agonist use, and COPD symptoms should be carefully monitored during withdrawal of oral corticosteroids. In addition, patients should be observed for signs and symptoms of adrenal insufficiency, such as fatigue, lassitude, weakness, nausea and vomiting, and hypotension.

Unmasking of Allergic Conditions Previously Suppressed by Systemic Corticosteroids
Transfer of patients from systemic corticosteroid therapy to BREZTRI AEROSPHERE may unmask allergic conditions previously suppressed by the systemic corticosteroid therapy (e.g., rhinitis, conjunctivitis, eczema, arthritis, eosinophilic conditions).

Corticosteroid Withdrawal Symptoms
During withdrawal from oral corticosteroids, some patients may experience symptoms of systemically active corticosteroid withdrawal (e.g., joint and/or muscular pain, lassitude, depression) despite maintenance or even improvement of respiratory function.

Hypercorticism and Adrenal Suppression
Inhaled budesonide is absorbed into the circulation and can be systemically active. Effects of budesonide on the HPA axis are not observed with the therapeutic doses of budesonide in BREZTRI AEROSPHERE. However, exceeding the recommended dosage or coadministration with a strong cytochrome P450 3A4 (CYP3A4) inhibitor may result in HPA dysfunction *[see Warnings and Precautions (5.9) and Drug Interactions (7.1) in the full Prescribing Information]*.

Because of the possibility of significant systemic absorption of ICS, patients treated with BREZTRI AEROSPHERE should be observed carefully for any evidence of systemic corticosteroid effects. Particular care should be taken in observing patients postoperatively or during periods of stress for evidence of inadequate adrenal response.

It is possible that systemic corticosteroid effects, such as hypercorticism and adrenal suppression (including adrenal crisis) may appear in a small number of patients who are sensitive to these effects. If such effects occur, appropriate therapy should be initiated as needed.

Drug Interactions with Strong Cytochrome P450 3A4 Inhibitors
Caution should be exercised when considering the coadministration of BREZTRI AEROSPHERE with long-term ketoconazole, and other known strong CYP3A4 inhibitors (e.g., ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, telithromycin) because adverse effects related to increased systemic exposure to budesonide may occur *[see Drug Interactions (7.1) and Clinical Pharmacology (12.3) in the full Prescribing Information]*.

Paradoxical Bronchospasm
As with other inhaled therapies, BREZTRI AEROSPHERE can produce paradoxical bronchospasm, which may be life-threatening. If paradoxical bronchospasm occurs following dosing with BREZTRI AEROSPHERE, it should be treated immediately with an inhaled, short-acting bronchodilator; BREZTRI AEROSPHERE should be discontinued immediately and alternative therapy should be instituted.

Hypersensitivity Reactions including Anaphylaxis
Immediate hypersensitivity reactions have been reported after administration of budesonide, glycopyrrolate or formoterol fumarate, the components of BREZTRI AEROSPHERE. If signs suggesting allergic reactions occur, in particular, angioedema (including difficulties in breathing or swallowing, swelling of tongue, lips, and face), urticaria, or skin rash, BREZTRI AEROSPHERE should be stopped at once and alternative treatment should be considered *[see Contraindications (4) in the full Prescribing Information]*.

Cardiovascular Effects
Formoterol fumarate, like other $beta_2$-agonists, can produce a clinically significant cardiovascular effect in some patients as measured by increases in pulse rate, systolic or diastolic blood pressure, and also cardiac arrhythmias, such as supraventricular tachycardia and extrasystoles *[see Clinical Pharmacology (12.2) in the full Prescribing Information]*.

If such effects occur, BREZTRI AEROSPHERE may need to be discontinued. In addition, beta-agonists have been reported to produce electrocardiographic changes, such as flattening of the T wave, prolongation of the QTc interval, and ST segment depression, although the clinical significance of these findings is unknown. Therefore, BREZTRI AEROSPHERE should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

Reduction in Bone Mineral Density
Decreases in bone mineral density (BMD) have been observed with long-term administration of products containing ICS. The clinical significance of small changes in BMD with regard to long-term consequences such as fracture is unknown. Patients with major risk factors for decreased bone mineral content, such as prolonged immobilization, family history of osteoporosis, postmenopausal status, tobacco use, advanced age, poor nutrition, or chronic use of drugs that can reduce bone mass (e.g., anticonvulsants, oral corticosteroids) should be monitored and treated with established standards of care. Since patients with COPD often have multiple risk factors for reduced BMD, assessment of BMD is recommended prior to initiating BREZTRI AEROSPHERE and periodically thereafter. If significant reductions in BMD are seen and BREZTRI AEROSPHERE

is still considered medically important for that patient's COPD therapy, use of therapy to treat or prevent osteoporosis should be strongly considered.

In a subset of COPD patients in a 24-week trial with a 28-week safety extension that evaluated BREZTRI AEROSPHERE 320/18/9.6 mcg and GFF MDI 18/9.6 mcg, the effects on BMD endpoints were evaluated. BMD evaluations were performed at baseline and 52-weeks using dual energy x-ray absorptiometry (DEXA) scans. Mean percent changes in BMD from baseline was -0.1% for BREZTRI AEROSPHERE 320/18/9.6 mcg and 0.4% for GFF MDI 18/9.6 mcg *[see Clinical Studies (14) in the full Prescribing Information]*.

