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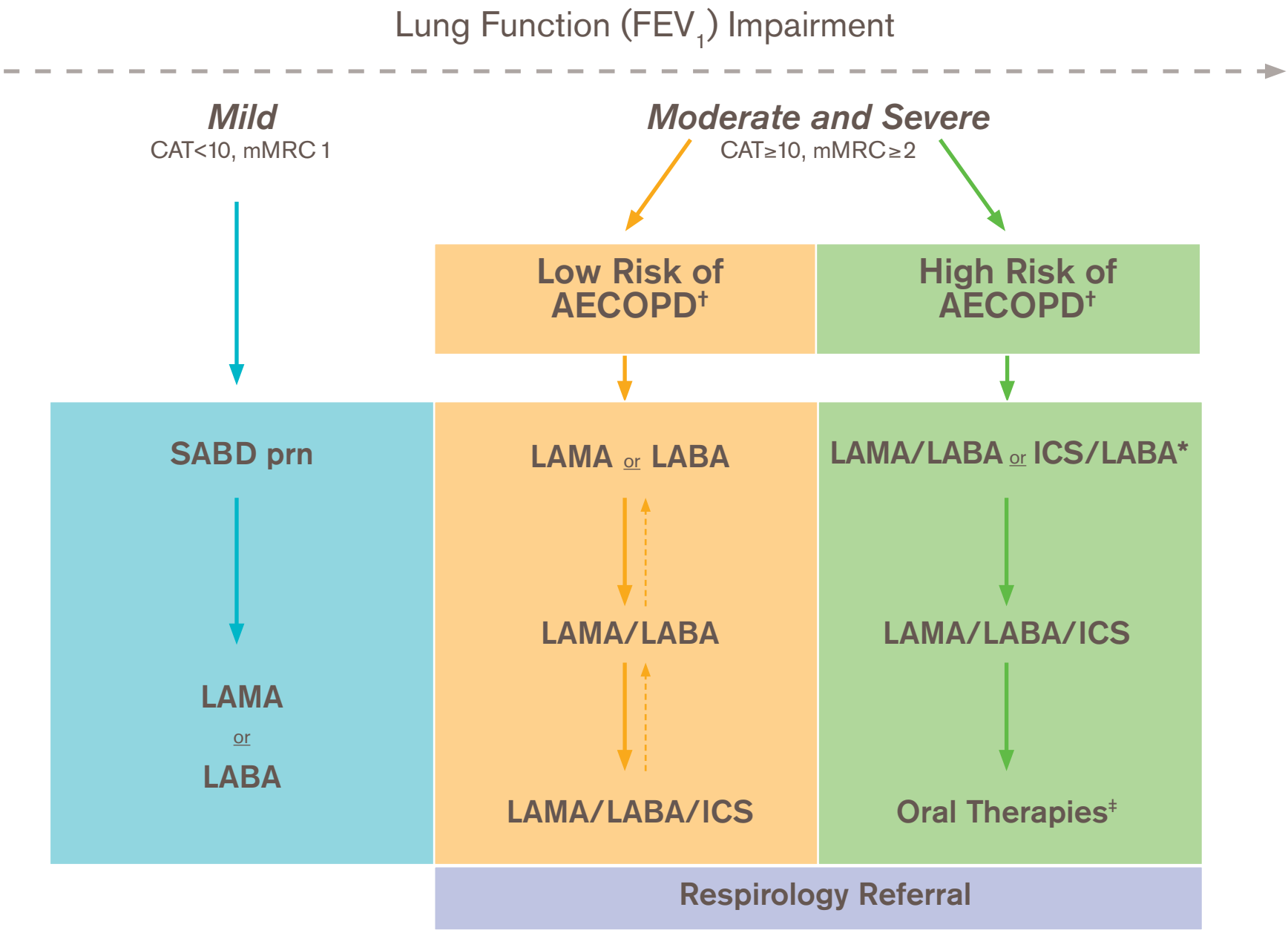
The Canadian Thoracic Society Treatment Algorithm 2019[1]



