Maxor
SPECIALTY PHARMACY

Your Guide to Cystic Fibrosis

PROGRAM OVERVIEW

Maxor's Disease Management Programs offer a unique approach to disease management. This includes information from disease overview to therapeutic outcome management and provides continuous, coordinated, and patient centered care plans carefully designated to fit your specific needs.

As part of the program, you will additionally have access to:

- Patient education materials providing disease specific information stressing the importance of medication compliance, ongoing physician follow up, scheduled lab work adherence, etc.
- Ongoing patient communication with documented patient feedback.
- Proactive refill calls to assist with patient compliance.
- Monitoring of timely and appropriate prescription refills to avoid product waste or misuse · Convenient ordering capabilities.
- Free delivery to home or other preferred location.
- Clinical pharmacist availability 24/7/365.
- Screening and education for drug/drug, drug/food, drug/lab, and drug/disease interactions as well as adverse drug reactions.
- Side effect management.

Through ongoing patient communication, education in lifestyle changes, clinical interventions, focused compliance efforts, market trend expertise, cost saving pharmacy practices, and outcome evaluation measures, our programs are dedicated to meeting your needs.

You can access your patient portal at Maxor.com or call us at 866-629-6779 for more information.

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UNDERSTANDING CYSTIC FIBROSIS (CF)

Cystic Fibrosis and Maxor's Role

Approximately 1,000 new cases of CF are diagnosed each year. Currently, there are close 40,000 adults and children living with CF within the United States.

Cystic fibrosis, at any time, can feel overwhelming. Our goal at Maxor Specialty Pharmacy is to provide you the tools and resources you need from initial diagnosis and onward. We aim to provide consistent support and navigation throughout the seasons of life. Understanding you or your family member's diagnosis of cystic fibrosis is the first step in taking control of your health. This program will provide key information about CF and ongoing initiatives to help get you started on your journey.

What is Cystic Fibrosis?

Cystic Fibrosis, or CF, is a genetic disease caused by a mutation or defect with the cystic fibrosis transmembrane conductance regulator (CFTR) gene. This gene plays a key role in regulating the exocrine glands. These glands control the production of sweat, digestive fluids, and mucus. Cystic Fibrosis causes the body to produce thick and sticky mucus that blocks airways, prevents normal digestive functions, and leads to bacterial infections.

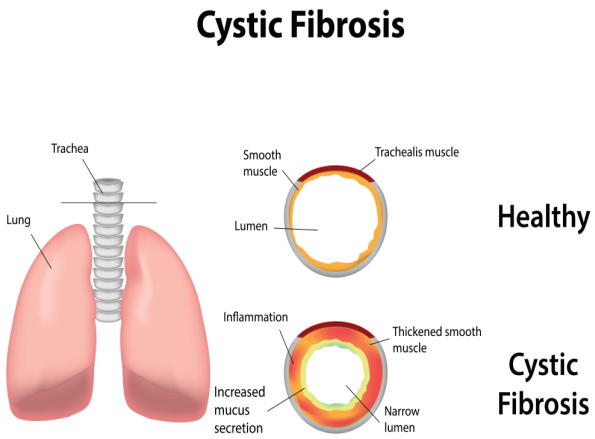

Figure 1

What causes CF?

In the United States, 1 in 31 people carry a mutation of the CF gene. A cystic fibrosis carrier has no related health problems, and probably has no idea they are carriers. When two people with the CF gene have a child, there is a 1 in 4 chances that the child will have cystic fibrosis.
A person born with CF has a protein called the cystic fibrosis transmembrane conductance regulator (CFTR). The CFTR proteins block the usual flow of water and salt in the lungs, pancreas,

colon, and genitourinary system. Because the salt and water is blocked, the body produces thicker mucus, which clogs the pathways of the body and leads to the symptoms of cystic fibrosis.

How is CF diagnosed?

The process of identifying cystic fibrosis may include multiple diagnostic tests such as:

- Newborn screening
- Sweat chloride testing
- Genetic (carrier) testing
- Clinical evaluation

There are many types of CFTR gene mutations that a person can carry. Knowing which specific gene mutation you or your child may have will help your healthcare team develop the best treatment plan.

What does CF look like?

Symptoms of cystic fibrosis can affect many organ systems and will primarily present in the lungs, digestive system, and sweat glands.

