Chronic Obstructive Pulmonary Disease (COPD) Agents

Executive Summary:

- Agent/inhaler device selection within each class should be individualized. Choice is guided by symptom severity, exacerbation risk, side effects, comorbidities, drug availability and cost/insurance coverage, as well as patient's response, preference and ability to use various delivery devices.
- All patients should be offered a short-acting bronchodilator (beta-2 agonist, antimuscarinic or combination) to use as needed for immediate symptom relief. Combination SABA+SAMA products are superior to either medication along in improving FEV_1 and symptoms.
- Long-acting muscarinic antagonist (LAMA) is the preferred drug class in patients with moderate to very severe COPD. Clinical trials have shown a greater reduction in exacerbations and hospitalizations for LAMAs (tiotropium) versus long-acting beta agonists (LABAs).
- LAMA and LABA combination devices have significantly greater improvement in lung function compared to LAMA or LABA monotherapy
- Patients with blood eosinophil counts > 300 cells/ mcL will obtain the greatest benefit from inhaled corticosteroids (ICS) therapy. ICS containing regimens are not beneficial in patients with blood eosinophil counts < 100 cells/mcL.

COMMONLY USED MAINTENANCE MEDICATIONS IN COPD

Beta2-agonists

- **SABAs Effect:** Short-acting beta2-agonists (SABAs) have an effect that lasts about 4 to 6 hours.
- **LABAs Effect:** Long-acting beta2-agonists (LABAs) last about 12 or more hours.
- Beta2-agonists haven't shown a mortality benefit, but do significantly improve forced expiratory volume in the first second (FEV1) and symptoms.
- **Cardiovascular Notes:** Over stimulation of beta2-adrenergic receptors can produce resting sinus tachycardia and tremors and has the potential to precipitate cardiac rhythm disturbances in susceptible patients. Hypokalemia can occur, especially in combination with thiazide diuretics. Moreover, tachyphylaxis is possible in patients with congestive heart failure (CHF) when oxygen consumption is increased under resting conditions with overuse.

Antimuscarinics

- **Ipratropium** → A systematic review of randomized controlled trials concluded that ipratropium, a short-acting muscarinic antagonist (SAMA), alone provided small benefits over SABAs in terms of lung function, health status, and requirement for oral steroids.
- **LAMA Treatment** → Long-acting antimuscarinic antagonists (LAMAs) treatments improve symptoms and health status. They also improve efficacy of pulmonary rehabilitation and reduce exacerbations and related hospitalizations. Clinical trials have shown a greater effect on exacerbation rates for LAMA treatment versus LABA treatment.
  - LAMA is the *preferred* drug class in patients with moderate to very severe COPD. Clinical trials have shown a greater reduction in exacerbations and hospitalizations for LAMAs (tiotropium) versus LABAs.
  - **Side Effects:** The main side effect is *dryness of mouth*, although some patients using ipratropium report a bitter, metallic taste. Use of solutions with a facemask can precipitate acute glaucoma, likely a direct result of contact between the solution and the eye.

Combination Bronchodilators

- Combining bronchodilators with different mechanisms and durations of action may increase the degree of bronchodilation with lower risk of side effects compared to increasing the dose of a single bronchodilator.
- SABA/SAMA combination products are superior to either medication alone in improving FEV1 and symptoms.
- There are numerous combinations of LAMA and LABA in a single delivery device available which have significantly greater improvement in lung function compared to LAMA or LABA monotherapy.
- **Dosing:** A lower-dose and twice-daily LAMA/LABA regimen has been shown to improve symptoms and health status in COPD patients compared to monotherapy.
- **Combination vs. Monotherapy:** combination of LAMA/LABA or LAMA/ICS products have a greater effect on symptoms, exacerbations and health status compared to their individual components as monotherapy.
  - **LAMA+LABA Combo Therapy** is recommended for severe COPD in patients who are highly symptomatic. Studies involving patient-related outcomes suggest improved response compared to single agents.
  - **LABA+ICS Combo Therapy** should be reserved for select patients who may benefit due to higher risk of pneumonia and side effects. Patients with asthma or blood eosinophils > 300 cells/microliter may benefit from ICS.

