Harvard Pilgrim Health Care | TUFTS Health Plan

Pharmacy Medical Necessity Guidelines:
Cystic Fibrosis Medications

Effective: May 14, 2024

Guideline Type	☒ Prior Authorization ☐ Non-Formulary ☐ Step-Therapy ☐ Administrative

Applies to:

Commercial Products

☒ Harvard Pilgrim Health Care Commercial products; Fax: 617-673-0988

☒ Tufts Health Plan Commercial products; Fax: 617-673-0988

CareLink℠ – Refer to CareLink Procedures, Services and Items Requiring Prior Authorization

Public Plans Products

☒ Tufts Health Direct – A Massachusetts Qualified Health Plan (QHP) (a commercial product); Fax: 617-673-0988

Note: While you may not be the provider responsible for obtaining prior authorization, as a condition of payment you will need to ensure that prior authorization has been obtained.

Overview

Food and Drug Administration – Approved Indications

The cystic fibrosis transmembrane conductance regulator (CFTR) potentiators are indicated for:

• Kalydeco (ivacaftor)

Treatment of cystic fibrosis (CF) in patients age 1 month and older who have at least one mutation in the *CFTR* gene that is responsive to ivacaftor based on clinical and/or in vitro assay data. 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.

• Orkambi (lumacaftor/ivacaftor)

Treatment of CF in patients aged 1 year and older who are homozygous for the *F508del* mutation in the *CFTR* gene. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the F508del mutation on both alleles of the *CFTR* gene. The efficacy and safety of Orkambi (lumacaftor/ivacaftor) have not been established in patients with CF other than those homozygous for the *F80del* mutation.

• Symdeko (tezacaftor/ivacaftor)

Treatment of patients with CF aged 6 years and older who are homozygous for the *F508del* mutation or who have at least one mutation in the *CFTR* gene that is responsive to tezacaftor/ivacaftor based on *in vitro* data and/or clinical evidence. 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.

• Trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor)

Treatment of CF in patients aged 2 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. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one *F508del* mutation or a mutation that is responsive based on *in vitro* data.

Clinical Guideline Coverage Criteria

The plan may authorize coverage of a Cystic Fibrosis Medication when all of the following criteria are met:

Kalydeco

1. Documented diagnosis of cystic fibrosis

AND

2. Prescribed by or in consultation with a pulmonologist or physician specializing in the treatment of cystic fibrosis

AND

3. The patient is at least 1 month of age

AND

4. Documentation of a cystic fibrosis mutation test confirming one of the CFTR gene mutations responsive to Kalydeco

Orkambi

1. Documented diagnosis of cystic fibrosis

AND

2. Prescribed by or in consultation with a pulmonologist or physician specializing in the treatment of cystic fibrosis

AND

3. The patient is at least 1 year of age

AND

4. Documentation confirming the patient is homozygous for the Phe508del (F508del) mutation in the CFTR gene

Symdeko

1. Documented diagnosis of cystic fibrosis

AND

2. Prescribed by or in consultation with a pulmonologist or physician specializing in the treatment of cystic fibrosis

AND

3. The patient is at least 6 years of age

AND

4. Documentation of **one (1)** of the following:
    a. Patient is homozygous for the Phe508del (F508del) mutation in the CFTR gene
    b. Patient has at least one mutation in the CFTR gene that is responsive to Symdeko

Trikafta

1. Documented diagnosis of cystic fibrosis

AND

2. Prescribed by or in consultation with a pulmonologist or physician specializing in the treatment of cystic fibrosis

AND

3. The patient is at least 2 years of age

AND

4. Documentation of **one (1)** of the following:
    a. Patient has at least one Phe508del (F508del) mutation in the CFTR gene
    b. Patient has at least one mutation in the CFTR gene that is responsive to Trikafta

Limitations

1. For a non-formulary medication request, please refer to the Pharmacy Medical Necessity Guidelines for Formulary Exceptions and submit a formulary exception request to the plan as indicated.

Codes

None

References

1. Ahrens R, Rodriguez S, Yen K, Davies J. VX-770 in subjects 6 to 11 years with cystic fibrosis and the G551D-CFTR mutation. Poster presented at: 25th North American Cystic Fibrosis Conference; November 3-5, 2011; Anaheim, CA
2. Cystic Fibrosis Foundation. Testing for CF. URL: http://www.cff.org/What-is-CF/Testing/. Available from Internet. Accessed 2018b April 5.
3. Davies JC, Alton EFW, Bush A. Cystic fibrosis. BMJ. 2007;335:1255-9.
4. Elborn J, Ramsey B, Boyle M, et al. Efficacy and safety of lumacaftor/ivacaftor combination therapy in patients with cystic fibrosis homozygous for Phe508del CFTR by pulmonary function subgroup: a pooled analysis. Lancet Respir Med. 2016 Aug;4(8):617-26.