Mucus can build up and make it easier for bacteria to grow, this causes lung and sinus infections. The heavy mucus in the lungs makes it increasingly difficult to breathe and sustain normal respiratory function. Daily breathing treatments and antibiotics are used to break down the mucus and fight bacteria growth.

Mucus can block tubes, plug air ducts, and even stop digestive enzymes from reaching the stomach. The pancreas needs these enzymes to break down food. Without them, the body cannot properly absorb key nutrients, minerals, and proteins.
Sodium is an essential electrolyte required to generate nerve impulses, for muscle contraction, and maintain water balance. Cystic Fibrosis patients will sweat out excessive amounts of sodium and chloride creating salt. An increase in daily salt intake is advised for CF patients, especially in hot weather or with increased exercise.

Complications of CF

Cystic fibrosis is a complex disease, each individuals experience may differ in symptoms and severity. While the most commonly affected organs are the lungs and in the pancreas, other parts of the body can experience serious complications. Common complications include:

- Cystic Fibrosis-Related Diabetes (CFRD)
- Chronic sinus and lung infection
- Gastroesophageal Reflux Disease (GERD)
- Bone Disease (fracture, osteopenia or osteoporosis)
- Lung damage requiring lung transplantation

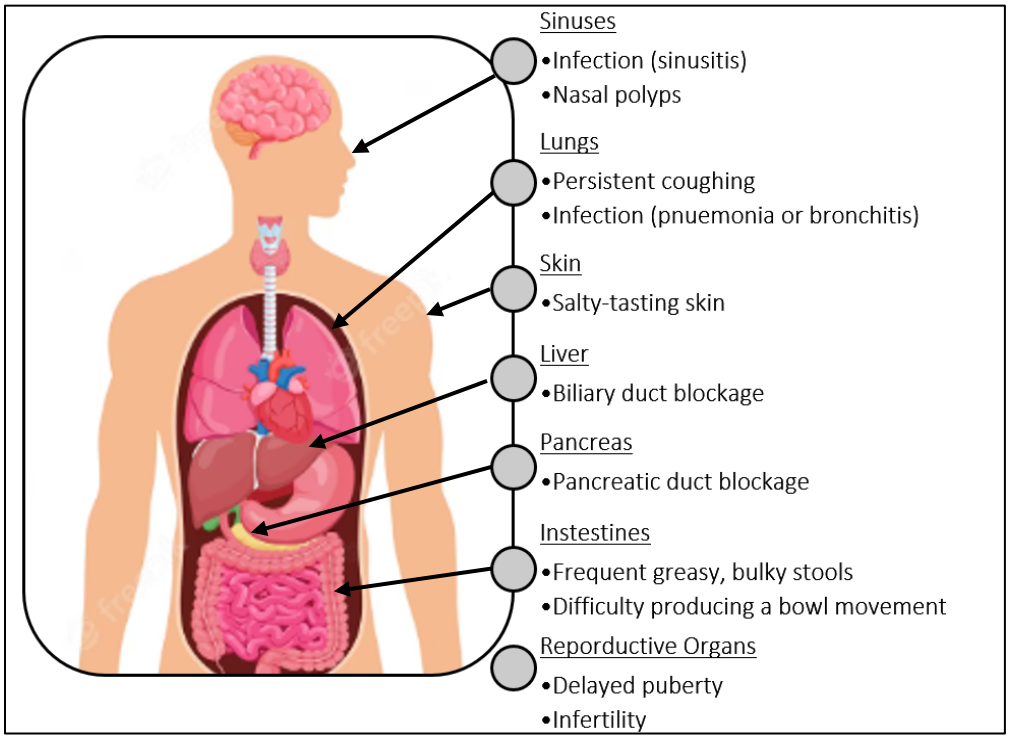

Figure 2: CF Symptoms by Organs

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2. About cystic fibrosis. Cystic Fibrosis Foundation website. Accessed September 6, 2023. https://www.cff.org/What-is-CF/About-Cystic-Fibrosis/
3. De Boeck K. Cystic fibrosis in the year 2020: A disease with a new face. Acta Paediatr. 2020 May;109(5):893-899. doi: 10.1111/apa.15155. Epub 2020 Jan 22. PMID: 31899933

CYSTIC FIBROSIS (CF) TREATMENTS

Cystic fibrosis is a complex disease and can affect multiple organs. The primary goal of CF treatment is to reduce symptom severity and **slow disease progression.** While there is not currently a cure for cystic fibrosis, CF is treatable. It is essential for patients to work closely with their care team to align their treatment plan with their health associated goals. In addition to supplying specialty genetic-based therapies, at Maxor our aim is to provide you with a list of five foundational goals that can be implemented to optimize you or your loved one's treatment plan.

