BlueCross BlueShield
Federal Employee Program

TRIKAFTA
(elexacaftor/tezacaftor/ivacaftor)

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Trikafta is a combination of ivacaftor, tezacaftor, and elexacaftor. Elexacaftor and tezacaftor bind to different sites on the CFTR protein and have an additive effect in facilitating the cellular processing and trafficking of select mutant forms of CFTR (including 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 CFTR at the cell surface, resulting in increased CFTR activity as measured by both CFTR mediated chloride transport in vitro and by sweat chloride in patients with CF (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 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 clinical and/or in vitro data (1).

If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one indicated mutation (see Appendix 2) (1).

Liver function tests (ALT, AST, alkaline phosphatase, and bilirubin) should be assessed prior to initiating Trikafta, every month during the first 6 months of treatment, then every 3 months for the next 12 months, and then at least 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).

Non-congenital lens opacities/cataracts have been reported in pediatric patients treated with ivacaftor-containing regimens. Baseline and follow-up examinations are recommended in pediatric

patients initiating treatment with Trikafta (1).

The safety and effectiveness of Trikafta in pediatric patients less than 2 years of age have not been established (1).

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 aged 2 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 clinical and/or in vitro data. Trikafta has warnings for elevated liver function tests, concomitant use with CYP3A inducers, and cataracts. The safety and efficacy of Trikafta in pediatric patients less than 2 years of age have not been established (1).

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

References

1. Trikafta [package insert]. Boston, MA: Vertex Pharmaceuticals Inc.; December 2024.