Inhaled Corticosteroids (ICS)

- In vitro evidence suggests that COPD-associated inflammation has limited responsiveness to corticosteroids. The clinical relevance of this effect has not been established.
- **ICS Alone** → Regular treatment with ICS alone does not modify the long-term decline of FEV1 nor mortality in patients with COPD.
- **ICS + LABA Combination** → In patients with moderate to severe COPD and exacerbations, a combination of ICS/LABA product is more effective than either component alone in improving lung function, health status and reducing exacerbations. ICS/LABA fixed dose combination therapy has shown better reduction in exacerbation rates over LABA alone.
- **Blood Eosinophil Count** → Several studies have shown that blood eosinophil counts predict the magnitude of effect of ICS therapy in preventing exacerbations. Almost no effect is observed at low blood eosinophil counts, while incrementally increasing effect is observed with higher eosinophil counts.
  - ICS-containing regimens are not beneficial in patients with blood eosinophil counts < 100 cells/mcL.
  - Patients with blood eosinophil counts > 300 cells/mcL will obtain the greatest benefit from ICS therapy. The use of blood eosinophil count to predict ICS effect should always be combined with clinical assessment of exacerbation risk.
- **Adverse Effects** → ICS use is associated with higher prevalence of oral candidiasis, hoarse voice, skin bruising and pneumonia.

Triple Therapy

- **Fixed-dose Triple vs. LAMA/LABA Combination** → Fixed-dose triple inhaled therapy has been shown to have a mortality benefit versus fixed-dose LAMA/LABA combinations in patients with symptomatic COPD with a history of frequent and/or severe exacerbations.

Phosphodiesterase-4 Inhibitors

- Reduce inflammation by inhibiting the breakdown of intracellular cyclic AMP.
- **Roflumilst Benefits** → Roflumilast (e.g. Daliresp®) reduces moderate and severe exacerbations treated with systemic corticosteroids in patients with chronic bronchitis, severe to very severe COPD and a history of exacerbations. The benefits of roflumilast have been reported to be greater in patients with a prior history of hospitalization for an acute exacerbation.
- **Adverse Effects** → More adverse effects than inhaled medications for COPD, including diarrhea, nausea, reduced appetite, weight loss, abdominal pain, sleep disturbances, and headache. Adverse effects tend to occur early in therapy and diminish over time with continued treatment. Roflumilast should also be used with caution in patients with depression as it can increase anxiety, thoughts of suicide and emotional instability.

Antibiotics

Antibiotics & Exacerbation Rates → Recent studies have shown regular use of certain antibiotics may reduce exacerbation rates.

- **Azithromycin, Erythromycin**
  - Azithromycin (250 mg/day or 500 mg 3x/week) and erythromycin (250 mg 2x/day) for one year in patients prone to exacerbations reduced the risk of exacerbations compared to usual care.
  - Azithromycin use was associated with higher rates of bacterial resistance, QTc interval prolongation, and impaired hearing tests. There is no data showing the efficacy of prolonging azithromycin use beyond one year in preventing COPD exacerbations.

Methylxanthines

- **Methylxanthines** → May act as non-selective phosphodiesterase inhibitors, however, they also have an extensive range of non-bronchodilator actions.
- Theophylline is metabolized by the cytochrome P-450 pathway and clearance declines with age. There is evidence of a modest bronchodilator effect compared to placebo in stable COPD. Addition of theophylline to salmeterol produces a greater improvement in FEV1 and less shortness of breath than salmeterol alone.
- **Adverse Effects** → Events include development of arrhythmias, palpitations, and seizures. More minor side effects include headaches, insomnia, nausea, and heartburn. These medications also have a wide variety of drug-drug interactions.

References:

1. 2021 GOLD Reports. Global Initiative for Chronic Obstructive Lung Disease - GOLD. . Accessed February 23, 2022.