The Five Goals of Cystic Fibrosis Treatment

1) Preventing Disease Progression
2) Prevent and treat lung infections
3) Clear the lungs of heavy mucus
4) Remove intestinal blockage
5) Promote a healthy lifestyle

Goal 1: Preventing Disease Progression

Cystic fibrosis transmembrane conductance regulator (CFTR) modulator therapies work to correct the malfunctioning protein produced by the CFTR gene. There are multiple protein defects that are a result of differing mutations in cystic fibrosis. The five CFTR modulator therapies work with these specific mutations to help the proteins function normally. Below is a brief overview of these specialty therapies:

- **Kalydeco® (ivacaftor):** Approved to treat ages ≥ 4 months old who have at least one copy of 97 specified mutations
- **Orkambi® (lumacaftor/ivacaftor):** Approved to treat ages ≥ 1 years old who have two copies of the F508del mutation
- **Symdeko® (tezavaftor/ivacaftor):** Approved to treat ages ≥ 6 years old with at least two copies of the F508del mutation or one single copy of 154 specified mutations
- **Trikafta® (elexacaftor/tezacaftor/ivacaftor):** Approved to treat ages ≥ 2 years old with at least one copy of the F508del mutation or at least one copy of 177 specified mutations
- **Alyftrek® (vanzacaftor/tezacaftor/deutivacaftor):** Approved to treat ages ≥ 6 years old who have at least one *F508del* mutation or another responsive mutation in the *CFTR* gene.

Goal 2: Prevent and Treat Lung Infections

Mucus buildup in the lungs can make people with cystic fibrosis more susceptible to bacterial infections. These infections or exacerbations can last for variable periods of time and sometimes many years. Most infections can be treated with antibiotics. For certain lung exacerbations, antibiotics may need to be given intravenously, orally, or inhaled through a nebulizer.

Inhaled antibiotics should be given after airway clearance therapies and treatments such as bronchodilators. This will allow the antibiotic to work its best after the lungs have been cleared.

Goal 3: Clear the Lungs of Heavy Mucus

Airway clearance therapies (ACT) are often used in combination with prescribed medications.

Airway clearance therapies help clear the lungs of mucus through the use of breathing techniques, movement, and coughing to loosen mucous and clear the lungs. Each ACT may vary in assistance and equipment needed and selection is determined by age, patient preference, cost, and each patient's individual airway pathophysiology.

Some ACTs include:

- Conventional chest physiotherapy (CPT): Combines different positions to use gravity to drain mucus from the five lobes of the lungs *(Assistance required)*
- Positive expiratory pressure (PEP) therapy: A small devices, such as a mask or mouthpiece, is used to help clear the lungs by forced exhalation and coughing (*Device required)*
- High-pressure PEP therapy:
- Active cycle of breathing techniques: Involves controlled breathing to expand the chest in order to forcefully cough out mucus *(No device or assistance is required)*
- Autogenic draining: Involves a series of three breathing techniques at different speeds to mobilize mucus secretions *(No device or assistance is required)*
- External high frequency chest compression device: Provides external wall chest compressions through the used of a vest (*Device required)*

Medications such as bronchodilators help to relax and open up the airways.

Bronchodilators relax and open up the airways and should be used prior to ACT as prescribed by your physician. Bronchodilators may come in various dosage forms and may require a device. Some of these devices include:

- Nebulized solution (*requires nebulizer device)*
- Handheld aerosol canisters $\pm$ spacer

Mucolytics or mucus thinners, make it easier to clear mucus from the airways. Mucolytics are intended to generally be used after bronchodilator therapy and before airway clearance therapies. It is important to consult with your physician to develop a care plan that works best for you.

- Inhaled hypertonic saline: Approved to treat ages $\geq$ 2 years old
- Pulmozyme® (Dornase alfa): Approved to treat ages $\geq$ 6 years old
- Inhaled mannitol: Approved for ages $\geq$ 18 years old

Goal 4: Remove Intestinal Blockage

Pancreatic insufficiency occurs in about 85% of people living with cystic fibrosis. Some are born with pancreatic insufficiency and others may develop it over time. Pancreatic insufficiency is a result of the CFTR mutation that results in the pancreas becoming blocked with mucus resulting in a buildup of enzymes that are needed for the stomach to digest food properly. This can lead to vitamin deficiencies, the inability to absorb fats, and constipation.

