Respiratory Medications

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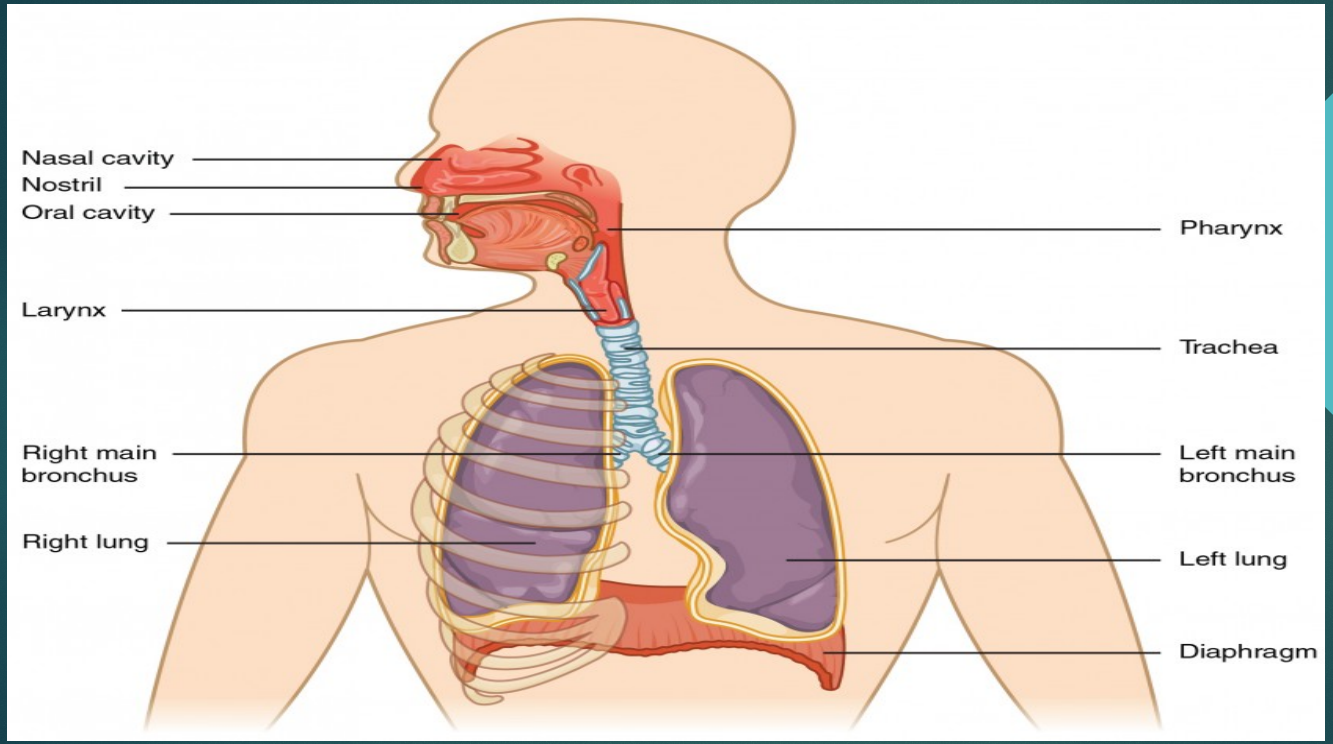
Outline

- Anatomy and physiology
- Pathophysiology
- Disease states: Asthma and COPD
- Drugs classes and Mechanism of actions
- New drugs in respiratory care
- Inhaler types and medication overview