Glaucoma and Cataracts, Worsening of Narrow-Angle Glaucoma

Glaucoma, increased intraocular pressure, and cataracts have been reported in patients with COPD following the long-term administration of ICS or with use of inhaled anticholinergics. BREZTRI AEROSPHERE should be used with caution in patients with narrow-angle glaucoma. Prescribers and patients should be alert for signs and symptoms of acute narrow-angle glaucoma (e.g., eye pain or discomfort, blurred vision, visual halos or colored images in association with red eyes from conjunctival congestion and corneal edema). Instruct patients to consult a physician immediately should any of these signs or symptoms develop. Consider referral to an ophthalmologist in patients who develop ocular symptoms or use BREZTRI AEROSPHERE long term.

In a 52-week trial that evaluated BREZTRI AEROSPHERE 320/18/9.6 mcg, GFF MDI 18/9.6 mcg, and BFF MDI 320/9.6 mcg in subjects with COPD, the incidence of cataracts ranged from 0.7% to 1.0% across groups.

Worsening of Urinary Retention

BREZTRI AEROSPHERE, like all therapies containing an anticholinergic, should be used with caution in patients with urinary retention. Prescribers and patients should be alert for signs and symptoms of prostatic hyperplasia or bladder-neck obstruction (e.g., difficulty passing urine, painful urination), especially in patients with prostatic hyperplasia or bladder neck obstruction. Instruct patients to consult a physician immediately should any of these signs or symptoms develop.

Coexisting Conditions

BREZTRI AEROSPHERE, like all therapies containing sympathomimetic amines, should be used with caution in patients with convulsive disorders or thyrotoxicosis and in those who are unusually responsive to sympathomimetic amines. Doses of the related $beta_2$-adrenoceptor agonist albuterol, when administered intravenously, have been reported to aggravate preexisting diabetes mellitus and ketoacidosis.

Hypokalemia and Hyperglycemia

Beta-adrenergic agonists may produce significant hypokalemia in some patients, possibly through intracellular shunting, which has the potential to produce adverse cardiovascular effects. The decrease in serum potassium is usually transient, not requiring supplementation. $Beta_2$-agonist therapies may produce transient hyperglycemia in some patients.

ADVERSE REACTIONS

The following adverse reactions are discussed in greater detail in other sections of the labeling.

- Serious asthma-related events – hospitalizations, intubations, death *[see Warnings and Precautions (5.1) in the full Prescribing Information]*
- Oropharyngeal candidiasis infection *[see Warnings and Precautions (5.4) in the full Prescribing Information]*
- Increased risk of pneumonia in COPD *[see Warnings and Precautions (5.5) in the full Prescribing Information]*
- Immunosuppression and risk of infections *[see Warnings and Precautions (5.6) in the full Prescribing Information]*
- Hypercorticism and adrenal suppression *[see Warnings and Precautions (5.8) in the full Prescribing Information]*
- Paradoxical bronchospasm *[see Warnings and Precautions (5.10) in the full Prescribing Information]*
- Hypersensitivity reactions including anaphylaxis *[see Contraindications (4) and Warnings and Precautions (5.11) in the full Prescribing Information]*
- Cardiovascular effects *[see Warnings and Precautions (5.12) in the full Prescribing Information]*
- Reduction in bone mineral density *[see Warnings and Precautions (5.13) in the full Prescribing Information]*
- Worsening of narrow-angle glaucoma and cataracts *[see Warnings and Precautions (5.14) in the full Prescribing Information]*
- Worsening of urinary retention *[see Warnings and Precautions (5.15) in the full Prescribing Information]*

Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of BREZTRI AEROSPHERE is based on the safety data from one 52-week exacerbation trial (Trial 1) and one 24-week lung function trial with a 28-week safety extension study, resulting in up to 52 weeks of treatment (Trial 2). In Trials 1 and 2, a total of 2783 subjects have received at least 1 dose of BREZTRI AEROSPHERE 320 mcg/18 mcg/9.6 mcg *[see Clinical Studies (14) in the full Prescribing Information]*.

In Trials 1 and 2, subjects received one of the following treatments: BREZTRI AEROSPHERE 320 mcg/18 mcg/9.6 mcg, glycopyrrolate and formoterol fumarate [GFF MDI 18 mcg/9.6 mcg], or budesonide and formoterol fumarate [BFF MDI 320 mcg/9.6 mcg]. Each treatment was administered twice daily.

In Trial 1, a 52-week, randomized, double-blind clinical trial, a total of 2144 subjects with COPD received at least 1 dose of BREZTRI AEROSPHERE 320 mcg/18 mcg/9.6 mcg (mean age: 64.7 years, 84.9% Caucasian, 59.7% male across all treatments) *[see Clinical Studies (14) in the full Prescribing Information]*.