Pancreatic enzyme replacement (PERT) is recommended by the Cystic Fibrosis Foundation for all patients with pancreatic insufficiency, including infants. These enzymes will contain lipase, protease, and amylase necessary for absorption of fats, proteins, carbohydrates, and fat-soluble vitamins. Overall, PERT will help to decrease fatty stools, other gastrointestinal complications, and help support appropriate weight gain. Ask your doctor and care team about the following FDA approved enzymes:

- **Creon®:** Copay assistance available through CFCareForward
- **Zenpep®:** Copay assistance available through Live2Thrive
- **Pancreaze®:** Copay assistance available through Engage
- **Viokace®:** Patient assistance program may be available through the manufacturer
- **Pertzye®:** Copay assistance available through Care & EPI Nutrition Program

Goal 5: Promote a Healthy Lifestyle

Ensuring you or your loved one receives adequate nutrition and hydration is essential to promoting a healthy lifestyle. Energy needs of people with CF are estimated to be up to 2 times greater than the need of people without CF. Body mass index, or BMI, is used to estimate growth percentiles for people between the ages of 2 and 20 years old. Maintaining an appropriate BMI can be done through high-calorie supplements, providing an estimated additional 500 calories per day in addition to daily calories of those with a similar height and weight, exercising regularly, and maintaining adequate hydration. All medicinal and non-medicinal therapies should be considered in partnership with your provider.

Promoting a healthy lifestyle also includes emotional health. Cystic fibrosis cannot only be difficult to manage but also emotionally challenging. Anxiety is fears or worries that can potentially prevent a person from participating in daily activities. People with chronic diseases are at a greater risk of developing clinical depression. Anxiety and depression can present differently for each individual, some common symptoms may include:

Symptoms of Anxiety

- Restlessness
- Irritability
- Muscle tension
- Headaches
- Difficulty concentrating
- Trouble falling asleep or staying asleep

Symptoms of Depression

- Sadness
- Loss of energy
- Feelings of hopelessness
- Loss of enjoyment
- Problems concentrating
- Sleep disturbances

- Fatigue
- Trembling
- Weight changes

There are many treatment options including antidepressant medications, anti-anxiety medications, counseling, and non-medicinal therapies such as counseling. Talk to your healthcare provider if you or a loved one are experiencing symptoms of anxiety or depression.

Keeping up with CF therapy can be overwhelming but it is important to maintain consistency. For more information on treating CF, the following chapter is dedicated to resources.

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RESOURCES

Center for Disease Control & Prevention (CDC)

https://www.cdc.gov/genomics/disease/cystic_fibrosis.htm | 800-232-4636
The CDC is the nation's leading science-based, data drive, services organization that protects the public's health. Their website provides an overview of cystic fibrosis including national statistics, links to CF associated health conditions, and treatments.

Cystic Fibrosis Foundation

www.cff.org | 800-344-4823
Facebook: www.facebook.com/ cysticfibrosisfoundation
Twitter: www.twitter.com/CF_Foundation
The CF Foundation is a donor-funded nonprofit whose mission is finding a cure for CF. The CF Foundation also supports a wide range of research initiatives including drug development to ultimately provide advancing high-quality specialized care. Its website features educational materials for patients and families, information about care centers, case management resources, guidance on insurance, and updates on the latest research developments. For more specific topics refer to the links below:

- Managing CF: https://www.cff.org/managing-cf
- Medications: https://www.cff.org/managing-cf/medications
- Nutritional Basics: https://www.cff.org/managing-cf/nutritional-basics
- Mental Health: https://www.cff.org/managing-cf/mental-health
- Emerging Treatments: https://apps.cff.org/trials/finder/

American Lung Association

https://www.lung.org/lung-health-diseases/lung-disease-lookup/cystic-fibrosis | 800-586-4872
The American Lung Association is a nonprofit organization dedicated to improving lung health and preventing lung disease through education, advocacy, and research. Their website provides information on understanding CF, symptoms and diagnosis, managing CF, and questions to ask your doctor about CF.