Anatomy and Physiology

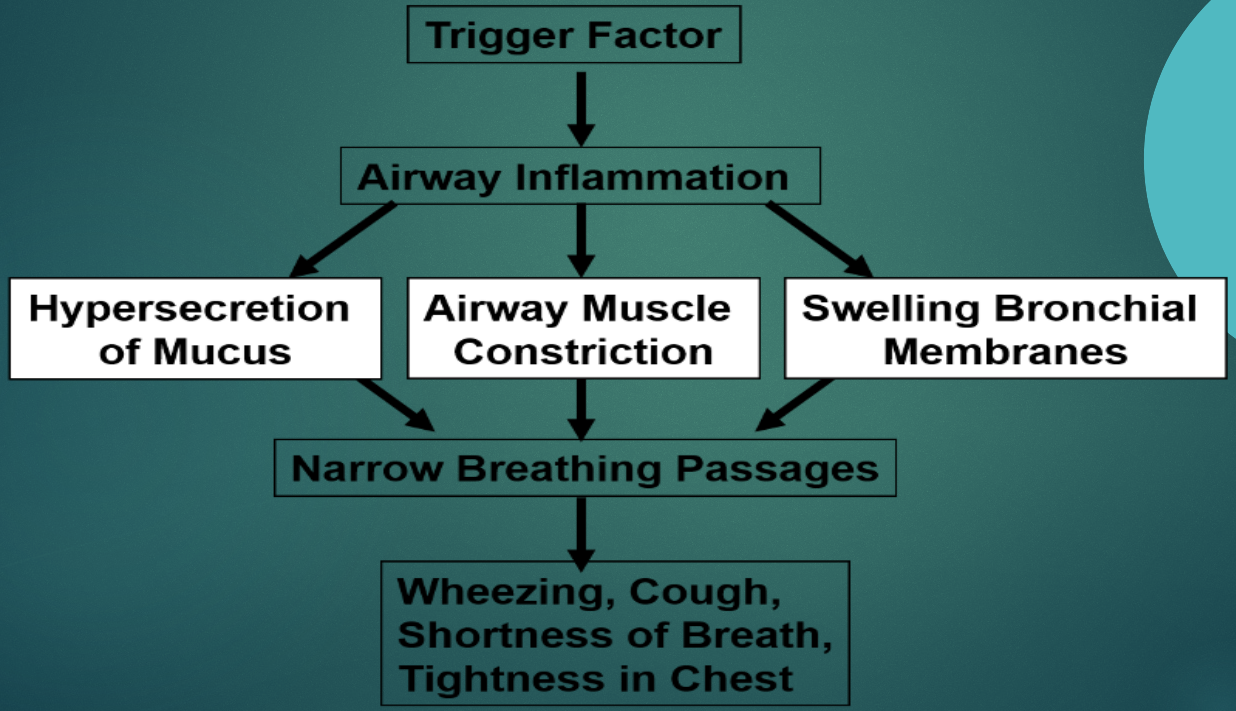


Asthma- Definition

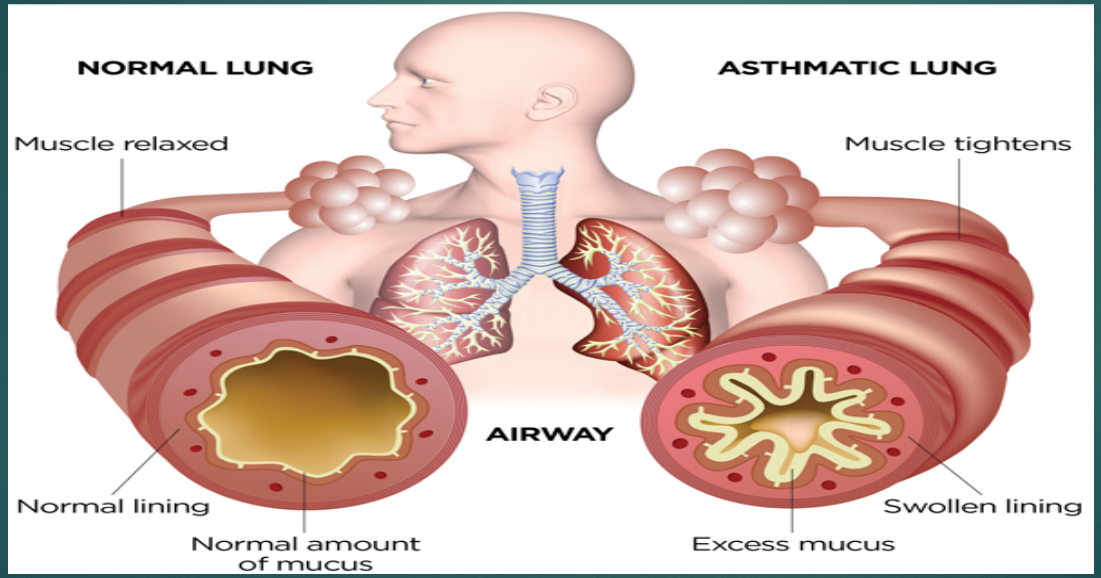
- Chronic Inflammatory disorder of the airways
- Recurrent episodes of wheezing, breathlessness, chest tightness, and Coughing
- Airflow obstruction that is often **reversible**
- Inflammation process leads to Bronchial hyperresponsiveness to different stimuli

