Proposed Addendum to Protocol for Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Products
April 2026

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

Addendum:
Alyftrek was approved in December 2024 for the treatment of cystic fibrosis in patients 6 years of age and older who have at least one F508del mutation or another responsive mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

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.

Criteria for initial approval must meet all of the following:
1. Patient is of the FDA-labeled or compendial approved age
2. The medication requested is prescribed in accordance with a 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
3. Patient does not have any contraindications to therapy
4. Documentation is provided confirming diagnosis of cystic fibrosis
5. Documentation is provided that indicates the patient has a CFTR gene mutation(s), confirmed by an FDA-cleared CF mutation test for which the requested drug is indicated.
6. Prescriber is a specialist in CF, a pulmonologist, or in consultation with one
7. The patient is not receiving another CFTR agent
8. Documentation of the patient's liver function is provided
9. For drugs with weight-based dosing, the patient's most recent weight is provided
10. For patient's receiving moderate and/or strong CYP3A4 inhibitors the CFTR dosing is adjusted based on the prescribing information for the requested drug

Trikafta and Alyftrek have a black box warning for drug-induced liver injury and liver failure. See full prescribing information for complete boxed warning.

Continuation of therapy:
1. The patient has demonstrated at least one of the following clinical improvement or stabilization with the product being requested (documentation must be received)
    a. Improvement in FEV1 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 exacerbation

2. The patient is not receiving another CFTR agent
3. Documentation of recent ALT and AST levels is provided
4. For dose increase requests, the patient's recent weight is provided
5. The medication requested is prescribed in accordance with a 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

Approval Duration and Quantity Restrictions:

Initial and Renewal Approval: 12 months

Quantity Level Limit:

- Kalydeco (ivacaftor) tablets 150mg blister carton: 1 carton (56 tablets) per 28 days
- Kalydeco (ivacaftor) tablets 150mg: 60 tablets per 30 days
- Kalydeco (ivacaftor) oral granules 5.8mg packets: 56 packets per 28 days
- Kalydeco (ivacaftor) oral granules 13.4mg packets: 56 packets per 28 days
- Kalydeco (ivacaftor) oral granules 25mg packets: 56 packets per 28 days
- Kalydeco (ivacaftor) oral granules 50mg packets: 56 packets per 28 days
- Kalydeco (ivacaftor) oral granules 75mg packets: 56 packets per 28 days
- Symdeko (tezacaftor-ivacaftor) 100mg/150 mg: 56 tablets per 28 days
- Symdeko (tezacaftor-ivacaftor) 50mg/75 mg: 56 tablets per 28 days
- Trikafta (elexacaftor-tezacaftor-ivacaftor) 50mg/25mg/37.5mg tablets: 84 tablets per 28 days
- Trikafta (elexacaftor-tezacaftor-ivacaftor) 100mg/50mg/75mg tablets: 84 tablets per 28 days
- Trikafta (elexacaftor-tezacaftor-ivacaftor) 80mg/40mg/60mg oral granules: 56 packets per 28 days
- Trikafta (elexacaftor-tezacaftor-ivacaftor) 100mg/50mg/75mg oral granules: 56 packets per 28 days
- Alyftrek (vanzacaftor-tezacaftor-deutivacaftor) 4mg/20 mg/50mg tablets: 1 carton (84 tablets) per 28 days
- Alyftrek (vanzacaftor-tezacaftor-deutivacaftor) 10mg/50mg/125mg tablets: 1 carton (56 tablets) per 28 days

References:

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