Common Inhalers for COPD Management

Generic Name	Brand Name	Generic Available?	Inhaler Type	Typical Dosing
Beta2-Agonists (Bronchodilators)				
Short-acting (SABA)				
Levalbuterol	Xopenex HFA®	Yes	MDI	1-2 puffs q4-6h PRN
Albuterol	Proair® HFA, Proair RespiClick®, Proventil® HFA, Ventolin® HFA	Yes	MDI, DPI	1-2 puffs q4-6h PRN
Long-acting (LABA)				
Salmeterol xinafoate	Serevent®	No	DPI	1 inhalation BID
Formoterol	Foradil Aerolizer®	Yes (nebs only)	DPI, Neb	1 inhalation/neb BID
Arformoterol	Brovana®	No	Neb	1 inhalation/neb BID
Olodaterol	Striverdi Respimat®	No	SMI	1 inhalation daily
Anticholinergics (Bronchodilators)				
Short-acting (SAMA)				
Ipratropium	Atrovent® HFA	No	MDI	2 inhalations 4XD
Long-acting (LAMA)				
Tiotropium	Spiriva® HandiHaler® Spiriva® Respimat®	No	DPI Slow-moving mist	Inhale 1 capsule BID 2 inhalations daily
Umeclidinium	Incruse® Ellipta®	No	DPI	1 inhalation daily
Aclidinium bromide	Tudorza Genuair	No	DPI	1 inhalation BID
Revefenacin	Yupelri®	No	Neb	1 nebulization daily
Combination Products				
SABA+SAMA				
Ipratropium/albuterol	Combivent® Respimat®	Yes (nebs only)	Slow-moving mist	1 inhalation 4XD
LAMA+LABA				
Umeclidinium/Vilanterol	Anoro® Ellipta®	No	DPI	1 inhalation daily
Olodaterol/Tiotropium	Stiolto Respimat®	No	SMI	1 inhalation daily
Formoterol/Glycopyrronium	Bevespi Aerosphere®	No	MDI	1 inhalation BID
Formoterol/Aclidiunium	Duaklir Pressair®	No	DPI	1 inhalation BID
ICS+LABA				
Budesonide/Formoterol	Symbicort®	Yes	MDI	2 inhalations BID
Fluticasone/Salmeterol	Advair®, AirDuo®, Wixela™ Inhub™	Yes	DPI	1 inhalation BID
Fluticasone/Vilanterol	Breo™ Ellipta™	No	DPI	1 inhalation daily
Formoterol/Mometasone	Dulera®	No	MDI	2 inhalations BID
ICS+LAMA+LABA				
Fluticasone/Umeclidinium/ Vilanterol	Trelegy™ Ellipta®	No	DPI	1 inhalation daily
Budesonide/Formoterol/ Glycopyrrolate	Breztri Aerosphere®	No	MDI	2 inhalations BID

Uncontrolled Chronic Obstructive Pulmonary Disease (COPD)

Executive Summary:
The initiation of chronic obstructive pulmonary disease **(**COPD) therapy is determined by the patients' individualized symptoms, exacerbation risk and the use of an assessment tool such as the mMRC dyspnea scale or CAT assessment. Follow-up therapy is determined by persistent dyspnea and/or further exacerbations, and the patient's current COPD treatment.

Initial Therapy for COPD

	☐ mMRC 0 to 1 **OR** ☐ CAT < 10 (less symptomatic)	☐ mMRC ≥ 2 **OR** ☐ CAT ≥ 10 (more symptomatic)
▪ **1 or less** moderate exacerbations per year	**Group A** Patient should be initiated on either a: ▪ Short-acting bronchodilator **OR** ▪ Long-acting bronchodilator	**Group B** Patients should be initiated on a ▪ Long-acting bronchodilator (LABA or LAMA) as they are more effective than short-acting bronchodilators
▪ **2 or more** moderate exacerbations **OR** ▪ **1 or more** exacerbations leading to hospitalization per year	**Group C** Patients should be initiated on a: ▪ LAMA as they are superior to LABAs in preventing exacerbations	**Group D** Patients should be initiated on a ▪ LAMA, ▪ LAMA/LABA *(LAMA/LABA combinations are superior to decreasing symptoms than either alone)* **OR** ▪ LABA/ICS *(LABA/ICS combinations have the greatest likelihood at reducing exacerbations)*

mMRC Dyspnea Questionnaire

Grade	Description of Breathlessness
0	I only get breathless with strenuous exercise
1	I get short of breath when hurrying on level ground or walking up a slight hill
2	On level ground, I walk slower than people of the same age because of breathlessness or have to stop for breath when walking at my own pace
3	I stop for breath after walking about 100 yards or after a few minutes on level ground
4	I am too breathless to leave the house or I am breathless while dressing

