Trikafta (elexacaftor/tezacaftor/ivacaftor)

Background
Trikafta is a combination of ivacaftor, tezacaftor, and elexacaftor. Trikafta is indicated for the treatment of cystic fibrosis (CF) in patients who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (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. 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 (1).

Regulatory Status
FDA-approved indication: 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 (1).

If the patient’s genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of at least one F508del mutation (1).
Liver function tests (ALT, AST, and bilirubin) should be assessed prior to initiating Trikafta, every 3 months during the first year of treatment, and annually thereafter. In patients with a history of hepatobiliary disease or liver function test elevations, more frequent monitoring should be considered. Patients with severe hepatic impairment (Child-Pugh Class C) should not be treated with Trikafta (1).

Concomitant use with strong CYP3A inducers (e.g., rifampin, St. John’s Wort) significantly decreases exposure of Trikafta which may diminish effectiveness. Therefore, co-administration is not recommended (1).

The safety and efficacy of Trikafta in pediatric patients less than 12 years of age have not been established (1).

**Related policies**
Kalydeco, Orkambi, Pulmozyme, Symdeko

**Policy**
This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Trikafta may be considered medically necessary in patients 12 years of age and older for the treatment of cystic fibrosis (CF) and if the conditions indicated below are met.

Trikafta is considered investigational in patients less than 12 years of age and for all other indications.

**Prior-Approval Requirements**

**Age**
12 years of age and older

**Diagnosis**

The patient must have the following:

Cystic fibrosis (CF)

AND ALL the following:
1. At least one F508del mutation in the CFTR gene confirmed by an FDA-cleared CF mutation test
2. Pretreatment percent predicted forced expiratory volume (ppFEV) must be
3. Baseline levels of ALT, AST, and bilirubin must be obtained and prescriber agrees to monitor at least yearly
4. Must be prescribed by a pulmonologist or gastroenterologist
5. **NO** severe hepatic impairment (Child-Pugh Class C)
6. **NO** dual therapy with another cystic fibrosis transmembrane conductance regulator (CFTR) potentiator (see Appendix 1)

### Prior – Approval *Renewal* Requirements

**Age**  
12 years of age and older

**Diagnosis**

Patient must have the following:
- Cystic fibrosis (CF)

**AND ALL** of the following:
1. Stable or improvement of ppFEV₁ from baseline
2. Prescriber agrees to monitor ALT, AST, and bilirubin levels at least yearly
3. **NO** severe hepatic impairment (Child-Pugh Class C)
4. **NO** dual therapy with another cystic fibrosis transmembrane conductance regulator (CFTR) potentiator (see Appendix 1)

### Policy Guidelines

**Pre – PA Allowance**

None

**Prior – Approval Limits**

**Quantity**  
12 blister packs (252 tablets) per 84 days  
(Blister packs contain 14 tablets of elexacaftor, tezacaftor, and ivacaftor and 7 tablets of ivacaftor for a 7 day supply)

**Duration**  
6 months
Prior – Approval Renewal Limits

Quantity  12 blister packs (252 tablets) per 84 days
(Blister packs contain 14 tablets of elexacaftor, tezacaftor, and ivacaftor and 7 tablets of ivacaftor for a 7 day supply)

Duration  12 months

Rationale

Summary
Trikafta is a combination of ivacaftor, a CFTR potentiator, tezacaftor, and elexacaftor. Trikafta is indicated for the treatment of cystic fibrosis (CF) in patients 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. 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 (1).

Prior approval is required to ensure the safe, clinically appropriate and cost effective use of Trikafta while maintaining optimal therapeutic outcomes.

References

Policy History

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Keywords
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on December 6, 2019 and is effective January 1, 2020.
### Appendix 1 - List of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Potentiators

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