Protocol for Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Products

Approved April 2021

Kalydeco® (ivacaftor)
Orkambi® (lumacaftor/ivacaftor)
Symdeko® (tezacaftor/ivacaftor)
Trikafta (elexacaftor/tezacaftor/ivacaftor)

Background:
Cystic fibrosis transmembrane conductance regulator (CFTR) modulators are a class of drugs that act by improving production, intracellular processing, and/or function of the defective CFTR protein. These drugs represent an important advance in management of cystic fibrosis (CF) because they target the production or function of the mutant CFTR protein rather than its downstream consequences. Their indications and efficacy depend upon the CFTR gene mutations in an individual patient.

Kalydeco *– Kalydeco is a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator indicated for the treatment of cystic fibrosis (CF) in patients age 4 months and older who have one mutation in the CFTR gene that is responsive to ivacaftor based on clinical and/or in vitro assay data.*

Orkambi - *Orkambi is a combination of lumacaftor and ivacaftor, a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator, indicated for the treatment of cystic fibrosis (CF) in patients age 2 years and older who are homozygous for the F508del mutation in the CFTR gene.*

Symdeko – *Symdeko is a combination of tezacaftor and ivacaftor, indicated for the treatment of cystic fibrosis (CF) in patients age 6 years and older who are homozygous for the F508del mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence.*

Trikafta *- TRIKAFTA is a combination of ivacaftor, a CFTR potentiator, tezacaftor, and elexacaftor indicated for the treatment of cystic fibrosis (CF) in patients aged 12 years and older who have at least one F508del mutation in the CFTR gene or a mutation in the CFTR gene that is responsive based on in vitro data.*

Criteria for approval:

1. Patient has a diagnosis of cystic fibrosis; **AND**

2. Documentation is provided that indicates that patient has a CFTR gene mutation(s), confirmed by an FDA-cleared CF mutation test for which the requested drug is indicated (see above). If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use

3. Patient meets the FDA approved age for the product requested (see above)
4. Prescriber is a specialist in CF, a pulmonologist, or in consultation with one
5. The patient is not currently being treated with another CFTR agent OR
6. Prescriber will discontinue current CFTR prior to initiating another
7. Baseline liver function tests (e.g., ALT, AST) are done prior to initiating treatment
8. Weight must be received for drugs that have weight-based dosing
9. For pediatric patients, an eye examination is required at baseline and periodically during therapy
10. Dose of CFTR product is reduced in patients taking CYP3A inhibitors such as fluconazole, erythromycin, ketoconazole, etc.
11. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence

Continuation of therapy:

1. Patient has demonstrated a clinical improvement or stabilization with the product being requested, e.g.,
   a. Improvement in FEV_1 from baseline
   b. Increase in weight or body mass index (BMI)
   c. Improvement in quality of life as demonstrated by CF Questionnaire-Revised (CFQ-R) Respiratory Domain Score
   d. Improvement in respiratory symptoms related to patients with CF (cough, sputum production, and difficulty breathing)
   e. Reduced number of pulmonary exacerbations
2. The patient is not concurrently receiving another CFTR agent
3. The prescriber is a specialist in CF, a pulmonologist or in consultation with one
4. Monitoring of ALT and AST is done annually
5. Monitoring of pediatric patients for possible development of cataracts
6. For dose increase requests, weight must be received for drugs that have weight-based dosing.
7. Medication is prescribed in accordance with Food and Drug Administration (FDA) established indication and dosing regimens or in accordance with medically appropriate off-label indication and dosing according to American Hospital Formulary Service, Micromedex, Clinical Pharmacology, Wolters Kluwer Lexi-Drugs (Lexicomp), national guidelines, or other peer-reviewed evidence

References:

1. Kalydeco® [package insert]. Vertex Pharmaceuticals In. Boston, MA 02210. December 2020.
2. Orkambi® [package insert]. Vertex Pharmaceuticals In. Boston, MA 02210. July 2019.
3. Symdeko® [package insert]. Vertex Pharmaceuticals In. Boston, MA 02210. December 2020.
4. Trikafta® [packet insert]. Vertex Pharmaceuticals In. Boston, MA 02210. December 2020
5. Clinical Pharmacology® Gold Standard Series [Internet database]. Tampa FL. Elsevier 2016. Updated periodically
6. Castellani C, Duff AJA, et al. ECFS best practice guidelines: 2018 revision. Journal of Cystic Fibrosis 17 (2018);153-178
7. Ren CL, Morgan RL, Oermann C, et al. Cystic Fibrosis Pulmonary Guidelines: Use of CFTR Modulator Therapy in Patients with Cystic Fibrosis. Ann Am Thorac Soc. 2018 Mar;15(3):271-280