In Trial 2, a 24-week, randomized, double-blind clinical trial, with a 28-week long-term safety extension resulting in up to 52 weeks of treatment, a total of 639 subjects received at least 1 dose of BREZTRI AEROSPHERE 320 mcg/18 mcg/9.6 mcg (mean age: 65.2 years, 50.1% Caucasian, 71.2% male across all treatments) *[see Clinical Studies (14) in the full Prescribing Information]*.

The incidence of adverse reactions from the 52-week trial (Trial 1) is presented in Table 1 for subjects treated with BREZTRI AEROSPHERE 320 mcg/18 mcg/9.6 mcg, GFF MDI 18 mcg/9.6 mcg, or BFF MDI 320 mcg/9.6 mcg.

Table 1: Adverse reactions occurring at an incidence of ≥ 2% of subjects and more common in BREZTRI AEROSPHERE compared to GFF MDI and/or BFF MDI (Trial 1)

Adverse Reaction	BREZTRI AEROSPHERE[1] 320 mcg/18 mcg/9.6 mcg N=2144 (%)	GFF MDI[1] 18 mcg/9.6 mcg N=2125 (%)	BFF MDI[1] 320 mcg/9.6 mcg N=2136 (%)
Upper Respiratory Tract Infection	123 (5.7)	102 (4.8)	115 (5.4)
Pneumonia	98 (4.6)	61 (2.9)	107 (5.0)
Back pain	67 (3.1)	55 (2.6)	64 (3.0)
Oral candidiasis	65 (3.0)	24 (1.1)	57 (2.7)
Influenza	63 (2.9)	42 (2.0)	61 (2.9)
Muscle spasms	60 (2.8)	19 (0.9)	53 (2.5)
Urinary tract infection	58 (2.7)	60 (2.8)	41 (1.9)
Cough	58 (2.7)	50 (2.4)	51 (2.4)
Sinusitis	56 (2.6)	47 (2.2)	55 (2.6)
Diarrhea	44 (2.1)	37 (1.7)	38 (1.8)

[1] BREZTRI AEROSPHERE = budesonide/glycopyrrolate/formoterol fumarate 320 mcg/18 mcg/9.6 mcg; GFF MDI = glycopyrrolate/formoterol fumarate 18 mcg/9.6 mcg; BFF MDI = budesonide/formoterol fumarate 320 mcg/9.6 mcg; all treatments were administered twice daily.

In 24-week data from Trial 2, adverse reactions that occurred in subjects treated with BREZTRI AEROSPHERE 320 mcg/18 mcg/9.6 mcg (n=639) at an incidence of ≥ 2% included dysphonia (3.1%) and muscle spasms (3.3%).

Additional Adverse Reactions

Other adverse reactions that have been associated with one or more of the individual components of BREZTRI AEROSPHERE include: hyperglycemia, anxiety, insomnia, headache, palpitations, nausea, hypersensitivity, depression, agitation, restlessness, nervousness, tremor, dizziness, angina pectoris, tachycardia, cardiac arrhythmias (e.g., atrial fibrillation, supraventricular tachycardia, and extrasystoles), throat irritation, bronchospasm, dry mouth, bruising, urinary retention, chest pain, sign or symptoms of systemic glucocorticoid steroid effects (e.g., hypofunctional adrenal gland), and abnormal behavior.

DRUG INTERACTIONS

No formal drug interaction studies have been performed with BREZTRI AEROSPHERE.

Inhibitors of Cytochrome P450 3A4

The main route of metabolism of corticosteroids, including budesonide, a component of BREZTRI AEROSPHERE, is via cytochrome P450 isoenzyme 3A4 (CYP3A4). After oral administration of ketoconazole, a strong inhibitor of CYP3A4, the mean plasma concentration of orally administered budesonide increased. Concomitant administration of a CYP3A4 inhibitor may inhibit the metabolism of, and increase the systemic exposure to, budesonide. Caution should be exercised when considering the coadministration of BREZTRI AEROSPHERE with long-term ketoconazole and other known strong CYP3A4 inhibitors (e.g., ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, telithromycin) *[see Warnings and Precautions (5.9) in the full Prescribing Information]*.

Adrenergic Drugs

If additional adrenergic drugs are to be administered by any route, they should be used with caution because the sympathetic effects of formoterol, a component of BREZTRI AEROSPHERE, may be potentiated *[see Warnings and Precautions (5.3) in the full Prescribing Information]*.

Xanthine Derivatives, Steroids, or Diuretics

Concomitant treatment with xanthine derivatives, steroids, or diuretics may potentiate the hypokalemic effect of $beta_2$-adrenergic agonists such as formoterol, a component of BREZTRI AEROSPHERE.

Non-Potassium Sparing Diuretics

The hypokalemia and/or ECG changes that may result from the administration of non-potassium sparing diuretics (such as loop or thiazide diuretics) can be acutely worsened by $beta_2$-agonists, especially when the recommended dose of the $beta_2$-agonist is exceeded.