FEV_1 = Forced expiratory volume in one second; CAT = COPD Assessment Test; mMRC = Modified Medical Research Council; AECOPD = Acute exacerbation of COPD; SABD = Short-acting bronchodilator; prn = As needed; LAMA = Long-acting muscarinic agent; LABA = Long-acting $beta_2$-agonist; ICS = Inhaled corticosteroid

Solid arrows indicate step up therapy to optimally manage symptoms of dyspnea and/or activity limitation, as well as the prevention of AECOPD where appropriate. Dashed arrows indicate potential step down of therapy, with caution, and with close monitoring of the patient symptoms, exacerbations, and lung function. Symbol "/" refers to combination products (in the same device) and combination regimens (in separate devices). ICS should ideally be administered in a combination inhaler.

†Patients are considered at **Low Risk of AECOPD** with ≤1 moderate AECOPD in the last year (moderate AECOPD is an event with prescribed antibiotic and/or oral corticosteroids), and did not require hospital admission/ED visit; or at **High Risk of AECOPD** with ≥2 moderate AECOPD or ≥1 severe exacerbation in the last year (severe AECOPD is an event requiring hospitalization or ED visit).

***Blood eosinophil** ≥300/μL in patients with previous AECOPD may be useful to predict a favourable response to ICS combination inhaler.

‡**Oral Therapies** = Roflumilast, N-acetylcysteine, daily dose Azithromycin could be considered with patients with high risk AECOPD despite on optimal long-acting inhaled therapy. Oral corticosteroids as maintenance therapy are not indicated in COPD.

Reference: 1. Bourbeau J, *et al. Canadian Journal of Respiratory, Critical Care, and Sleep Medicine* 2019; DOI: 10.1080/24745332.2019.1668652.

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02/20

Consider the GSK COPD portfolio

INCRUSE ELLIPTA
umeclidinium

ONE inhaler
ONE inhalation
ONE daily

62.5 mcg
LAMA

ANORO ELLIPTA
umeclidinium/vilanterol

ONE inhaler
ONE inhalation
ONE daily

62.5/25 mcg
LAMA/LABA

TRELEGY ELLIPTA
fluticasone furoate/umeclidinium/vilanterol

ONE inhaler
ONE inhalation
ONE daily

100/62.5/25 mcg
LAMA/LABA/ICS

Consider INCRUSE ELLIPTA (a LAMA) for appropriate patients.
Consider ANORO ELLIPTA (a LAMA/LABA) for appropriate patients.
Consider TRELEGY ELLIPTA (a LAMA/LABA/ICS) for appropriate patients.

Indications and Clinical Use:
INCRUSE ELLIPTA (umeclidinium) is indicated for the long-term once-daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

INCRUSE ELLIPTA is **not** indicated for the relief of acute deterioration of COPD.

INCRUSE ELLIPTA should not be used in patients under 18 years of age.

Contraindications:
- Patients with severe hypersensitivity to milk proteins.

Warnings and Precautions:
- INCRUSE ELLIPTA is not indicated for the treatment of acute episodes of bronchospasm (i.e., as rescue therapy).
- INCRUSE ELLIPTA should not be initiated in patients during rapidly deteriorating or potentially life-threatening episodes of COPD.
- Patients should be instructed to discontinue regular use of short-acting bronchodilators and to use them only for acute respiratory symptoms.
- Exacerbations may occur during treatment. Patients should be advised to continue treatment and seek medical advice if COPD symptoms remain uncontrolled or worsen after initiation of therapy.
- INCRUSE ELLIPTA should not be used more often or at higher doses than recommended. INCRUSE ELLIPTA should not be used in conjunction with other medicines containing a short- or long-acting muscarinic antagonist.
- Headache or blurred vision may influence the ability to drive or to use machinery.
- Anticholinergic effects: Use with caution in patients with narrow-angle glaucoma or urinary retention.
- Cardiovascular effects: INCRUSE ELLIPTA should be used with caution in patients with severe cardiovascular disorders, particularly cardiac arrhythmias. In some cases, treatment may need to be discontinued.
- Respiratory: Treatment should be discontinued if paradoxical bronchospasm occurs and alternative therapy considered if necessary.
- Hypersensitivity: As with all medications, immediate hypersensitivity reactions may occur after administration of INCRUSE ELLIPTA. Patients with severe milk protein allergy should not take INCRUSE ELLIPTA.
- Use during pregnancy, labour and in breastfeeding women should only occur if the potential benefit justifies the potential risk.
- Avoid co-administration with other anticholinergics.