Asthma- Triggers

Asthma - Pathophysiology



Asthma- Pathophysiology



Asthma- Pathophysiology

- **Acute Phase**

  - Histamine release (IgE specific) and mast cell involvement.

  - Bronchoconstriction and narrowing of the airways lumen

  - Minutes to Hours.

Asthma Pathophysiology

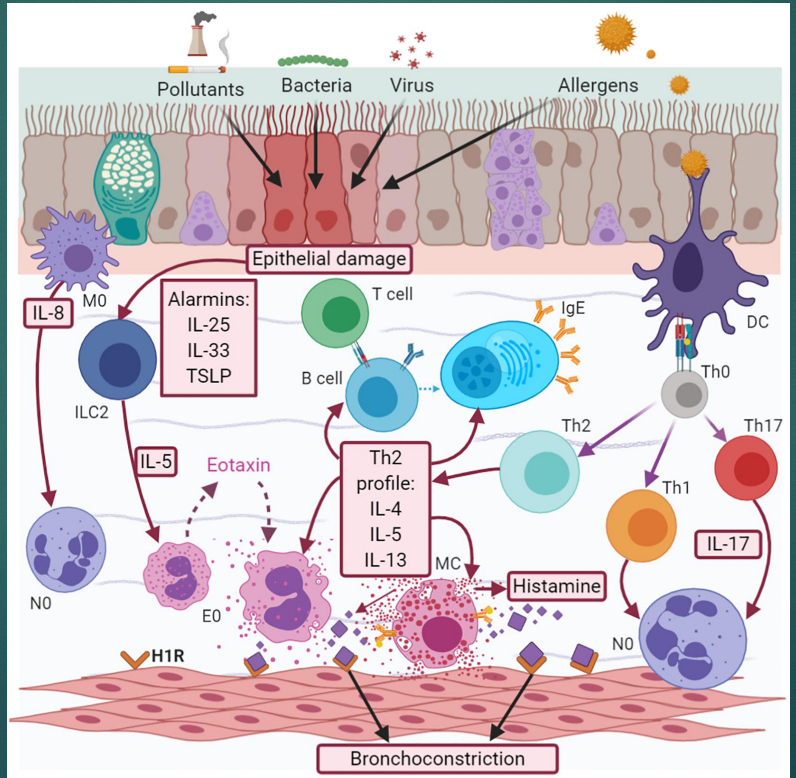
- **Chronic Phase**

  - Eosinophils, T Cells, mast cells, macrophages, epithelial cells, fibroblasts, bronchial smooth muscle cells proliferation

  - Bronchial Hyperresponsiveness and remodeling

  - Days to weeks

Asthma - Pathophysiology



Asthma - Diagnosis

- **Physical Exam**
  - Symptoms, triggers, family and social history
  - Wheezing, use of accessory muscles, presence of nasal polyps

Asthma - Diagnosis

- Spirometry
  - Use in kids 5 and older.
  - Pulmonary function (Reversibility of obstruction)
  - Beta Agonist challenge

Asthma - Diagnosis

- Spirometry

  - FVC (forced vital capacity) - total volume of air that can be exhaled during a maximal forced expiration effort

  - FEV1 (Forced Expiratory volume in one second) - volume of air exhaled in the first second under force after a maximal inhalation

  -Normal is **80 - 120%** predicted.

Asthma- Diagnosis

- Methacholine test: Used when spirometry test is normal. Used to provoke bronchoconstriction to test the reactivity of the airways
- Doses given in increasing increments until 20% of constriction is achieved, which is indicative of asthma.
- Methacholine is a cholinergic agonist, at the M3 receptor and induces bronchoconstriction.