Monoamine Oxidase Inhibitors, Tricyclic Antidepressants, QTc Prolonging Drugs

BREZTRI AEROSPHERE, as with other $beta_2$-agonists, should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants or other drugs known to prolong the QTc interval because the action of adrenergic agonists on the cardiovascular system may be potentiated by these agents. Drugs that are known to prolong the QTc interval may be associated with an increased risk of ventricular arrhythmias.

Beta-adrenergic Receptor Blocking Agents

Beta-adrenergic receptor antagonists (beta-blockers) and BREZTRI AEROSPHERE may interfere with the effect of each other when administered concurrently. Beta-blockers not only block the therapeutic effects of $beta_2$-agonists, but may produce severe bronchospasm in COPD patients. Therefore, patients with COPD should not normally be treated with beta-blockers. However, under certain circumstances, e.g., as prophylaxis after myocardial infarction, there may be no acceptable alternatives to the use of beta-blockers in patients with COPD. In this setting, cardioselective beta-blockers could be considered, although they should be administered with caution.

Anticholinergics

There is a potential for an additive interaction with concomitantly used anticholinergic medications. Therefore, avoid coadministration of BREZTRI AEROSPHERE with other anticholinergic-containing drugs as this may lead to an increase in anticholinergic adverse effects *[see Warnings and Precautions (5.9, 5.10) and Adverse Reactions (6) in the full Prescribing Information]*.

OVERDOSAGE

No cases of overdose have been reported with BREZTRI AEROSPHERE. BREZTRI AEROSPHERE contains budesonide, glycopyrrolate, and formoterol fumarate; therefore, the risks associated with overdosage for the individual components described below apply to BREZTRI AEROSPHERE. Treatment of overdosage consists of discontinuation of BREZTRI AEROSPHERE together with institution of appropriate symptomatic and/or supportive therapy. The judicious use of a cardioselective beta-receptor blocker may be considered, bearing in mind that such medication can produce bronchospasm. Cardiac monitoring is recommended in case of overdosage.

Budesonide

If used at excessive doses for prolonged periods, systemic corticosteroid effects, such as hypercorticism may occur *[see Warnings and Precautions (5.8) in the full Prescribing Information]*.

Glycopyrrolate

High doses of glycopyrrolate, a component of BREZTRI AEROSPHERE, may lead to anticholinergic signs and symptoms such as nausea, vomiting, dizziness, lightheadedness, blurred vision, increased intraocular pressure (causing pain, vision disturbances or reddening of the eye), obstipation, or difficulties in voiding.

Formoterol Fumarate

An overdose of formoterol fumarate would likely lead to an exaggeration of effects that are typical for $beta_2$-agonists: seizures, angina, hypertension, hypotension, tachycardia, atrial and ventricular tachyarrhythmias, nervousness, headache, tremor, palpitations, muscle cramps, nausea, dizziness, sleep disturbances, metabolic acidosis, hyperglycemia, hypokalemia. As with all sympathomimetic medications, cardiac arrest, and even death may be associated with overdosage of formoterol fumarate.

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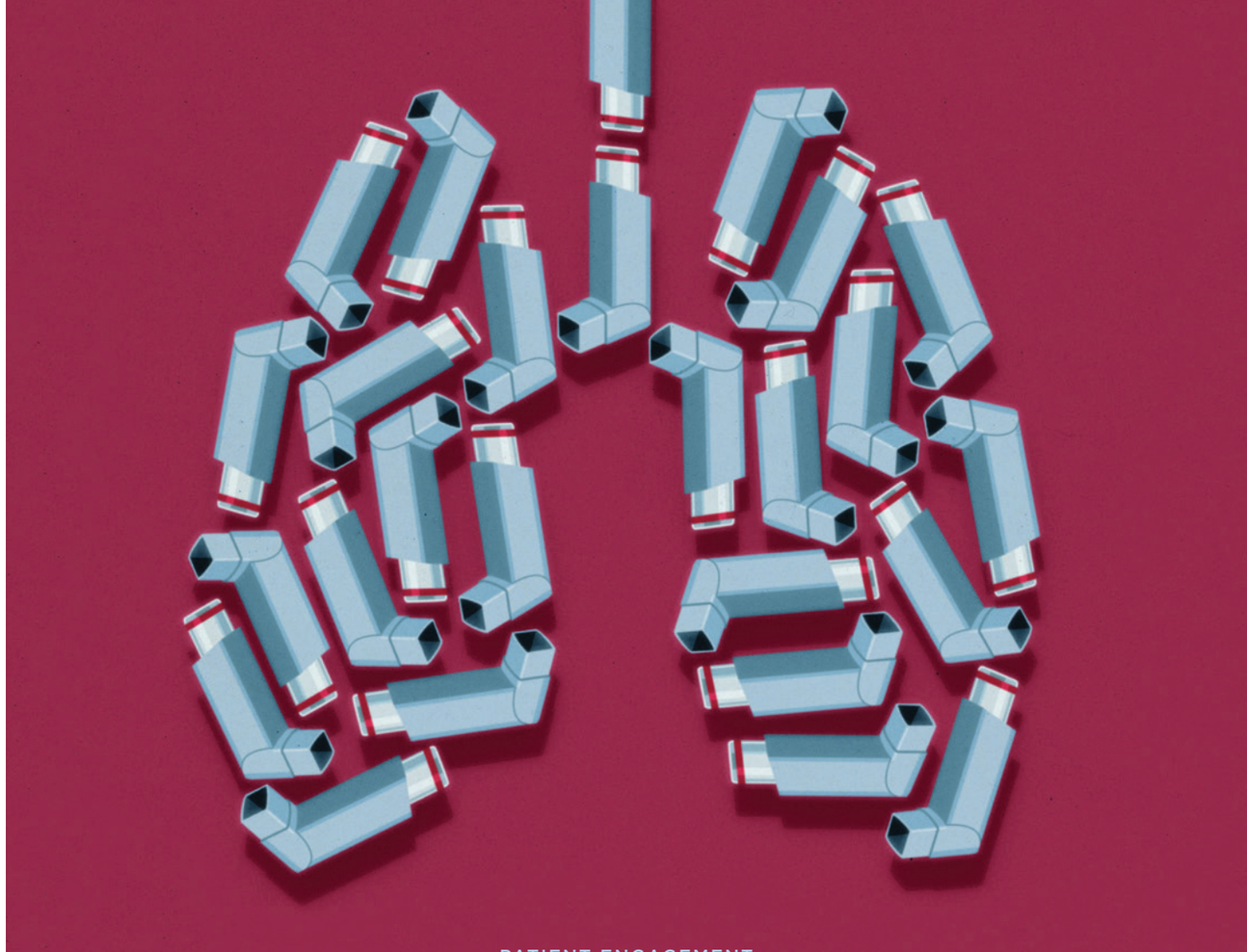

