Mass General Brigham
Health Plan

Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Potentiators: Kalydeco (ivacaftor) Orkambi (lumacaftor/ivacaftor) Symdeko (tezacaftor/ivacaftor) Trikafta (elexacaftor/tezacaftor/ivacaftor) Effective 02/01/2025

<table>
<tr><td>Plan</td><td>☐ MassHealth UPPL
☒Commercial/Exchange</td><td rowspan="2">Program Type</td><td rowspan="2">☒ Prior Authorization
☐ Quantity Limit
☐ Step Therapy</td></tr>
<tr><td>Benefit</td><td>☒ Pharmacy Benefit
☐ Medical Benefit</td></tr>
<tr><td>Specialty Limitations</td><td colspan="3">This medication has been designated specialty and must be filled at a contracted specialty pharmacy.</td></tr>
<tr><td rowspan="4">Contact Information</td><td colspan="3">Medical and Specialty Medications</td></tr>
<tr><td>All Plans</td><td>Phone: 877-519-1908</td><td>Fax: 855-540-3693</td></tr>
<tr><td colspan="3">Non-Specialty Medications</td></tr>
<tr><td>All Plans</td><td>Phone: 800-711-4555</td><td>Fax: 844-403-1029</td></tr>
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Overview

Cystic fibrosis (CF) is caused by genetic mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) protein. The CFTR protein is present in the respiratory epithelium and plays an important role in the regulation of airway surface liquid. Genetic mutations in the protein result in abnormal airway secretions, chronic endobronchial infection, and progressive airway obstruction. The CFTR potentiators treat the underlying cause of CF by targeting the defective CFTR protein to help facilitate increased chloride transport.

Kalydeco (ivacaftor) is a CFTR potentiator indicated for the treatment of 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 is a combination of ivacaftor and lumacaftor indicated for the treatment of CF in patients 1 year of age or 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 *F508del* mutation on both alleles of the CFTR gene. The efficacy and safety of Orkambi has not been established in patients with CF other than those who are homozygous for the F508del mutation.

Symdeko is a combination of tezacaftor and ivacaftor indicated for the treatment of CF in patients 6 years of age and older who are homozygous for the *F508del* mutation or who have at least one mutation in the CFTR gene that is response 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 is a combination of ivacaftor (a CFTR potentiator), tezacaftor, and elexacaftor indicated for the 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.

Coverage Guidelines:
Authorization may be granted for members new to the plan within the last 90 days who are currently receiving treatment with the requested medication and are stable, excluding when the product is obtained as samples or via manufacturer's patient assistance programs
OR
Authorization may be granted when all of the following criteria are met:

Kalydeco (ivacaftor)

1. Documentation of genetic testing to detect a mutation in the *CFTR* gene
2. Member has at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is response to ivacaftor (Note: specific gene must be documented)
3. The member is 1 month of age or older
4. Kalydeco will not be used in combination with Symdeko, Orkambi, or Trikafta

Orkambi (lumacaftor/ivacaftor)

1. Documentation of genetic testing to detect a mutation in the *CFTR* gene
2. The member is positive for the *F508del* mutation on both alleles of the *CFTR* gene
3. The member is 1 year of age or older
4. Orkambi will not be used in combination with Kalydeco, Symdeko, or Trikafta

Symdeko (tezacaftor/ivacaftor)

1. Documentation of genetic testing to detect a mutation in the *CFTR* gene
2. The member meets at least ONE of the following:
   a. Member is positive for the *F508del* mutation on both alleles of the CFTR gene
   b. Member has at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor (Note: specific gene must be documented)
3. The member is 6 years of age or older
4. Symdeko will not be used in combination with Kalydeco, Orkambi, or Trikafta

Trikafta (elexacaftor/tezacaftor/ivacaftor)

1. Documentation of genetic testing to detect a mutation in the *CFTR* gene
2. The member meets at least ONE of the following:
   a. Member is positive for at least one *F508del* mutation on the CFTR gene
   b. Member has at least one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to elexacaftor/tezacaftor/ivacaftor (Note: specific gene must be documented)
3. The member is 2 years of age or older
4. Trikafta will not be used in combination with Kalydeco, Symdeko, or Orkambi

Continuation of Therapy
All members (including new members) requesting authorization for continuation of therapy must meet all initial authorization criteria.

Limitations

1. Initial approvals will be granted for 6 months
2. Reauthorizations will be granted for 12 months
3. The following quantity limits apply:

Drug Name and Dosage Form	Quantity Limit
Kalydeco 150mg tablets	56 tablets per 28 days
Kalydeco 5.8 mg, 13.4 mg, 25mg, 50mg, or 75mg packets	56 packets per 28 days
Orkambi 100-125 mg tablets, 200-125mg tablets	112 tablets per 28 days
Orkambi 75-94 mg granules, 150-188mg granules, 100-125 mg granules	56 packets per 28 days
Symdeko 50-75mg tablets, 100-150 mg tablets	56 tablets per 28 days
Trikafta 50-25-37.5 mg tablets, 100-50-75mg tablets	84 tablets per 28 days
Trikafta 80-40-60 mg granules, 100-50-75 mg granules	56 granules per 28 days

References

1. Kalydeco (ivacaftor) [prescribing information]. Boston, MA: Vertex Pharmaceuticals Inc.; August 2023.
2. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med*. 2013;187:680-689.
3. Orkambi (lumacaftor and ivacaftor) [prescribing information]. Boston, MA: Vertex Pharmaceuticals Inc.; August 2023.
4. Rowe SM, Daines C, Ringshausen FC, Kerem E, Wilson J, Tullis E, Nair N, Simard C, Han L, Ingenito EP, McKee C, Lekstrom-Himes J, Davies JC. Tezacaftor-Ivacaftor in Residual Function Heterzygotes with Cystic Fibrosis. *N Engl J Med*. 2017; 377:2024-2035
5. Symdeko (tezacaftor/ivacaftor) [prescribing information]. Boston, MA: Vertex Pharmaceuticals Inc.; August 2023.
6. Taylor-Cousar JL, Munck A, McKone EF, et al. Tezacaftor–ivacaftor in patients with cystic fibrosis homozygous for Phe508del *N Engl J Med* 2017; 377:2013-2023
7. Trikafta (elexacaftor/tezacaftor/ivacaftor) [prescribing information]. Boston, MA: Vertex Pharmaceuticals Inc., August 2023.

Review History

05/20/2020 – Created and Reviewed P&T Mtg; Merged Orkambi, Symdeko, Trikafta and Kalydeco into one program. Effective 7/1/20.
05/19/2021 – Updated and Reviewed May P&T Mtg; Separated out Comm/Exch vs. MH UPPL; Added duration of approval to Limitations.
07/21/2021 – Updated and Reviewed July P&T; removed previous failure or inadequate response to Orkambi, Symdeko and Kalydeco for the drug Trikafta. Age requirement for Trikafta updated to ≥ 6 years old. Effective 10/01/2021.
11/13/2024 – Updated and reviewed at November P&T. Updated Kalydeco criteria to decrease approval age from 6 months to 1 month to reflect updated FDA-approved indication. Updated Orkambi criteria to decrease approval age from 2 years to 1 year to reflect updated FDA-approved indication. Updated Trikafta criteria from 6

years of 2 years to reflect up dated FDA-approved indication. Updated language for Kalydeco, Symdeko, and Trikafta to remove specific mutations and instead require member has at least one mutation in the CFTR gene that is responsive. to the requested agent. Updated quantity limitations grid to include all doses and formulations. Effective 02/01/2025.