Asthma - Diagnosis

- Spirometry

  - FEV1/FVC - % of the FVC expired in 1 second.

  - Normal is > 0.70 of predicted. **<0.70 = airway obstruction.**

  Beta 2 agonist test

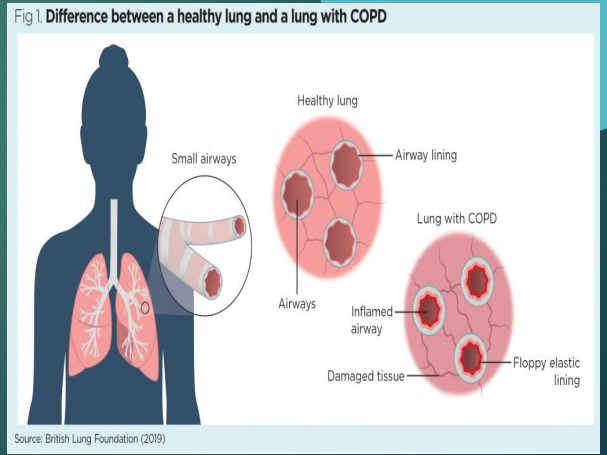
  - >12 % increase if FEV1 and 200 ml increase in FVC or FEV1 diagnostic for asthma.

COPD - Definition

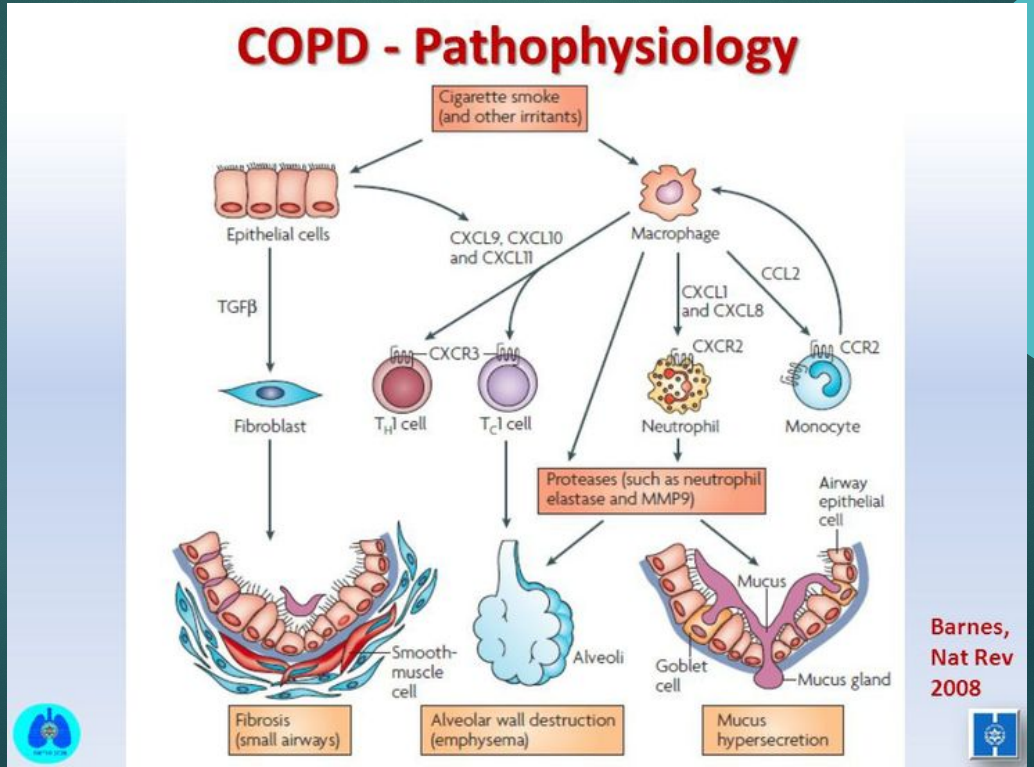
- Characterised by Persistent airflow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the airways.
- Innate and adaptive immune responses to long term exposure to noxious gases particularly cigarette smoke.
- **Persistent and Progressive**