PATIENT ENGAGEMENT

OVERCOMING BARRIERS TO PROPER INHALER TECHNIQUE

By Alex Evans, PharmD, MBA

Illustration by Dan Page

CONTINUED ON NEXT PAGE

According to the Centers for Disease Control and Prevention (CDC), chronic obstructive pulmonary disease (COPD) affects approximately 16 million Americans and ranks as the third leading cause of death in the United States.[1] The World Health Organization (WHO) estimates that COPD is also the third-leading cause of death globally, accounting for over 3 million deaths in 2019 alone.[2]

Despite the prevalence and severity of the disease, a significant proportion of COPD patients do not use their inhaler devices correctly and miss out on the full benefits of treatment. While the percentage of patients who use incorrect technique varies greatly between studies, the TIE-study, a prospective multicenter study conducted in primary and secondary care centers in Sweden, found that 50% of patients demonstrated incorrect technique.[3] Another notable study of 180 patients with COPD found that at least 80% demonstrated incorrect technique.[4]

Improper inhaler technique can lead to suboptimal drug delivery and is tied to poor outcomes. A 2018 systematic analysis of over 100 studies showed a significant association between a higher frequency of inhaler errors and COPD or asthma exacerbations. These studies spanned a broad range of inhaler types, further supporting the need to ensure correct inhaler use.[5]

As healthcare professionals, understanding and promoting correct inhaler technique is an important part of COPD management. We interviewed Vanessa Pomarico, EdD, APRN, FNP-BC, FAANP, nurse practitioner and faculty at Fitzgerald Health Education Associates, to get her expert advice on common inhaler pitfalls and how providers can help patients overcome them.

Barrier 1: Poor coordination

Coordinating inhaler activation and medication inhalation can be a significant challenge for many patients. In 2016, a systematic review of 144 articles representing close to 55,000 patients found that coordination was the most common inhaler use error, with a prevalence of 45%.[6] Poor coordination can result in a significant proportion of the drug being deposited in the mouth or throat rather than the lungs, reducing treatment efficacy.

Pomarico has seen this firsthand in her office. "It takes a lot of coordination for patients to use a metered dose inhaler correctly. They will often call me and tell me the medicine isn't working, when in fact the issue is their technique."

How to overcome it: Guiding patients through inhaler use, demonstrating the correct technique, and then allowing patients to try it themselves can help providers identify and correct mistakes early. Asking them to periodically demonstrate their technique again at follow-up visits can also help catch coordination mistakes before they lead to an exacerbation. "I review inhaler technique in the office when I am prescribing it as well as give them a printed handout. If someone is really struggling, I encourage them to ask the pharmacist to show them how to use the inhaler when they pick it up. I emphasize that proper technique is essential to feeling better, so it is important to use the inhaler correctly," notes Pomarico.

Spacers are one of the best ways to overcome poor coordination, and they aren't just for those struggling to use their inhaler correctly, either—nearly anyone can benefit from one. Pomarico says, "I even tell patients that I use a chamber when I need an inhaler [for bronchospasm due to respiratory infection] because I want to be sure that the medication gets to where it needs to be and doesn't just sit on my tongue where it will do nothing to help me breathe." Even though spacers aren't always covered by insurance, writing a prescription will allow the pharmacy to attempt to bill the patient's insurance.