★**TIP:** COPD Assessment Test (CAT) can be found on the Guidelines and Algorithms KnowledgeNet page under "Pharmacy Pearls"

When to Start an Inhaled Corticosteroids (ICS):

Strong Support to Use if:	• The patient has a history of hospitalizations for exacerbations, or • 2 or more moderate exacerbations per year despite long-acting bronchodilator therapy, eos > 300 cells/mcL or • A history of asthma
Consider Use if:	• One moderate exacerbation per year despite long-acting bronchodilator therapy or • eos between 100 and 300 cells/mcL
Do Not Use if:	• The patient has repeated pneumonia events, eos < 100 cells/mcL or • A history of mycobacterial infection

Abbreviation Key	
CAT	COPD Assessment Test
COPD	Chronic Obstructive Lung Disease
eos	Blood Eosinophil Count in Cells per Microliter (mcL or µL)
ICS	Inhaled Corticosteroids
LABA	Long-Acting Beta Agonist
LAMA	Long-Acting Antimuscarinic
mMRC	Modified Medical Research Council Dyspnea Questionnaire
SABA	Short-Acting Beta Agonist
SAMA	Short-Acting Antimuscarinic

Follow-up Management:

When following up on a patient's COPD medications, the review, assess and adjust method should be utilized. Review the patient's dyspnea symptoms and exacerbation risk. Assess the patient's inhaler technique, adherence and non-pharmacological approaches. Adjust pharmacological treatment accordingly. If dyspnea or exacerbation risk is identified, consider the following adjustments.

Dyspnea

For patients with persistent breathlessness or exercise limitation on:

- A single long-acting bronchodilator, should be initiated on a LAMA/LABA combination product
- A LABA/ICS, should be initiated on a LABA/LAMA/ICS triple therapy product
  - Switching from a LABA/ICS to a LAMA/LABA could be considered if ICS is not indicated
- A LABA/LAMA/ICS, should consider switching inhaler device or formulation and investigate other causes for dyspnea

Exacerbations

For patients who develop further exacerbations with or without dyspnea on:

- A single long-acting bronchodilator, should be initiated on either a LABA/LAMA or LABA/ICS
  - LABA/ICS may be preferred in patients with a history of asthma or with frequent exacerbations as ICS has a greater effect in patients with more frequent or severe exacerbations
- A LABA/LAMA, should escalate therapy based on the patient's eos
  - > 100 cells/mcl – Initiate a LABA/LAMA/ICS triple therapy product
  - < 100 cells/mcl – Consider adding roflumilast or azithromycin
- A LABA/ICS, should be initiated on a LABA/LAMA/ICS triple therapy product
  - Switching from a LABA/ICS to a LAMA/LABA could be considered if ICS is not indicated
- A LABA/LAMA/ICS, should consider adding one of the following:
  - Roflumilast – may consider for patients with a FEV1 < 50% predicted and chronic bronchitis
  - Macrolide – azithromycin or erythromycin in patients that are not current smokers (consider local antimicrobial resistance)
  - Stopping ICS – may consider for patients experiencing adverse effects of the ICS including frequent pneumonia infections. Patients with an eos > 300 have the greatest likelihood of experiencing withdrawal and relapse exacerbations

References

- Global Initiative for Chronic Obstructive Lung Disease (GOLD). *Global Strategy for Prevention, Diagnosis, and Management of COPD*. 2020. Retrieved from https://goldcopd.org/wp-content/uploads/2019/12/GOLD-2020-FINAL-ver1.2-03Dec19_WMV.pdf
- https://www.uptodate.com/contents/stable-copd-initial-pharmacologic-management?search=copd%20treatment&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1