COPD - Pathophysiology

- Chronic inflammation of bronchioles.
- Peripheral disease and narrowing of the airways
- Progressive and Chronic



COPD - Pathophysiology



COPD - Diagnosis

- **Symptoms:** Cough, Sputum, Shortness of breath

- **Spirometry**
  - Challenge after adequate administration of bronchodilator
  - FEV/FVC < 0.70 - confirms airflow limitation that is not fully reversible (COPD)

Differential Diagnosis: COPD and Asthma

Asthma

- Onset early if life (often childhood)
- Symptoms vary from day to day
- Symptoms at night/early morning
- Allergy, rhinitis, and/or eczema also present
- Family history of asthma
- Largely **reversible**

COPD

- Onset in mid life
- Symptoms slowly progressive
- Long smoking history
- Dyspnea during exercise
- Largely **irreversible**

Respiratory Medications classes

A. Bronchodilators - open the airway

- SABA - Short-acting Beta Agonist
- LABA - Long-acting Beta Agonist
- Anticholinergics
- Methylxanthines: Theophylline

A. Anti-inflammatory - target underlying process

- Corticosteroids
- Leukotriene Modifiers
- Mast cell stabilizers

Bronchodilators - SABA

- **Albuterol (Proair,® Ventolin®, Proventil®), Levalbuterol (Xopenex®)**
- MOA: Acts on beta-2 adrenergic receptors to relax the bronchial smooth muscle
- Use for quick relief of acute symptoms.
- Lasts about 4 - 8 hours
- Side effects: tachycardia, tremor

Bronchodilators - LABA

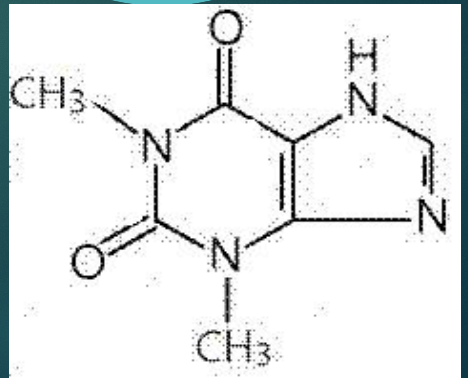
- **Indacaterol, Salmeterol, Formoterol, Arformoterol**
  - MOA: Acts on beta-2 adrenergic receptors to relax the bronchial smooth muscle
  - Use in combination with other classes of drugs.
  - Lasts 12 - 24 hours.

Bronchodilators - Anticholinergics

- **Ipratropium, Tiotropium, Aclidinium, Umeclidinium**
  - Muscarinic receptor antagonists. Specifically targets M3 receptors in the lungs which leads to smooth muscle relaxation.
  - Can be used alone or in combination with other drug classes
  - Lasts 12 - 24 hours
  - Side effects: Dry mouth, metallic taste,

Bronchodilators - Methylxanthines

- **Aminophylline, Theophylline**
  - MOA: PDE-3 (Phosphodiesterase) Inhibitor in the smooth muscle of the airways, which leads to bronchodilation.
  - Not used very often due to interactions with other drugs, and interpatient variability. Also requires monitoring due to narrow therapeutic index.
  - Side effects: N/V, diarrhea, tachycardia, arrhythmias, seizures.



Anti-Inflammatory - corticosteroids

- **Fluticasone, Beclomethasone, Mometasone, Budesonide**
  - MOA: Binds and activate glucocorticoid receptors. Leads a cascading events that eventually blocks the release of proinflammatory factors such as prostaglandins and leukotrienes and block late phase reaction to allergen
  - Beneficial actions
    - Increase number and responsiveness of B2 receptors
    - reduce mucus production
    - Reduce Bronchial Hyperresponsiveness
    - Reduce airway edema

Anti-inflammatory - Corticosteroids

- Staple of respiratory care. Most effective long-term control medications.
- Used in combination with Beta-2 agonists for most effective results.
- Do not alter progression or underlying severity

Oral steroids: **Prednisone**

- Used in acute exacerbations
- Fast acting.

Anti-inflammatory

- Side effects
  - Local

    Thrush, Hoarseness

    Rinse mouth after use (**swish and spit**)

  - Systemic

    Long term use can lead to cataracts, reduce bone density, and decreased growth in children.

