CYSTIC FIBROSIS Western Australia

CF Fact
cystic fibrosis fact sheet

CFTR Modulator Therapies

Cystic fibrosis transmembrane conductance regulator (CFTR) modulators are a type of medication that differ from conventional CF treatments because they aim to improve or restore the malfunctioning CFTR protein, rather than treat the symptoms.

If the CFTR protein is absent or defective, this results in thick, sticky mucus in the lungs, damage to the pancreas and problems in many other parts of the body. People on modulators often experience improvements in lung function, reduction in respiratory infections and overall quality of life. While they have shown significant clinical improvements, they are not a cure.

Who can take modulators

Different modulator therapies are suited to different people depending on their CF gene mutation and their individual medical needs.

CFTR modulators are now available for approximately 90% of those who carry the most common mutations, however, approximately 10-20% of people with rare and ultra-rare CF causing mutations are still without any efficient, corrective therapy. There are also people who may be ineligible due to the inability to tolerate the medication or due to side effects experienced.

Clinical trials continue so that effective treatments become available for all people living with CF. For more information on clinical trials click here.

CFTR modulators

Trikafta® (Elexacaftor/Ivacaftor/Tezacaftor)
Trikafta® is the first triple combination therapy to be added to the PBS in Australia. Elexacaftor and Tezacaftor work together to help more CFTR proteins reach the cell surface, with Ivacaftor working to open the channels for longer. Trikafta® is indicated for people aged 2 years and older who have at least one F508del mutation in the CFTR gene; approximately 90% of the CF population.

Kalydeco® (Ivacaftor)
Kalydeco® binds to the defective CFTR protein, helping to open the channel so that more chloride and water can move in and out of the cells, thinning the mucus in the lungs and other organs. Kalydeco is indicated for people aged 1 month and older with at least one responsive gene; approximately 4-16% of the CF population.

Orkambi® (Lumacaftor/Ivacaftor)
Lumacaftor helps the CFTR protein to become the right shape, move to the cell surface and remain there longer. Used with Ivacaftor, this combination therapy reduces the symptoms of CF. Orkambi® is indicated in people aged one year and older with two copies of the most common CF mutation, F508del; approximately 50% of the CF population.

Symdeko® (Tezacaftor/Ivacaftor and Ivacaftor)
Tezacaftor increases the amount of mature CFTR protein delivered to the cell surface, while Ivacaftor helps to open the chloride channel. Symdeko is indicated in people aged 6 and older with two copies of F508del, as well as for individuals who have a single copy of one of 26 specified mutations; approximately 55% of the CF population.

Alyftrek® (vanzacaftor/tezacaftor/deutivacaftor)
Vanzacaftor and tezacaftor help the protein fold correctly and reach the cell's surface, while deutivacaftor opens the chloride channel on the surface to improve protein function. Alyftrek® is a once-daily triple-combination therapy for people aged 6 years and older with at least one F508del or another responsive CFTR mutation.

Are traditional CF treatments still needed?

Traditional treatments like airway clearance are still recommended for most people on modulators. Many people are tempted to stop other treatments because a lot of their CF symptoms reduce. However, even though modulator therapies can be very effective, there may still be established lung disease or residual CFTR protein defects that make people more vulnerable to infection and other CF complications.

It is important to discuss any changes with the CF team and make decisions about type and frequency of treatments on an individual basis. There are a number of clinical trials looking at the outcome of withdrawal of treatments in people on modulator medications. The results of these will help guide clinicians as to the best approach.

Mental health and wellbeing

Modulator therapies can have an impact on both physical and mental health. People might find additional mental health challenges arise as a side-effect of the new medication or as a result of the psychological effect of taking a potentially life-altering drug.

The CFWA Services team are available to help, or patients can talk to their hospital team. We also have lots of information on our CF Futures webpage.

For more information about eligibility for modulator medications, or being involved in a trial, please talk to the CF team.

Useful resources

- Drug Pipeline (CFA)
- Community Modulator Stories (CFWA)