Adverse Events:
Adverse events reported at a frequency of ≥1% and greater than placebo include: nasopharyngitis, upper respiratory tract infection, cough, arthralgia, abdominal pain upper, contusion, myalgia, pharyngitis, tachycardia, toothache and viral upper respiratory tract infection. Adverse reactions occurring with INCRUSE ELLIPTA in combination with an ICS/LABA, at an incidence of greater than or equal to 1% and exceeding ICS/LABA alone were oropharyngeal pain and dysgeusia.

Recommended Dose:
The recommended dose is one inhalation of INCRUSE ELLIPTA 62.5 mcg once daily.

Dosing Considerations:
No dosage adjustment is required in patients over 65 years of age, in patients with renal impairment, or in patients with mild or moderate hepatic impairment. INCRUSE ELLIPTA has not been studied in patients with severe hepatic impairment.

Indications and Clinical Use:
ANORO ELLIPTA (umeclidinium/vilanterol) is a combination of a long-acting muscarinic antagonist (LAMA) and a long-acting beta$_2$-agonist (LABA) indicated for the long-term once-daily maintenance bronchodilator treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema.

ANORO ELLIPTA is not indicated for the relief of acute deterioration of COPD. ANORO ELLIPTA is not indicated for the treatment of asthma.

The safety and efficacy of ANORO ELLIPTA in asthma have not been established. ANORO ELLIPTA should not be used in patients under 18 years of age.

Contraindications:
- Patients with severe hypersensitivity to milk proteins.
- All LABAs are contraindicated in patients with asthma without use of a long-term asthma control medication.

Most Serious Warnings and Precautions:
Asthma-related death: Long-acting beta$_2$-adrenergic agonists (LABA) increase the risk of asthma-related death. Data from a large placebo-controlled US study that compared the safety of salmeterol (SEREVENT Inhalation Aerosol) or placebo added to patients' usual asthma therapy showed an increase in asthma-related deaths in patients receiving salmeterol. This finding with salmeterol is considered a class effect of LABA, including vilanterol, one of the active ingredients in ANORO ELLIPTA.

The safety and efficacy of ANORO ELLIPTA in patients with asthma have not been established.

Other Relevant Warnings and Precautions:
- Do not initiate in patients during rapidly deteriorating or potentially life-threatening episodes of COPD.
- Instruct patients to discontinue regular use of short-acting beta$_2$-agonists, use them only for acute respiratory symptoms.
- Continue treatment and seek medical advice if COPD symptoms remain uncontrolled or worsen after initiation of therapy.
- Concomitant use with other medicines containing a LABA or a short- or long-acting muscarinic antagonist.
- Headache and blurred vision may influence ability to drive or use machinery.
- Patients with narrow-angle glaucoma or urinary retention.
- Increase in pulse rate, systolic or diastolic blood pressure, or cardiac arrhythmias.
- Myocardial ischemia, angina pectoris, hypertension or hypotension. Should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, acute myocardial infarction, cardiac arrhythmias, and hypertension.
- Electrocardiogram changes (e.g., QTc prolongation).
- Patients with convulsive disorders or thyrotoxicosis.
- Hypokalemia and Hyperglycemia.
- Paradoxical bronchospasm.
- Patients with severe hepatic impairment.

Relevant Adverse Events (≥1% incidence and greater than placebo):
- **Infections and Infestations:** Pharyngitis, Sinusitis, Lower respiratory tract infection.
- **Gastrointestinal Disorders:** Diarrhea, Constipation.
- **Musculoskeletal and Connective Tissue Disorders:** Pain in extremity, Muscle spasms, Neck pain.
- **General disorders and administration site conditions:** Chest pain.