Common Inhalers for COPD Management

Generic Name	Brand Name	Generic Available?	Inhaler Type	Typical Dosing
Beta2-Agonists (Bronchodilators)				
Short-acting (SABA)				
Levalbuterol	Xopenex HFA®	Yes	MDI	1-2 puffs q4-6h PRN
Albuterol	Proair® HFA, Proair RespiClick®, Proventil® HFA, Ventolin® HFA	Yes	MDI, DPI	1-2 puffs q4-6h PRN
Long-acting (LABA)				
Salmeterol xinafoate	Serevent®	No	DPI	1 inhalation BID
Formoterol	Foradil Aerolizer®	Yes (nebs only)	DPI, Neb	1 inhalation/neb BID
Arformoterol	Brovana®	No	Neb	1 inhalation/neb BID
Olodaterol	Striverdi Respimat®	No	SMI	1 inhalation daily
Anticholinergics (Bronchodilators)				
Short-acting (SAMA)				
Ipratropium	Atrovent® HFA	No	MDI	2 inhalations 4XD
Long-acting (LAMA)				
Tiotropium	Spiriva® HandiHaler® Spiriva® Respimat®	No	DPI Slow-moving mist	Inhale 1 capsule BID 2 inhalations daily
Umeclidinium	Incruse® Ellipta®	No	DPI	1 inhalation daily
Aclidinium bromide	Tudorza Genuair	No	DPI	1 inhalation BID
Revefenacin	Yupelri®	No	Neb	1 nebulization daily
Combination Products				
SABA+SAMA				
Ipratropium/albuterol	Combivent® Respimat®	Yes (nebs only)	Slow-moving mist	1 inhalation 4XD
LAMA+LABA				
Umeclidinium/Vilanterol	Anoro® Ellipta®	No	DPI	1 inhalation daily
Olodaterol/Tiotropium	Stiolto Respimat®	No	SMI	1 inhalation daily
Formoterol/Glycopyrronium	Bevespi Aerosphere®	No	MDI	1 inhalation BID
Formoterol/Aclidiunium	Duaklir Pressair®	No	DPI	1 inhalation BID
ICS+LABA				
Budesonide/Formoterol	Symbicort®	Yes	MDI	2 inhalations BID
Fluticasone/Salmeterol	Advair®, AirDuo®, Wixela™ Inhub™	Yes	DPI	1 inhalation BID
Fluticasone/Vilanterol	Breo™ Ellipta™	No	DPI	1 inhalation daily
Formoterol/Mometasone	Dulera®	No	MDI	2 inhalations BID
ICS+LAMA+LABA				
Fluticasone/Umeclidinium/ Vilanterol	Trelegy™ Ellipta®	No	DPI	1 inhalation daily
Budesonide/Formoterol/ Glycopyrrolate	Breztri Aerosphere®	No	MDI	2 inhalations BID

Smoking Cessation

Executive Summary:

In the U.S., smoking is the leading cause of preventable death, resulting in over 480,000 deaths annually.[1] Roughly 90% of all lung cancer deaths were caused by smoking. Esophagus, larynx, trachea, stomach, bladder and numerous other cancers can develop with smoking. According to the Centers for Disease Prevention and Control (CDC), one of every three cancer deaths would be prevented if no one smoked. Additionally, patients are at an increased risk of developing coronary heart disease and strokes.

The table below depicts the five 'As' and the five 'Rs' to use at every patient visit[2] and includes a few leading questions to prompt discussion during visits.

To Assess Willingness:	To Enhance Motivation:
Ask: Are you a smoker? How many cigarettes per day? How soon after waking up?	**Relevance:** How would quitting benefit you?
Advise: Educate on risks of smoking and benefits of quitting.	**Risks:** What are the dangers of tobacco use?
Assess: How willing are you to quit?	**Rewards:** How would quitting benefit you?
Assist: If ready to quit: set a date and determine therapy. If not ready to quit: use the five Rs!	**Roadblocks:** What is preventing you from quitting?
Arrange: Follow up visit/phone call one week after quit date.	**Repetition:** Keep motivating patients to quit at every visit!