Barrier 2: Weak hand strength

Weak hand strength can make inhalers hard to use, significantly impacting both inhaler technique and adherence. Pomarico sees this regularly in her office. "Rheumatoid arthritis, osteoarthritis, Parkinson's disease and any neuromuscular disorder that makes it difficult for the patient to use the pump correctly can lead to poor technique. Elderly patients who have a weak hand grasp will have difficulty pressing the decanter so they generally do not get a full dose or it is so painful for them that they don't even bother to use the inhaler."

This issue recently hit close to home for Pomarico: "My mom got a pretty severe upper respiratory infection this past spring. She has bilateral hand neuropathies and was so weak that she couldn't use the inhaler correctly, so that just made it more difficult for her to get better. It was frightening to see her struggle to breathe and not be able to use the inhaler. My sister and I visited her twice a day and gave her the steroid inhaler."

How to overcome it: Considering the patient's entire medical history, and not just their pulmonary history, will help alert you to potential trouble ahead. This is another issue you can catch when the patient is demonstrating their technique in the office. Breath activated inhalers, dry powder inhalers, and nebulized solutions are all great options for patients who lack the hand strength to activate a metered dose inhaler. For Pomarico's mom, "I finally had her primary care provider order a breath activated pump for her until she got stronger." Keep in mind, though, that spacers should not be used with breath activated inhalers.

Illustration by Neil Leslie / Ikon Images

Barrier 3: Treatment complexity

The presence of multiple health conditions also complicates the patient's overall treatment regimen and can leave patients feeling overwhelmed and confused, making it easy for inhaler mistakes to start creeping in. Compared to many of Pomarico's patients with other pulmonary conditions, like asthma, "COPD patients tend to be older and sicker with other comorbid conditions that impede their ability to use an inhaler correctly."

Some of the most common mistakes? According to Pomarico, "If we write for 2 puffs every 4 hours the patients will often do both puffs at the same time and inhale rather than waiting between each puff. I explain that this just wastes a dose and provides no extra benefit. Another common mistake I see is mixing up the rescue and inhaled corticosteroid (ICS) inhalers."

How to overcome it: Managing medications is where pharmacists can shine. Pill boxes and blister packaging help with oral medications, while automated refills and medication reminders help patients with their entire regimen. Furthermore, 80% of community pharmacies offer Medication Therapy Management (MTM)[7], and many now

offer medication synchronization, both of which can improve adherence.[8,9] Partnering with your community pharmacists to help with complex regimens gives patients the space to focus on things like inhaler technique.

But Pomarico also offers a word of caution on refills, despite their adherence benefits. "I do not give a year of refills on rescue inhalers. While I want my patients to have easy access, I also need to know how often they are using it because if they are requesting a refill on their albuterol every month, then I give them a call to find out what is going on. The vast majority of the time, it is because they mixed up their inhalers." Keeping tabs on it during office visits is equally important. "I always ask my patients to bring their inhalers with them to every visit so I can review what they are using and how they are using it," says Pomarico.

Barrier 4: Lack of education

Unfortunately, despite our best efforts, many patients still fall through the cracks and receive an inhaler without learning how to use it. In one study in Saudi Arabia, approximately 40% of patients presenting to the ED for an asthma exacerbation had received no formal education from a healthcare professional on inhaler technique. This lack of knowledge was identified as a major contributor to improper inhaler use.[10]

Furthermore, even if a patient does receive inhaler education, different kinds of inhalers, such as metered-dose inhalers (MDIs) and dry powder inhalers (DPIs), require different techniques. That can make it even more challenging for COPD patients, who often require multiple inhaler types to manage their symptoms.

How to overcome it: Implementing a comprehensive COPD education program is essential to ensure correct inhaler technique among patients. Here again, pharmacists can help fill in the gaps. "We have great relationships with our local pharmacists so we sometimes will call them to say, 'please demonstrate to the patient how to use it when they pick it up.' I even had one pharmacist go out to the parking lot and show the patient how to use the inhaler," says Pomarico.

Minimizing the types of inhalers, when possible, is another good solution. Prescribing two MDIs, for example, rather than one MDI and one DPI, reduces the potential for errors. This may depend on insurance and also on the patient's clinical needs, but MDIs are available for multiple medication classes, including corticosteroids and combination products.[11]