Recommended Dose:
The recommended and maximum dose is one inhalation of ANORO ELLIPTA 62.5/25 mcg once daily.

Indications and Clinical Use:
TRELEGY ELLIPTA (fluticasone furoate/umeclidinium/vilanterol) 100/62.5/25 mcg is a combination of an inhaled corticosteroid (ICS), long-acting muscarinic antagonist (LAMA), and a long-acting beta$_2$-adrenergic agonist (LABA), indicated in patients who are not adequately treated by a combination of an ICS/LABA or a combination of a LAMA/LABA:
- For the long-term, once daily, maintenance treatment of airflow obstruction in patients with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and/or emphysema.
- To reduce exacerbations of COPD in patients with a history of exacerbations.

TRELEGY ELLIPTA is not indicated for the relief of acute bronchospasm or for the treatment of asthma. TRELEGY ELLIPTA should not be used in patients under 18 years of age.

Contraindications:
- Severe hypersensitivity to milk proteins.

Most Serious Warnings and Precautions:
- **Not indicated for the treatment of asthma. Asthma-Related Events – Hospitalizations, Intubations, Death:** Use of LABA as monotherapy (without ICS) for asthma is associated with an increased risk of asthma-related death.

Other Relevant Warnings and Precautions:
- Discontinue regular use of rapid onset, short duration inhaled bronchodilators and use only for symptomatic relief if acute symptoms develop.
- Do not initiate in patients with acutely deteriorating COPD.
- Risk of exacerbations.
- Do not use higher than recommended dose, or with other LABAs or LAMAs.
- Caution in patients with cardiovascular disease, especially coronary insufficiency, cardiac arrhythmias (including tachyarrhythmias), or hypertension.
- Risk of headache or blurred vision that may influence ability to drive or use machinery.
- Risk of localized infections of the mouth and pharynx with *Candida albicans*.
- Risk of systemic effects include Cushing's syndrome, Cushingoid features, hypothalamic-pituitary-adrenal (HPA) axis suppression, decrease in bone mineral density (BMD), cataracts, glaucoma and central serous chorioretinopathy (CSCR).
- Hypercorticism and adrenal suppression in patients sensitive to these effects.
- Risk of death due to adrenal insufficiency for patients transferred from systemically active corticosteroids.
- Beta-adrenergic agonist medications may produce significant hypokalemia and transient hyperglycemia in some patients.
- Co-existing convulsive disorders, thyrotoxicosis, or those unusually responsive to sympathomimetic amines.
- Physicians should be alerted to eosinophilia, vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy.
- Risk of immediate hypersensitivity effects.
- Increased susceptibility to infections.
- Risk of urinary retention.
- Risk of paradoxical bronchospasm and wheezing after dosing.
- Risk of pneumonia.
- Monitoring recommendations: serum potassium levels in patients predisposed to low levels of serum potassium; blood glucose in diabetic patients; bone and ocular effects (cataract, glaucoma, and central serous chorioretinopathy) for patients at risk; corticosteroid effects for patients with hepatic impairment.
- Adverse reactions reported at a frequency of ≥1% in clinical studies included: constipation, nasopharyngitis, upper respiratory tract infection, pneumonia, oral candidiasis, bronchitis, pharyngitis, rhinitis, influenza, sinusitis, urinary tract infection, viral respiratory tract infection, headache, back pain, arthralgia, cough, oropharyngeal pain.

Dosage and Method of Administration:
Recommended and maximum dose is one oral inhalation once daily, administered at the same time every day. Do not use more than once every 24 hours. If a dose is missed, wait for next scheduled dose. Rinse mouth with water (without swallowing) after dosing.

For More Information:
Please consult the Product Monographs for INCRUSE ELLIPTA, ANORO ELLIPTA, and TRELEGY ELLIPTA at gsk.ca/incruse/en, gsk.ca/anoro/en, and gsk.ca/trelegy/pm, respectively, for important information relating to adverse reactions, drug interactions, and dosing information. The Product Monograph is also available by calling 1-800-387-7374. To report an adverse event, please call 1-800-387-7374.

COPD = Chronic obstructive pulmonary disease