MEDICATION POLICY:
Alyftrek (vanzacaftor–tezacaftor–deutivacaftor)

Applicable Drugs: Alyftrek (vanzacaftor–tezacaftor–deutivacaftor)

Preferred: N/A

Non-preferred: N/A

Date of Origin: 6/2/2025

Date Last Reviewed / Revised: N/A

Prior Authorization Criteria

(May be considered medically necessary when criteria I through VIII are met)

I. Documented diagnosis of Cystic Fibrosis including elevated sweat chloride concentration (60 mmol/L) and genetic testing confirming two copies of CFTR mutations.

II. Documentation of at least one *F508del* mutation in the *CFTR* gene or another responsive mutation in the CFTR gene (List of mutations available in drug package insert Table 5).

III. Documentation of liver function tests (AST, ALT, alkaline phosphatase and bilirubin) prior to starting treatment.

IV. Minimum age requirement: 6 years old.

V. Documented treatment failure or contraindication to Trikafta (elexacaftor-tezacaftor-ivacaftor).

VI. The medication is prescribed by or in consultation with a pulmonologist or a physician who specializes in the treatment of cystic fibrosis.

VII. Request is for a medication with the appropriate FDA labeling, or its use is supported by current clinical practice guidelines.

VIII. Refer to plan document for the list of preferred products. If requested agent is not listed as a preferred product, must have a documented failure, intolerance, or contraindication to a preferred product(s).

Exclusion Criteria

- Severe liver impairment (Child-Pugh Class C)
- Prior solid organ or hematological transplant

Other Criteria

- Liver function tests recommended to be obtained prior to initiation, then assessed monthly for the first six months of therapy, then every three months for the next 12 months. Afterwards may be obtained at least yearly.

Quantity / Days Supply Restrictions

- Strengths available include the following;
    - vanzacaftor 4 mg/tezacaftor 20 mg/deutivacaftor 50 mg
    - vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg
- Max 90 tablets of vanzacaftor 4 mg/tezacaftor 20 mg/deutivacaftor 50 mg per 30 day supply
- Max 60 tablets of vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg per 30 day supply

APPROVAL LENGTH

- **Authorization:** 6 months
- **Re-Authorization:** An updated letter of medical necessity or progress notes confirming the current medical necessity criteria are met and showing the medication is effective. Document tolerating therapy and response of disease stabilization (improved lung function, stable lung function). Liver function tests (AST, ALT, alkaline phosphatase, and bilirubin) to be obtained for renewal

APPENDIX

N/A

REFERENCES

1. Alyftrek Prescribing information. Vertex Pharmaceuticals Incorporated.; 2025. Accessed June 2, 2025. https://pi.vrtx.com/files/uspi_vanzacaftor_tezacaftor_deutivacaftor.pdf.
2. Keating C, Yonker LM, Vermeulen F, et al. VX20-121-102 Study Group; VX20-121-103 Study Group. Vanzacaftor-tezacaftor-deutivacaftor versus elexacaftor-tezacaftor-ivacaftor in individuals with cystic fibrosis aged 12 years and older (SKYLINE Trials VX20-121-102 and VX20-121-103): results from two randomised, active-controlled, phase 3 trials. Lancet Respir Med. 2025;13(3):256-271. doi: 10.1016/S2213-2600(24)00411-9.
3. Hoppe JE, Kasi AS, Pittman JE, et al.VX21-121-105 Study Group. Vanzacaftor-tezacaftor-deutivacaftor for children aged 6-11 years with cystic fibrosis (RIDGELINE Trial VX21-121-105): an analysis from a single-arm, phase 3 trial. Lancet Respir Med. 2025;13(3):244-255. doi: 10.1016/S2213-2600(24)00407-7

DISCLAIMER: Medication Policies are developed to help ensure safe, effective and appropriate use of selected medications. They offer a guide to coverage and are not intended to dictate to providers how to practice medicine. Refer to Plan for individual adoption of specific Medication Policies. Providers are expected to exercise their medical judgement in providing the most appropriate care for their patients.