References

1. **Chronic obstructive pulmonary disease (COPD). Centers for Disease Control and Prevention. June 30, 2023. Available at *cdc.gov/copd/index.html*.**
2. **Chronic obstructive pulmonary disease (COPD). World Health Organization. Available at *who.int*.**
3. **Johanna S, et al. Incorrect inhaler technique is common in patients with COPD – Data from the TIE study. Eur. Respir. J Sep 2016;48(suppl 60):PA3945.**
4. **Harb HS, et al. Determinants of incorrect inhaler technique in chronic obstructive pulmonary disease patients. Int J Clin Pract. 2021;75(6):e14073.**
5. **Usmani OS, et al. Critical inhaler errors in asthma and COPD: a systematic review of impact on health outcomes. Respir Res. Jan 16;19(1):10.**
6. **Sanchis J, Gich I, Pedersen S; Aerosol Drug Management Improvement Team (ADMIT). Systematic review of errors in inhaler use: has patient technique improved over time? Chest. 2016;150(2):394-406.**
7. **NCPA releases 2022 digest report. National Community Pharmacists Association. October 2, 2022. Available at *ncpa.org/newsroom/news-releases/2022/10/02/ncpa-releases-2022-digest-report*.**
8. **Erku DA, et al. The impact of pharmacist-led medication therapy management on medication adherence in patients with type 2 diabetes mellitus: a randomized controlled study. Pharm Pract (Granada). 2017;15(3):1026.**
9. **Nsiah I, et al. The impact of medication synchronization programs on medication adherence: A meta-analysis. J Am Pharm Assoc (2003). 2021;61(4):e202-e211.**
10. **Al-Jahdali H, et al. Improper inhaler technique is associated with poor asthma control and frequent emergency department visits. Allergy Asthma Clin Immunol. 2013;9(1):8.**
11. **COPD Resource Center. Ensuring safe transitions of care in patients with chronic obstructive pulmonary disease. Published in Guide to Device Selection. Available at *copdcare.org/guide-device-selection.php*.**

PATIENT: JOHN, 66, WAS A RETIRED FIREFIGHTER WITH A HISTORY OF OCCUPATIONAL EXPOSURES TO FIRE SMOKE. HE WAS NEVER A CIGARETTE SMOKER. HE DEVELOPED ASTHMA ABOUT 10 YEARS AGO.

"Occupational exposure and comorbidities made John's case challenging"

PHYSICIAN:

David Mannino, MD, FCCP, FERS

Medical Director/ Co-Founder of the COPD Foundation

Illustration by Juhee Kim

History:
John was referred by his PCP. He is a bit overweight and was diagnosed with diabetes 5 years ago. He told me he did have instances of fire smoke exposure while working as a firefighter, without respiratory protection. He has been on a dual-inhaled therapy for the past 5 years. John was referred because his symptoms—mostly shortness of breath with exertion, wheezing and cough—were getting worse, though with no exacerbations. He has been using his rescue inhaler 2 to 3 times daily.

Pulmonary function testing revealed a CAT score of 15, an FEV1 of 50%, which increased to 55% with bronchodilator, and FEV1/FVC of 0.65. His chest X-ray showed hyper-inflammation—trapped air in the lungs.

John qualified for triple therapy because his ongoing symptoms were not responsive to current treatment. We checked with his insurance, and he was approved to go from a dual-inhaled therapy to triple therapy. He was not interested in pulmonary rehabilitation, the reason being he is still fairly active even though his lung function was suboptimal.

We also discussed addressing his weight. I recommended he try to include more exercise. And because he has diabetes, he needs to pay attention to his diet; we discussed that he may need referral to a dietitian.

Initiating treatment:
John was started on triple therapy in a single inhaler, used twice daily. His dual-inhaled therapy was stopped. Our respiratory therapist also used training devices to demonstrate to him the proper technique and steps used to correctly administer this medication.

> "John qualified for triple therapy because his ongoing symptoms were not responsive to current treatment."

John was seen at follow-up 3 months later. At this visit, his pulmonary function test was repeated. His FEV1 was now 60%, with no change after an inhaled bronchodilator, and his FEV1/FVC was 0.67. His CAT improved to 10. John relates that he feels his symptoms have improved; he is now able to climb a flight of stairs without having to stop and he no longer reports cough.

He also notes that he has decreased his need for the rescue inhaler to just 1 to 2 times a week. When asked to demonstrate the correct use of his inhaler, he was able to complete all of the steps without error.

Considerations:
John had a couple of interesting challenges. He had occupational exposure, which sometimes can make this diagnosis a little more challenging. He also had the comorbidity diabetes, and that can complicate things, specifically because oral steroids can make diabetes worse. Both of those factors make triple therapy an excellent treatment option for patients like John.

Q&A

Expert insight on COPD management

Signs of worsening disease

Q: Do patients have trouble recognizing when their COPD is getting worse? How do you educate them about this?

A: This is interesting because the answer is yes and no. For the most part, once a person knows they have COPD, they tend to be fairly in tune to their symptoms. The cardinal symptom is shortness of breath, and this is challenging for patients. All of us get short of breath at times. If I climb three or four flights of stairs, I will be huffing and puffing at the top. That's normal. With COPD, this happens at low levels of exertion and people have trouble getting air in. Also, as we age, respiratory symptoms increase, and patients may wrongly attribute worse symptoms to getting older or being out of shape.

Another challenge is cough. Coughing is not normal. Sometimes they tend to call it a smoker's cough, but that is still not normal. A chronic, productive cough is never normal, especially if you stopped smoking long ago. Education becomes important once they are diagnosed. The undiagnosed person is the biggest challenge. The COPD Foundation tries to educate people about what is normal aging and what is abnormal aging. If a person is coughing, if they can't keep up with people of their own age because of breathing problems, that's not normal, and it's time to investigate what could be the cause.

