RXADVANCE
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| **Clinical Policy Title:** | elexacaftor/ivacaftor/tezacaftor; ivacaftor |
| **Policy Number:** | RxA.523 |
| **Drug(s) Applied:** | Trikafta® |
| **Original Policy Date:** | 09/05/2020 |
| **Last Review Date:** | 09/14/2020 |
| **Line of Business Policy Applies to:** | All lines of business |

## Background

Elexacaftor/ivacaftor/tezacaftor (Trikafta®) is a triple combination drug for cystic fibrosis (CF).

- Elexacaftor and tezacaftor bind to different sites on the cystic fibrosis transmembrane conductance regulator (CFTR) protein and have an additive effect in facilitating the cellular processing and trafficking of F508del-CFTR to increase the amount of CFTR protein delivered to the cell surface compared to either molecule alone.
- Ivacaftor potentiates the channel open probability (or gating) of the CFTR protein at the cell surface.
- The combined effect of elexacaftor, tezacaftor, and ivacaftor is increased quantity and function of F508del-CFTR at the cell surface, resulting in increased CFTR activity as measured by CFTR mediated chloride transport.

It is 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.

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.

## Dosing Information

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| elexacaftor/ivacaftor/tezacaftor ; ivacaftor (Trikafta®) | CF | Adults and pediatric patients age 12 years and older:<br>• Morning dose: 2 tablets (each containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg)<br>• Evening dose: 1 tablet of ivacaftor 150 mg<br>• Morning and | elexacaftor 200 mg/ tezacaftor 100 mg/ ivacaftor 300 mg per day |

## Dosing Information

| Drug Name | Indication | Dosing Regimen | Maximum Dose |
|---|---|---|---|
| | | evening dose should be taken approximately 12 hours apart with fat-containing food. | |

## Dosage Forms

- Tablets: co-packaged fixed dose combination containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg and ivacaftor 150 mg

## Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

**I. Initial Approval Criteria**

**A. Cystic Fibrosis** (must meet all)**:**

1. Diagnosis of CF with genetic testing confirming the presence of two disease-causing mutations in CFTR gene;
2. Age ≥ 12 years;
3. Prescribed by or in consultation with a pulmonologist;
4. Chart notes indicate that pulmonary function tests, performed within the last 90 days, show a percent predicted forced expiratory volume in 1 second (ppFEV1) that is between 40-90%;
5. Member has at least one F508del mutation in the CFTR gene;
6. Trikafta® is not prescribed concurrently with other CFTR modulators (e.g., Orkambi®, Kalydeco®, Symdeko®);
7. Dose does not exceed elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 300 mg per day.

**Approval Duration**
**Commercial:** 6 months
**Medicaid:** 6 months
**HIM:** 6 months

**II. Continued Therapy Approval**

**A. Cystic Fibrosis** (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy as evidenced by a stabilization in ppFEV1 if baseline was ≥ 70% or increase in ppFEV1 if baseline was < 70%;
3. Trikafta® is not prescribed concurrently with other CFTR modulators (e.g., Orkambi®, Kalydeco®, Symdeko®);
4. If request is for a dose increase, new dose does not exceed elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 300 mg per day.

**Approval Duration**
**Commercial:** 12 months

**Medicaid:** 12 months
**HIM:** 12 months

## III. Appendices

**APPENDIX A: Abbreviation/Acronym Key**
CF: cystic fibrosis
CFTR: cystic fibrosis transmembrane conductance regulator
FDA: Food and Drug Administration
ppFEV1: percent predicted forced expiratory volume in 1 second

**APPENDIX B: Therapeutic Alternatives**
Not applicable

**APPENDIX C: Contraindications/Boxed Warnings**

- Contraindication(s):
  - None reported

- Boxed Warning(s):
  - None reported

**APPENDIX D: General Information**

- Elexacaftor and tezacaftor bind to different sites on the CFTR protein and have an additive effect in facilitating the cellular processing and trafficking of F508del-CFTR to increase the amount of CFTR protein delivered to the cell surface compared to either molecule alone. Ivacaftor potentiates the channel open probability (or gating) of the CFTR protein at the cell surface. The combined effect of elexacaftor, tezacaftor and ivacaftor is increased quantity and function of F508del-CFTR at the cell surface, resulting in increased CFTR activity as measured by CFTR mediated chloride transport.
- Should not be used in patients with severe hepatic impairment.

**References**

1. Trikafta® Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc.; January 2020. Available at: https://www.trikafta.com/. Accessed September 5, 2020.
2. Ren CL, Morgan RL, Oermann C, et al. Cystic Fibrosis Foundation pulmonary guidelines: Use of cystic fibrosis transmembrane conductance regulator modulator therapy in patients with cystic fibrosis. Ann Am Thorac Soc. 2018; 15(3): 271-280. Accessed September 5, 2020.
3. Elexacaftor, Tezacaftor, and Ivacaftor, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed September 05, 2020.
4. Clinical Pharmacology [database online] powered by ClinicalKey. Tampa, FL: Elsevier, 2020. Accessed with subscription at: http://www.clinicalkey.com. Updated January 14, 2020. Accessed September 05, 2020.

| Review/Revision History | Review/Revision Date | P&T Approval Date |
|---|---|---|
| Policy established. | 09/05/2020 | 09/14/2020 |