Anti-inflammatory - Leukotriene Modifiers

- **Montelukast, Zafirlukast, Zileuton**
  - MOA: blocks leukotriene receptors. Leukotrienes are responsible for constriction of smooth muscle in the airways. Swelling, edema and leakage into airway passages.
  - Used mostly in Asthma.
  - Adjunctive therapy with steroids.
  - Side effects: well tolerated. Reports of suicidal thoughts.

Anti-Inflammatory - Mast cell stabilizers

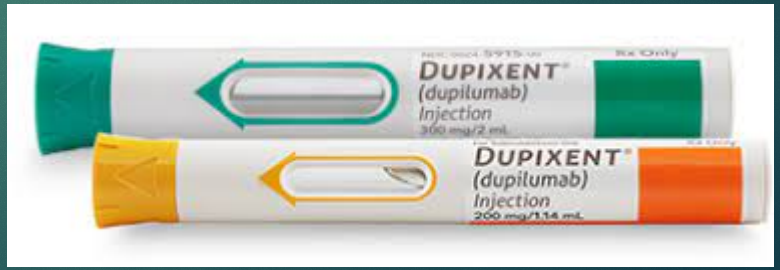
- **Cromolyn sodium, Nedocromil sodium**
  - Inhibit degranulation of mast cells, which prevents the release of inflammatory mediators.
  - Oral solution that comes with a special nasal applicator
  - Not use often. Alternative anti-inflammatory.
  - Short duration of action. Dosed 4 to 6 times a day.

New respiratory drugs - Biologics

- **Dupilumab (Dupixent)**
  - MOA: Monoclonal antibody. Blocks IL4 and IL13 signaling pathways, which are involved in inflammation in asthma.
  - Biologics. Has to be injected.
  - Comes in pre-filled syringes of 200 mg or 300 mg
  - Dosed every 2 weeks
  - Approved for adolescents 12 years and older with chronic severe

Biologics - Dupixent

- **Side effects**
  - Injections side reactions
  - Conjunctivitis
  - Mouth or throat pain
  - Cold sores



Biologics - Xolair

- Omalizumab (Xolair)
  - MOA:
    - Blocks IgE, main mediator in allergic reactions
    - Downregulates IgE receptor on multiple cells (Basophils, mast cells..)
    - Limits mast cell degranulation
    - Prevents IgE cross-linking

Biologics - Xolair

- Approved for patients 6 years or older with severe persistent allergic asthma
- Dosing based on patient eosinophils level and body weight. Typically dosed 75 mg to 375 mg every 2 to 4 weeks.
- Available in vial and prefilled syringes
- Side effects: Injections side reactions, tiredness, sore throat.

Biologics - Nucala

- **Mepolizumab (Nucala)**
  - MOA:

    - IL-5 cytokine antagonist. IL-5 is involved in the growth, recruitment and activation of eosinophils.

    - Ultimately reduces blood levels of eosinophils, which helps reduce allergic reactions and inflammation.

Biologics - Nucala

- Approved for patients 6 years or older with severe persistent allergic asthma.
- Dosing is 100 mg every 4 weeks. Injected subcutaneously.
- Comes in a lyophilized powder in a single dose vial.
- Side effects: Injection site reaction, headache, back pain, and fatigue.

Biologics - Fasenra

- **Benlarizumab (Fasenra)**
  - MOA:
    - Targets and depletes blood eosinophils.
    - Binds to IL-5 receptors on eosinophils.
    - Attracts natural killer cells and induces apoptosis of eosinophils.

Biologics - Fasenra

- Indicated as add on maintenance for adolescents 12 years and older with asthma of eosinophilic type.
- Comes in a prefilled syringe.
- Dosed every 4 weeks for the first 3 months then every 8 weeks thereafter.
- Side effects include: Injection site reaction, headache, Pharyngitis.

Biologics – Cinqair

- **Reslizumab (Cinqair)**
  - MOA:
    - Targets and depletes blood eosinophils.
    - Binds to IL-5 receptors on eosinophils.
    - Attracts natural killer cells and induces apoptosis of eosinophils.