Abbreviation Key	
BID	An abbreviation meaning "two times a day". Commonly used in drug dosing instructions.
CAT	COPD Assessment Test
COPD	Chronic Obstructive Lung Disease
eos	Blood Eosinophil Count in Cells per Microliter (mcL or µL)
QAM	quadrature amplitude modulation
ICS	Inhaled Corticosteroids
LABA	Long Acting Beta Agonist
LAMA	Long Acting Antimuscarinic
mMRC	Modified Medical Research Council Dyspnea Questionnaire
SABA	Short Acting Beta Agonist
SAMA	Short Acting Antimuscarinic

Here are a few key points related to outcomes when using the five 'As' and the five 'Rs':

- Evidence shows higher odds of smoking cessation when providers go beyond ask, advise and assess. Even when patients are not interested, or are hesitant, to quit it's important to discuss quitting options, their effectiveness and plan a follow-up. Doing so can increase the odds of patients quitting by 40%.[3]
- Repetition is key! Evidence shows the more often providers utilize the five 'As' and the five 'Rs' the more likely patients are to quit smoking.
- There is clear evidence that medications and/or nicotine replacement therapy (NRT) roughly doubles likelihood of smoking cessation (25 to 33% vs. 14%), yet approximately 60% of people still try to quit cold turkey.[4]

The information below discusses the treatment options available for smoking cessation. Discuss therapy options, including advantages and disadvantages, with each patient to create a treatment plan.

Nicotine Replacement Therapy (NRT) Options Available[5]:

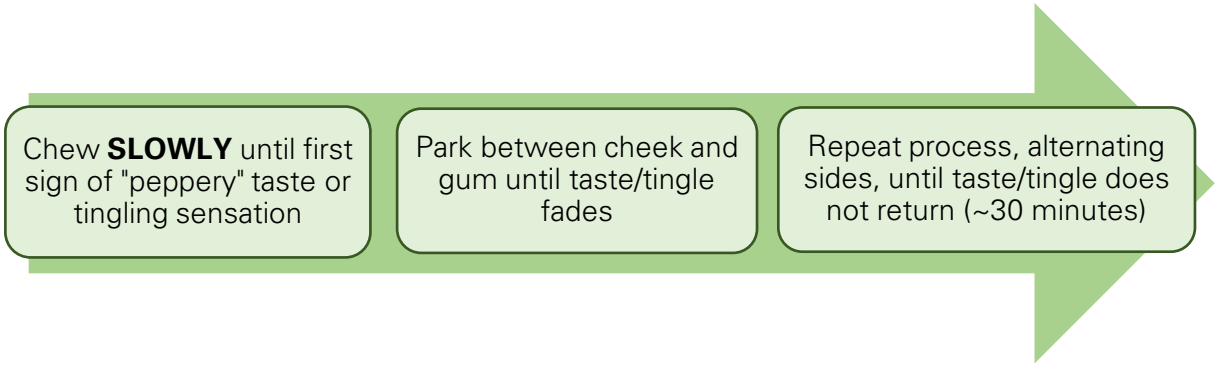
Nicotine Replacement Therapy		
	Dosing	**Schedule**
Gum	2 mg – 30 minutes **after** waking 4 mg – **within** 30 minutes of waking	Weeks 1-6: 1 piece Q1-2hrs* Weeks 7-9: 1 piece Q2-4hrs Weeks 10-12: 1 piece Q4-8hrs
Lozenge	2 mg – 30 minutes **after** waking 4 mg – **within** 30 minutes of waking	Weeks 1-6: 1 piece Q1-2hrs** Weeks 7-9: 1 piece Q2-4hrs Weeks 10-12: 1 piece Q4-8hrs
Patch	14 mg – ≤ 10 cigarettes/day	Weeks 1-6: 14 mg Weeks 7-8: 7 mg
	21 mg – >10 cigarettes/day	Weeks 1-6: 21 mg Weeks 7-8: 14 mg Weeks 9-10: 7 mg

* Recommended to use at least 9 pieces/day to start but do not exceed 24 pieces/day
** Recommended to use at least 9 pieces/day to start but do not exceed 20 pieces/day

NRT GUM

Nicotine replacement therapy (NRT) gum and lozenges are available over-the-counter at most pharmacy locations. While these options requires frequent dosing, both are easily titratable, which allows for more patient-specific management of breakthrough cravings. Additionally, both NRT gum and lozenges cab delay weight gain associated with smoking cessation.