–David Mannino, MD, FCCP, FERS,
Medical Director and Co-Founder of the COPD Foundation

Treating exacerbations

Q: How should worsening symptoms be managed?

A: One of the key changes in the GOLD Report is the use of triple therapy in the management of exacerbations. GOLD is now advocating for treatment with triple therapy (LABA/LAMA/ICS) because there are recent trial data showing a mortality benefit for symptomatic patients with COPD. Previously, the guidelines focused on dual therapy with LABA/LAMA, or each one given individually. Based on claims data, the revised guidelines also recommend initiation of a pulmonary rehab program within 4 weeks of a hospitalization for an exacerbation, rather than the 90 days that was recommended previously. There is also new information on the pros and cons of specific inhalation devices and what clinicians should consider when prescribing these different therapies.

–Isaretta Lee Riley, MD, *Assistant Professor, Pulmonary, Allergy and Critical Care Medicine, Duke School of Medicine*

Psychosocial challenges

Q: What are common challenges of living with COPD?

A: I will highlight three of them. First, a lot of COPD patients live with shame, blame or guilt. Society plays a part in that. The thinking is, *I did this to myself. It's my fault.* You don't have the same judgment in other diseases. So, identifying that and calling it out—yes, you made some unfortunate decisions in your life, such as smoking, but this is a disease process, and it can be dealt with.

The second is isolation. COPD patients tend to be limited in their activity and subsequently tend to be more isolated. One benefit of pulmonary rehab is that they see other people like them. Some patients may be self-conscious about needing oxygen, and a great answer is, "We all need oxygen to live. I just need a little more than you do."

The third challenge: They tend to have multimorbidities, including depression and anxiety. Having difficulty catching your breath makes you anxious. In addition, social isolation and loneliness can cause depression. The first step is to identify those and encourage patients to talk about their struggles with other like-minded folks. One way to do that is through the COPD Foundation's social network, COPD 360, which is a community of more than 55,000 members (*copdfoundation.org*). The patient can go online and find educational resources, and they'll also see me weighing in on medical questions. Most important, it's a judgment-free zone. It's not the patient's fault if they aren't able to quit smoking—that's the nature of addiction.

–David Mannino, MD, FCCP, FERS

Patient engagement

Q: How do you counsel patients on self-management?

A: We review the American Lung Association's COPD Action Plan with each patient so they can better understand their symptoms and which ones require action on their part, such as shortness of breath, increased coughing or sputum production or greater use of their rescue inhalers. Also, we make sure they know their medications—which ones they should be taking every day and which ones they can take as needed—and how to use their inhalers properly.

It's also important to ask patients open-ended questions. One I always ask is, "How do you use your device?" This opens up an opportunity to correct them or congratulate them. I also talk about smoking cessation and whether they need help with quitting.

–Isaretta Lee Riley, MD

SPECIAL THANKS TO OUR MEDICAL REVIEWER:
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Health Monitor

Clinician Update

EXAM TOOL

Assessing severity of COPD symptoms

Updates in the 2024 Global Initiative for Chronic Obstructive Lung Disease (GOLD) Report reflect the latest evidence-based strategies for proactively managing COPD at all levels of disease severity. One feature to note: a treatment algorithm that highlights escalating therapy after a moderate-to-severe exacerbation or hospitalization to help prevent future episodes. Other things to weigh include a change in how patients feel or their level of activity. When assessing worsening symptoms—which may require more aggressive therapy—consider the following criteria.

DYSPNEA *(based on mMRC Dyspnea Scale)*

Ask patients which of the following best describes them:

Mild

- ☐ I only get breathless with strenuous exercise.

Moderate

- ☐ I get short of breath when hurrying on level ground or walking up a slight hill.

Moderate-to-severe

- ☐ I walk slower than people of my same age because of breathlessness.
- ☐ I have to stop for breath when walking at my own pace on level ground.
- ☐ I can't do my usual exercise routine, or I don't do it as often, because I get breathless.

Severe

- ☐ I stop for breath after walking a few yards, or a few minutes, on level ground.
- ☐ I get breathless walking to or back from the mailbox.

Most severe

- ☐ I am too breathless to leave the house.
- ☐ I am breathless when dressing or undressing.

OTHER SIGNS *(based on COPD Assessment Test)*

Ask patients to rate the following based on a scale of 0 (not a problem) to 5 (a major problem):

- ☐ **Cough**
  0 1 2 3 4 5
- ☐ **Mucus in chest**
  0 1 2 3 4 5
- ☐ **Chest tightness**
  0 1 2 3 4 5
- ☐ **Limited in doing activities at home**
  0 1 2 3 4 5
- ☐ **Not confident leaving home because of lung problems**
  0 1 2 3 4 5
- ☐ **Poor sleep**
  0 1 2 3 4 5
- ☐ **Little or no energy for everyday activities**
  0 1 2 3 4 5

Source: Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global Strategy for Prevention, Diagnosis and Management of COPD: 2024 Report. For complete information, visit *goldcopd.org*.