Biologics – Cinqair

- Indicated as add on maintenance for adults with asthma of eosinophilic type.
- Administered Intravenously.
- Dosed every 4 weeks for a minimum of 4 months too determine efficacy.
- Side effects include: increased serum CPK , Oropharyngeal pain.

Biologics - Tezspire

- **Tezepelumab (Tezspire)**
  - MOA:
    - Binds to human thymic stromal lymphopoietin (TSLP) preventing TSLP receptor activation and reducing cytokines and biomarkers of inflammation.

Biologics - Tezspire

- Approved for patients 12 years or older with severe asthma and a history of sever exacerbations.
- Dosed 210mg subcutaneously once every 4 weeks.
- Available in auto-injector and prefilled syringes.
- Side effects: Arthralgia, Back Pain, and Pharyngitis.

Biologics

- Expensive. $$$$$$$$$$
- Usually requires a prior authorization
- Manufacturer assistance program for non-medicare patients.
- Can get to no copays.

Respiratory Treatments

2023

Allergy & Asthma Network

AllergyAsthmaNetwork.org

800.878.4403

American College of Allergy, Asthma & Immunology

CHEST FOUNDATION

DOSE INDICATOR = DOSE INDICATOR | G = GENERIC AVAILABLE | DISEASE STATES: A = ASTHMA | C = COPD

Allergy & Asthma Network is a national nonprofit organization dedicated to ending needless death and suffering due to asthma, allergies and related conditions through outreach, education, advocacy and research.

SHORT-ACTING BETA$_2$-AGONIST BRONCHODILATORS

relax tight muscles in airways and offer quick relief of symptoms such as coughing, wheezing and shortness of breath for 3-6 hours

- **ProAir® Digihaler™** — 90 mcg, albuterol sulfate inhalation powder — DOSE INDICATOR A
- **ProAir RespiClick®** — 90 mcg, albuterol sulfate inhalation powder — DOSE INDICATOR A
- **Proventil® HFA** — 90 mcg, albuterol sulfate — DOSE INDICATOR A G
- **Ventolin® HFA** — 90 mcg, albuterol sulfate — DOSE INDICATOR A G
- **Xopenex HFA®** — 45 mcg, levalbuterol tartrate — A G

LONG-ACTING BETA$_2$-AGONIST BRONCHODILATORS

relax tight muscles in airways and offer lasting relief of symptoms such as coughing, wheezing and shortness of breath for at least 12 hours

- **Serevent® Diskus®** — 50 mcg, salmeterol xinafoate inhalation powder — DOSE INDICATOR A C
- **Striverdi® Respimat®** — 2.5 mcg, olodaterol hydrochloride — DOSE INDICATOR C

INHALED CORTICOSTEROIDS

reduce and prevent swelling of airway tissue; they do not relieve sudden symptoms of coughing, wheezing or shortness of breath

- **Alvesco® HFA** — 80, 160 mcg, ciclesonide — DOSE INDICATOR A
- **ArmonAir® Digihaler™** — 55, 113, 232 mcg, fluticasone propionate inhalation powder — DOSE INDICATOR A
- **Arnuity® Ellipta®** — 50, 100, 200 mcg, fluticasone furoate inhalation powder — DOSE INDICATOR A
- **Asmanex® HFA** — 50, 100, 200 mcg, mometasone furoate — DOSE INDICATOR A
- **Asmanex® Twisthaler®** — 110, 220 mcg, mometasone furoate inhalation powder — DOSE INDICATOR A
- **Flovent® Diskus®** — 50, 100, 250 mcg, fluticasone propionate inhalation powder — DOSE INDICATOR A
- **Flovent® HFA** — 44, 110, 220 mcg, fluticasone propionate — DOSE INDICATOR A
- **Pulmicort Flexhaler®** — 90, 180 mcg, budesonide inhalation powder — DOSE INDICATOR A
- **QVAR® Redihaler™** — 40, 80 mcg, beclomethasone dipropionate — DOSE INDICATOR A

MUSCARINIC ANTAGONISTS (ANTICHOLINERGIC)

relieve cough, sputum production, wheeze and chest tightness associated with chronic lung diseases