5. Farrell PM, White TB, Ren CL et al. Diagnosis of cystic fibrosis: consensus guidelines from the Cystic Fibrosis Foundation. J Pediatr. 2017; 181S:S4-S15.
6. Flume PA, Mogayzel PJ, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Am J Resp Crit Care Med. 2009:180:802-8.
7. Gershman AJ, Mehta AC, Infeld M, et al. Cystic fibrosis in adults: an overview for the internist. Cleve Clin J Med. 2006; 73(12):1065-74.
8. Grasemann H. CFTR modulatory therapy for cystic fibrosis. N Engl J Med. 2017; 377:2085-88
9. Kalydeco (ivacaftor) [prescribing information]. Boston, MA: Vertex Pharmaceuticals Inc.; May 2023.
10. Mogayzel PJ, Flume PA. Update in Cystic Fibrosis 2009. Am J Respir Crit Care Med. 2010:181:539- 44.
11. Mogayzel PF, Flume PA. Update in Cystic Fibrosis 2010. Am J Respir Crit Care Med. 2011:183:1620- 4.
12. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Pulmonary Clinical Practice Guidelines Committee. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. Am J Respir Crit Care Med. 2013 Apr 1;187(7):680-9.
13. Orkambi (lumacaftor/ivacaftor) [prescribing information]. Boston, MA: Vertex Pharmaceuticals Inc.; August 2023.
14. O'Sullivan BP, Freedman SD. Cystic fibrosis. Lancet. 2009;373(9678):1891-1904.
15. Pittman J, Ferkol T. The evolution of cystic fibrosis care. Chest. 2015 Aug;148(2):533-42.
16. Rehman A, Baloch N, Janahi I. Lumacaftor-ivacaftor in patients with cystic fibrosis homozygous for Phe508del CFTR. N Engl J Med. 2015 Oct;373(18):1783.
17. Staab D. Cystic fibrosis-therapeutic challenge in cystic fibrosis children. Eur J Endicrinol. 2004; 151:S77-S80.
18. Stoltz D, Meyerholz D, Welsh M. Origins of cystic fibrosis lung disease. N Engl J Med. 2015; 372(4):351-362.
19. Symdeko (tezacaftor/ivacaftor) [prescribing information]. Boston, MA: Vertex Pharmaceuticals Inc.; August 2023.
20. Trikafta (elexacaftor/tezacaftor/ivacaftor and ivacaftor) [prescribing information]. Boston, MA: Vertex Pharmaceuticals, Inc.; August 2023.
21. Wainwright CE, Elborn JS, Ramsey BW, et al. Lumacaftor-ivacaftor in patients with cystic fibrosis homozygous for Phe508del CFTR. N Engl J Med. 2015 Jul;373(3):220-31.
22. Wainwright CE, Elborn JS, Ramsey BW, et al. Lumacaftor-ivacaftor in patients with cystic fibrosis homozygous for Phe508del CFTR. N Engl J Med. 2015 Oct;373(18):1783-4.
23. Zhang W, Zhang X, Zhang YH, et al. Lumacaftor/ivacaftor combination for cystic fibrosis patients homozygous for Phe508del-CFTR. Drugs Today (Barc). 2016 Apr;52(4):229-37.

Approval And Revision History

September 13, 2022: Reviewed by the Pharmacy & Therapeutics Committee.

- July 11, 2023: Expanded age requirements of Kalydeco and Trikafta based on updated package labeling (effective August 1, 2023).
- May 14, 2024: No changes

Background, Product and Disclaimer Information

Pharmacy Medical Necessity Guidelines have been developed for determining coverage for plan benefits and are published to provide a better understanding of the basis upon which coverage decisions are made. The plan makes coverage decisions on a case-by-case basis considering the individual member's health care needs. Pharmacy Medical Necessity Guidelines are developed for selected therapeutic classes or drugs found to be safe, but proven to be effective in a limited, defined population of patients or clinical circumstances. They include concise clinical coverage criteria based on current literature review, consultation with practicing physicians in the service area who are medical experts in the particular field, FDA and other government agency policies, and standards adopted by national accreditation organizations. The plan revises and updates Pharmacy Medical Necessity Guidelines annually, or more frequently if new evidence becomes available that suggests needed revisions.

For self-insured plans, coverage may vary depending on the terms of the benefit document. If a discrepancy exists between a Pharmacy Medical Necessity Guideline and a self-insured Member's benefit document, the provisions of the benefit document will govern.

Treating providers are solely responsible for the medical advice and treatment of members. The use of this policy is not a guarantee of payment or a final prediction of how specific claim(s) will be adjudicated. Claims payment is subject to member eligibility and benefits on the date of service, coordination of benefits, referral/authorization and utilization management guidelines when applicable, and adherence to plan policies and procedures and claims editing logic.