Lightheadedness, nausea, vomiting, mouth or throat irritation and indigestion can occur with gum use but is mostly well tolerated. Nausea, hiccups, heartburn, flatulence and cough can occur with lozenge use and may be less well tolerated than with nicotine replacement therapy gum. For proper gum administration, patients must use the "chew and park method" which can be easily explained using the graphic below:



If gum is chewed too quickly or swallowed, the patient is at an increased risk of side effects due to excessive nicotine release. For proper lozenge administration, patients must place lozenge between the cheek and gum, rotating occasionally, until completely dissolved. Lozenges should not be chewed or swallowed as there is an increased risk of side effects due to excessive nicotine release. Additionally, counsel patient to avoid eating or drinking for 15 minutes before and during NRT gum and lozenge use.

NRT PATCHES

NRT patches are available over-the-counter at most pharmacy locations. This is a once daily patch that should be applied to clean, dry, hairless skin on the upper body or outer arm. Patches should be applied to a new location daily with no duplication for at least one week.

Skin irritation is the most common adverse effect, so it's not recommended for patients with dermatologic conditions including psoriasis, eczema and atopic dermatitis. Vivid dreams and insomnia were also reported, thus the patch can be removed at bedtime if needed.

Oral Prescription Medications Available:

	Bupropion SR	Varenicline
Dose	150 mg QAM for 3 days then 150 mg BID for 7-12 weeks *Start 1-2 weeks before quit date*	0.5 mg daily for 3 days, then 0.5 mg BID for 4 days, then 1 mg BID for up to 12 weeks *Start 1 week before quit date*
Adverse Effects	Insomnia, dry mouth, rash Serious: neuropsychiatric symptoms, suicide risk, seizures	Insomnia, abnormal dreams, nausea Serious: neuropsychiatric symptoms, suicide risk*
Contraindications	Known seizure disorder, bulimia or anorexia diagnosis, currently tapering or discontinuing alcohol/benzo/barb/antiepileptic	-
Notes		Varenicline, brand name Chantix, is also available generically now.
**The Black Box Warning was removed by the FDA in 2016 following the EAGLES trial.*[6]		

Medication Effectiveness and Outcomes:

- In clinical trials, each NRT agent had similar efficacy rates, thus choice of therapy should be made based on patient preference. A combination of patches with gum and/or lozenges for acute cravings is more efficacious than NRT alone.
- Bupropion short-release (SR) has similar efficacy rates to NRT. A combination of bupropion SR and NRT patch is more efficacious than either bupropion or NRT alone.
- Studies show that Varenicline may be more efficacious than single NRT or bupropion sustained-release (SR) use. Combining with bupropion SR was studied and significantly improves cessation rates at 12 and 26 weeks, but not 52 weeks. While there is a lack of proven benefit of combination with NRT agents, it's normally well tolerated.

E-cigarettes[7]:

At this time, e-cigarette use is not an FDA approved smoking cessation aid. Some research may suggest improved smoking cessation with e-cigarettes containing nicotine than e-cigarettes without nicotine but is otherwise uncertain. E-cigarettes are not regulated, so it's unknown how much nicotine patients would be receiving. Therefore, it's recommended to use the FDA approved smoking cessation aids listed above before considering e-cigarette use.

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Asthma-COPD Overlap

Executive Summary:
Asthma-COPD overlap is a general term for patients who display features of both asthma and chronic obstructive pulmonary disease (COPD); however, asthma-COPD Overlap does not refer to a single disease entity. While both asthma and COPD are airflow obstruction diseases, asthma-COPD overlap are patients with persistent airflow limitation with clinical features that are consistent with both asthma and COPD.

Patients who do not fall neatly into diagnostic category of asthma or COPD, or have several clinical phenotypes that are indicative of COPD or asthma, may be diagnosed with asthma-COPD overlap. This condition is also known as 'Asthma-COPD Overlap Syndrome', 'Asthma+COPD' or 'Adults with features of asthma, COPD or both'.

While little is known about asthma-COPD overlap, most patients with features of both asthma and COPD have more symptoms, more frequent exacerbations, poorer quality of life, more rapid lung function decline, higher mortality and require more health care resources compared to a single diagnosis of asthma or COPD. Concurrent asthma and COPD diagnosis represent 15% to 32% of patients with a previous diagnosis of the asthma or COPD.

