Commercial PA Criteria

Effective: March 24, 2025

Prior Authorization: Alyftrek

Products Affected: Alyftrek (vanzacaftor/tezacaftor/deutivacaftor) tablets

Medication Description: Alyftrek, a cystic fibrosis transmembrane conductance regulator (CFTR), is indicated for the treatment of cystic fibrosis (CF) in patients ≥ 6 years of age who have at least one F508del mutation or another responsive mutation in the CFTR gene.

Covered Uses: Cystic fibrosis (CF) in patients 6 years of age and older who have at least one F508del mutation or another responsive mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

Exclusion Criteria:

1. **Cystic Fibrosis, Patient with Unknown Cystic Fibrosis Transmembrane Conductance Regulator Gene Mutation.** An FDA-cleared cystic fibrosis mutation test should be used to detect the presence of at least one indicated mutation prior to use of Alyftrek.
2. **Combination Therapy with other Cystic Fibrosis Transmembrane Conductance Regulator Modulator(s).** Alyftrek contains tezacaftor, which is a component of Symdeko® (tezacaftor/ivacaftor tablets; ivacaftor tablets) and Trikafta® (elexacaftor/tezacaftor/ivacaftor; ivacaftor tablets and granules). Note: Examples of other cystic fibrosis transmembrane conductance regulator modulators are: Kalydeco® (ivacaftor tablets and oral granules), Orkambi® (lumacaftor/ivacaftor tablets and oral granules), Symdeko® (tezacaftor/ivacaftor; ivacaftor tablets), Trikafta® (elexacaftor/tezacaftor/ivacaftor; ivacaftor tablets and oral granules).
3. **Infertility.** Alyftrek is indicated for the treatment of cystic fibrosis in patients ≥ 6 years of age who have at least one F508del mutation or another responsive mutation in the cystic fibrosis transmembrane conductance regulator gene. *Note: A patient with a diagnosis of cystic fibrosis should be reviewed using criteria for the FDA-approved indication.*

Required Medical Information:

1. Diagnosis
2. Medical History
3. F508del mutation or another responsive mutation in the CFTR gene

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

Age Restriction: Patient is ≥ 6 years of age

Coverage Duration: 12 months

Other Criteria:

Initial Approval Criteria

1. Cystic Fibrosis. Approve for 1 year if the patient meets ALL of the following (A, B, C, D, **AND** E):

A. Patient is ≥ 6 years of age; **AND**

B. Patient has at least ONE of the following variants in the cystic fibrosis conductance regulator gene that is considered to be a pathogenic or likely pathogenic variant: F508del, A455E, G551D, L1077P, R352Q, S549N, V754M, D1152H, G85E, L206W, R75Q, S549R, W1098C, H1054D, M1101K, S1159F, S945L, W1282R, G1244E, I336K, R1066H, S1251N, V562I, Y563N, 1507_1515del9, E116Q, G424S, I556V, P140S, R334L, T1053I, 2183A→G, E193K, G463V, I601F, P205S, R334Q, T1086I, 3141del9, E292K, G480C, I618T, P499A, R347H, T1246I, 3195del6, E403D, G480S, I807M, P5L, R347L, T1299I, 3199del6, E474K, G551A, I980K, P574H, R347P, T338I, 546insCTA, E56K, G551S, K1060T, P67L, R352W, T351I, A1006E, E588V, G576A, K162E, P750L, R516G, T604I, A1067P, E60K, G576A;R668C, K464E, P99L, R516S, V1153E, A1067T, E822K, G622D, L1011S, Q1100P, R553Q, V1240G, A107G, E92K, G628R, L102R, Q1291R, R555G, V1293G, A120T, F1016S, G91R, L1065P, Q1313K, R560S, V201M, A234D, F1052V, G970D, L1324P, Q237E, R560T, V232D, A309D, F1074L, G970S, L1335P, Q237H, R668C, V392G, A349V, F1099L, H1085P, L137P, Q359R, R709Q, V456A, A46D, F1107L, H1085R, L1480P, Q372H, R74Q, V456F, A554E, F191V, H1375P, L15P, Q452P, R74W, V520F, A559T, F200I, H139R, L165S, Q493R, R74W;D1270N, V603F, A559V, F311del, H199R, L320V, Q552P, R74W;V201M, W361R, A561E, F311L, H199Y, L333F, Q98R, R74W;V201M;D, 1270N, Y1014C, A613T, F508C, H609R, L333H, R1048G, R75L, Y1032C, A62P, F508C;S1251N, H620P, L346P, R1066C, R751L, Y109N, A72D, F575Y, H620Q, L441P, R1066L, R792G, Y161D, C491R, F587I, H939R, L453S, R1066M, R933G, Y161S, D110E, G1047R, H939R;H949L, L619S, R1070Q, S1045Y, Y301C, D110H, G1061R, I1027T, L967S, R1070W, S108F, Y569C, D1270N, G1069R, I105N, L997F, R1162L, S1118F, Y913C, D1445N, G1123R, I1139V, M1101R, R117C, S1159P, D192G, G1247R, I1234Vdel6aa, M1137V, R117C;G576A;R668C, S1235R, D443Y, G1249R, I125T, M150K, R117G, S1255P, D443Y;G576A;R668C, G126D, I1269N, M152V, R117H, S13F, D513G, G1349D, I331N, M265R, R117L, S341P, D565G, G149R, I1366N, M952I, R117P, S364P, D579G, G178E, I1398S, M952T, R1283M, S492F, D614G, G178R, I148N, N1088D, R1283S, S549I, D836Y, G194R, I148T, N1303I, R170H, S589N, D924N, G194V, I175V, N1303K, R258G, S737F, D979V, G27E, I502T, N186K, R297Q, S912L, D993Y, G27R, I506L, N187K, R31C, S977F, E116K, G314E, I506T, N418S, R31L, T1036N, 1341G→A, 2789+2insA, 3041-15T→G, 3849+10kbC→T, 3850-3T→G, 5T;TG13, 711+3A→G, 1898+3A→G, 2789+5G→A, 3272-26A→G, 3849+4A→G, 4005+2T→C, 621+3A→G, E831X 2752-26A→G, 296+28A→G, 3600G→A, 3849+40A→G, 5T;TG12; **AND**

C. Patient meets at least ONE of the following (i, ii, **OR** iii):
   i. Positive cystic fibrosis newborn screening test; **OR**
   ii. Family history of cystic fibrosis; **OR**
   iii. Clinical presentation consistent with signs and symptoms of cystic fibrosis; AND
   Note: Examples of clinical presentation of cystic fibrosis include but are not limited to meconium ileus, sino-pulmonary symptoms (e.g., persistent cough, wheezing, pulmonary function tests consistent with obstructive airway disease, excess sputum production), bronchiectasis, sinusitis, failure to thrive, pancreatic insufficiency.

D. Patient has evidence of abnormal cystic fibrosis transmembrane conductance regulator function as demonstrated by at least ONE of the following (i, ii, **OR** iii):
   i. Elevated sweat chloride test; **OR**
   ii. Two cystic fibrosis-causing cystic fibrosis transmembrane conductance regulator mutations; **OR**
   iii. Abnormal nasal potential difference; **AND**

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

Renewal Criteria

1. Member has responded positively to therapy according to the prescriber; **AND**
2. Member has not experienced unacceptable toxicity from the medication

References:

1. Alyftrek™ tablets [prescribing information]. Boston, MA: Vertex; December 2024.

Policy Revision history

Rev #	Type of Change	Summary of Change	Sections Affected	Date
1	New Policy	New Policy	All	03/24/2025