

Clinical Policy: Elexacaftor/Ivacaftor/Tezacaftor; Ivacaftor (Trikafta)

Reference Number: CP.PHAR.440

Effective Date: 12.01.19

Last Review Date: 02.20

Line of Business: Commercial, HIM, Medicaid

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

Description

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.

FDA Approved Indication(s)

Trikafta 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.

Policy/Criteria

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

It is the policy of health plans affiliated with Centene Corporation® that Trikafta is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cystic Fibrosis (must meet all):

1. Diagnosis of CF confirmed by all of the following (a, b, and c):
 - a. Clinical symptoms consistent with CF in at least one organ system, or positive newborn screen or genetic testing for siblings of patients with CF;
 - b. Evidence of CFTR dysfunction confirmed by one of the following (i or ii) (*see Appendix D*):
 - i. Evidence of clinical severity as defined by an average sweat chloride > 86 mmol/L;
 - ii. Genetic testing confirming the presence of two disease-causing mutations in CFTR gene, one from each parental allele;

- c. Member has at least one *F508del* mutation in the CFTR gene;
2. Age \geq 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. In vitro testing demonstrates both of the following (a and b):
 - a. Baseline chloride transport that is $<$ 10% of wild type CFTR;
 - b. Lack of responsiveness to tezacaftor, ivacaftor, or tezacaftor/ivacaftor as evidenced by failure to increase chloride transport over baseline by $>$ 10%;
6. Trikafta is not prescribed concurrently with other CFTR modulators (e.g., Orkambi[®], Kalydeco[®], Symdeko[®]);
7. For members currently taking another CFTR modulator (e.g., Orkambi, Kalydeco, Symdeko) and switching to Trikafta, evidence of an increase in chloride transport of $<$ 10% over baseline;
8. Dose does not exceed elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 300 mg (2 tablets elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg and 1 tablet ivacaftor 150 mg) per day.

Approval duration: 4 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Cystic Fibrosis (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
2. Member is responding positively to therapy as evidenced by both of the following after at least 12 weeks of therapy (a and b):
 - a. Stabilization in ppFEV1 if baseline was \geq 70% or increase in ppFEV1 if baseline was $<$ 70%;
 - b. Increase in chloride transport \geq 10% since baseline;
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 (2 tablets elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg and 1 tablet ivacaftor 150 mg) per day.

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PHAR.21 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

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

None reported

Appendix D: General Information

- Regarding the diagnostic criteria for CF:
 - 1) Although the Cystic Fibrosis Foundation guidelines state that CFTR dysfunction needs to be confirmed with an elevated sweat chloride ≥ 60 mmol/L, the criteria above incorporates the study inclusion criteria’s definition of clinical severity as “average sweat chloride > 86 mmol/L”.
 - 2) In regards to the criteria of “genetic testing confirming the presence of two disease-causing mutations in CFTR gene,” this is to ensure that whether heterozygous or homozygous, there are two disease-causing mutations in the CFTR gene, one from each parental allele. One of those two mutations must be a *F508del* mutation but does not necessarily require both.
- Most children can do spirometry by age 6, though some preschoolers are able to perform the test at a younger age. Some young children aren’t able to take a deep enough breath and blow out hard and long enough for spirometry. Forced oscillometry is another way to test lung function in young children. This test measures how easily air flows in the lungs (resistance and compliance) with the use of a machine.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CF	Adults and pediatric patients age 12 years and older:	elexacaftor 200 mg/ tezacaftor 100 mg/ ivacaftor 300 mg per day

Indication	Dosing Regimen	Maximum Dose
	<ul style="list-style-type: none"> • <u>Morning dose</u>: 2 tablets (each containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg) • <u>Evening dose</u>: 1 tablet of ivacaftor 150 mg • Morning and evening dose should be taken approximately 12 hours apart with fat-containing food 	

VI. Product Availability

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

VII. References

1. Trikafta Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc.; October 2019. Available at: <https://www.trikafta.com/>. Accessed October 21, 2019.
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.
3. Farrell PM, White TB, Ren CL, et al. Diagnosis of cystic fibrosis: consensus guidelines from the Cystic Fibrosis Foundation. J Pediatr. 2017 Feb;181S:S4-S15.e1.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	10.29.19	11.19
1Q 2020 annual review: Finalized line of businesses on policy to include HIM per SDC and prior clinical guidance; for initial approval: added comprehensive diagnostic criteria to confirm CF diagnosis (e.g., clinical symptoms in at least one organ, positive newborn screen, siblings genetic testing, and evidence of CFTR dysfunction confirmed by sweat chloride or genetic testing); added in vitro testing demonstrates a baseline chloride transport < 10% of wild type CFTR; added requirement for lack of responsiveness to other CFTR modulators; added for members currently using another CFTR modulator switching to Trikafta must show increase in chloride transport of < 10% over baseline; added positive response after at least 12 weeks of therapy of a) stabilization in ppFEV1 in lieu of an increase is acceptable if baseline was ≥ 70% and b) chloride transport ≥ 10% since baseline; modified initial approval duration to 4 months with reauthorization for 12 months; added Appendix D.	12.17.19	02.20
Clarify continuation of therapy requires an increase in chloride transport of 10% or greater.	02.11.20	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:

For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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