Diagnosis begins with a history and clinical assessment discussing the patient's respiratory symptoms, history of asthma diagnosis – during childhood or later in life – and previous exposure to smoking or other COPD risk factors.

Spirometry should be conducted to confirm persistent expiratory airflow limitation and variable expiratory airflow limitation. Based on the clinical phenotype, the patient should then be classified as 'highly likely asthma', 'features of both asthma + COPD', or 'likely COPD'. Treatment recommendations are listed in the table below.

Abbreviation Key	
CAT	COPD Assessment Test
COPD	Chronic Obstructive Lung Disease
eos	Blood Eosinophil Count in Cells per Microliter (mcL or µL)
ICS	Inhaled Corticosteroids
LABA	Long Acting Beta Agonist
LAMA	Long Acting Antimuscarinic
mMRC	Modified Medical Research Council Dyspnea Questionnaire
PRN	PRN prescription stands for 'pro re nata,' which means that the administration of medication is not scheduled. Instead, the prescription is taken as needed.
SABA	Short Acting Beta Agonist
SAMA	Short Acting Antimuscarinic

Clinical Phenotype Assessment

Highly Likely Asthma	Features of Both Asthma + COPD	Likely COPD
↓	↓	↓
Treat as Asthma	Treat as Asthma	Treat as COPD
Initial Pharmacologic Treatment		
• Inhaled Corticosteroid • PRN ICS+formoterol • DO NOT GIVE LABA and/or LAMA without ICS • Avoid maintenance oral corticosteroid	• Inhaled Corticosteroid • Add-on LABA and/or LAMA usually also needed • Additional COPD treatments per GOLD guidelines • DO NOT GIVE LABA and/or LAMA without ICS • Avoid maintenance oral corticosteroid	• Treat as COPD • Initially LAMA and/or LABA • Add ICS per GOLD guidelines • Avoid high dose ICS • Avoid maintenance oral corticosteroids • Reliever containing ICS is not recommended.
Review patient after 2 to 3 months. Refer for expert advice if diagnostic uncertainty or inadequate response.		

**GOLD: Global Initiative for Obstructive Lung Disease; ICS: inhaled corticosteroid; LABA: long acting beta-2 agonist; LAMA: long acting muscarinic antagonist*

Asthma Pharmacy Pearls

- Asthma Guideline Updates: 2020 NHLBI Focused Update and 2020 GINA
- Overview of Available Agents for Asthma Treatment
- Asthma – Checklist Prior to Initiating Biologics
- Outpatient Treatment of Asthma Exacerbations in Adults

Understanding the patient's clinic phenotype of asthma-COPD overlap is crucial to creating a treatment plan for the patient. It's important to note the risks associated with mismatched drug to clinical phenotype. For example, initial treatment for COPD calls for LAMA and/or LABA; however, LAMA or LABA mono- or combination therapy for asthma is contraindicated due to the risk of severe exacerbations or death. Another example is patients with concurrent asthma and COPD diagnosis being treated with LABA monotherapy have a higher risk of hospitalization and death compared to those treated with an ICS-LABA.

In all patients diagnosed with airflow obstruction diseases, recommend non-pharmacologic interventions including smoking cessation, regular physical activity, eating a healthy diet, avoidance of occupational exposures and avoiding allergens that may trigger an exacerbation. All patients should also remain up to date on influenza, pneumococcal and COVID-19 vaccinations.

Asthma-COPD overlap is a poorly-understood disease state, and is diagnosed primarily from the clinical phenotype. In recent research, patients with concurrent asthma and COPD were typically excluded from randomized controlled trials. The recommendations continually change for asthma-COPD overlap as new data comes available.

Further research is needed to identify additional clinical and physiologic characteristics, biomarkers, underlying mechanisms and outcomes to better guide interventions and pharmacotherapy for asthma-COPD overlap.

References:

Global Initiative for Asthma (GINA). Diagnosis and initial treatment of adults with features of asthma, COPD, or both ('asthma-COPD overlap'). 2021. Retrieved from https://ginasthma.org/wp-content/uploads/2021/05/GINA-Main-Report-2021-V2-WMS.pdf