Short-acting

- **Atrovent® HFA** — 17 mcg, ipratropium bromide — DOSE INDICATOR C

Long-acting

- **Incruse® Ellipta®** — 62.5 mcg, umeclidinium inhalation powder — DOSE INDICATOR C
- **Spiriva® HandiHaler®** — 18 mcg, tiotropium bromide inhalation powder — C
- **Spiriva® Respimat®** — 1.25, 2.5 mcg, tiotropium bromide — DOSE INDICATOR A C
- **Tudorza™ Pressair™** — 400 mcg, aclidinium bromide inhalation powder — DOSE INDICATOR C

COMBINATION MEDICATIONS

contain both short-acting beta$_2$-agonist and short-acting muscarinic antagonist

- **Combivent® Respimat®** — 20/100 mcg, ipratropium bromide and albuterol — DOSE INDICATOR C

COMBINATION MEDICATIONS

contain both inhaled corticosteroid and long-acting beta$_2$-agonist (LABA)

- **Advair Diskus®** — 100/50, 250/50, 500/50 mcg, fluticasone propionate and salmeterol inhalation powder — DOSE INDICATOR A C G
- **Advair® HFA** — 45/21, 115/21, 230/21 mcg, fluticasone propionate and salmeterol xinafoate — DOSE INDICATOR A G
- **AirDuo® Digihaler™** — 55/14, 113/14, 232/14 mcg, fluticasone propionate and salmeterol inhalation powder — DOSE INDICATOR A
- **AirDuo® RespiClick®** — 55/14, 113/14, 232/14 mcg, fluticasone propionate and salmeterol inhalation powder — DOSE INDICATOR A G
- **Breo® Ellipta®** — 100/25, 200/25 mcg, fluticasone furoate and vilanterol inhalation powder — DOSE INDICATOR A C
- **Dulera®** — 50/5, 100/5, 200/5 mcg, mometasone furoate and formoterol fumarate dihydrate — DOSE INDICATOR A
- **Symbicort®** — 80/4.5, 160/4.5 mcg, budesonide and formoterol fumarate dihydrate — DOSE INDICATOR A C G
- **Wixela™ Inhub™** — 100/50, 250/50, 500/50 mcg, fluticasone propionate and salmeterol xinafoate, approved generic of Advair Diskus — DOSE INDICATOR A C

contain both long-acting beta$_2$-agonist (LABA) and long-acting muscarinic antagonist (LAMA)

- **Anoro® Ellipta®** — 62.5/25 mcg, umeclidinium and vilanterol inhalation powder — DOSE INDICATOR C
- **Bevespi Aerosphere®** — 9/4.8 mcg, glycopyrrolate and formoterol fumarate — DOSE INDICATOR C
- **Duaklir® Pressair®** — 400, 12 mcg, aclidinium bromide and formoterol fumarate — DOSE INDICATOR C
- **Stiolto™ Respimat®** — 2.5/2.5 mcg, tiotropium bromide and olodaterol — DOSE INDICATOR C

contain inhaled corticosteroid, long-acting beta$_2$-agonist (LABA) and long-acting muscarinic antagonist (LAMA)

- **Trelegy® Ellipta®** — 200/62.5/25 mcg, 100/62.5/25 mcg, fluticasone furoate, umeclidinium and vilanterol inhalation powder — DOSE INDICATOR A C
- **Breztri Aerosphere™** — 160/9/4.8 mcg, budesonide, glycopyrrolate and formoterol fumarate — DOSE INDICATOR C

BIOLOGICS

target cells and pathways that cause airway inflammation; delivered by injection or IV

- **Cinqair®** — reslizumab — A
- **Dupixent®** — dupilumab — A
- **Fasenra™** — benralizumab — A
- **Nucala®** — mepolizumab — A
- **Tezspire™** — tezepelumab-ekko — A
- **Xolair®** — omalizumab — A

BRONCHIAL THERMOPLASTY

A minimally invasive procedure that uses mild heat to reduce airway smooth muscle, leading to fewer severe asthma flares, ER visits, and days lost from activities. www.btforasthma.com — A

PDE4 INHIBITORS

ease lung inflammation and reduce exacerbations

- **Daliresp®** — 250, 500 mcg, roflumilast — C

References

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Questions