Effective Date: 8/1/2025
Reviewed: 05/2025
Scope: Medicaid

SPECIALTY GUIDELINE MANAGEMENT

ALYFTREK (vanzacaftor, tezacaftor, and deutivacaftor)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indication
Alyftrek is indicated for the treatment of patients with cystic fibrosis (CF) aged 6 years and older who have at least one F508del mutation or another responsive 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 indicated mutation.

All other indications are considered experimental/investigational and not medically necessary.

II. CRITERIA FOR INITIAL APPROVAL

Cystic Fibrosis
Authorization of 6 months may be granted for treatment of cystic fibrosis when all of the following criteria are met:

A. Documentation that genetic testing was conducted to detect a mutation in the CFTR gene.
B. The member has one of the following mutations in the CFTR gene: A455E, G551D, L1077P, R352Q, S549N, V754M, D1152H, G85E, L206W, R75Q, S549R, W1098C, F508del, H1054D, M1101K, S1159F, S945L, W1282R, G1244E, I336K, R1066H, S1251N, V562I, Y563N, 1507_1515del9, 2183A→G, 3141del9, 3195del6, 3199del6, 546insCTA, A1006E, A1067P, A1067T, A107G, A120T, A234D, A309D, A349V, A46D, A554E, A559T, A559V, A561E, A613T, A62P, A72D, C491R, D110E, D110H, D1270N, D1445N, D192G, D443Y, D443Y;G576A;R 668C, D513G, D565G, D579G, D614G, D836Y, D924N, D979V, D993Y, E116K, E116Q, E193K, E292K, E403D, E474K, E56K, E588V, E60K, E822K, E92K, F1016S, F1052V, F1074L, F1099L, F1107L, F191V, F200I, F311del, F311L, F508C, F508C;S1251N, F575Y, F587I, G1047R, G1061R, G1069R, G1123R, G1247R, G1249R, G126D, G1349D, G149R, G178E, G178R, G194R, G194V, G27E, G27R, G314E, G424S, G463V, G480C, G480S, G551A, G551S, G576A, G576A;R668C, G622D, G628R, G91R, G970D, G970S, H1085P, H1085R, H1375P, H139R, H199R, H199Y, H609R, H620P, H620Q, H939R, H939R;H949L, I1027T, I105N, I1139V, I1234Vdel6aa, I125T, I1269N, I331N, I1366N, I1398S, I148N, I148T, I175V, I502T, I506L, I506T, I556V, I601F, I618T, I807M, I980K, K1060T, K162E, K464E, L1011S, L102R, L1065P, L1324P, L1335P, L137P, L1480P, L15P, L165S, L320V, L333F, L333H, L346P, L441P, L453S, L619S, L967S, L997F, M1101R, M1137V, M150K, M152V, M265R, M952I, M952T, N1088D, N1303I, N1303K, N186K, N187K, N418S, P140S, P205S, P499A, P5L, P574H, P67L, P750L, P99L, Q1100P, Q1291R, Q1313K, Q237E, Q237H, Q359R, Q372H, Q452P, Q493R, Q552P, Q98R, R1048G, R1066C, R1066L, R1066M, R1070Q, R1070W, R1162L, R117C, R117C;G576A;R668C, R117G, R117H, R117L, R117P, R1283M, R1283S, R170H, R258G, R297Q, R31C, R31L, R334L, R334Q, R347H, R347L,

R347P, R352W, R516G, R516S, R553Q, R555G, R560S, R560T, R668C, R709Q, R74Q, R74W, R74W;D1270N, R74W;V201M, R74W;V201M;D1270N, R75L, R751L, R792G, R933G, S1045Y, S108F, S1118F, S1159P, S1235R, S1255P, S13F, S341P, S364P, S492F, S549I, S589N, S737F, S912L, S977F, T1036N, T1053I, T1086I, T1246I, T1299I, T338I, T351I, T604I, V1153E, V1240G, V1293G, V201M, V232D, V392G, V456A, V456F, V520F, V603F, W361R, Y1014C, Y1032C, Y109N, Y161D, Y161S, Y301C, Y569C, Y913C, 1341G→A, 1898+3A→G, 2752-26A→G, 2789+2insA, 2789+5G→A, 296+28A→G, 3041-15T→G, 3272-26A→G, 3600G→A, 3849+10kbC→T, 3849+4A→G, 3849+40A→G, 3850-3T→G, 4005+2T→C, 5T;TG12, 5T;TG13, 621+3A→G, 711+3A→G, E831X

C. The member is at least 6 years of age.
D. The medication is prescribed by or in consultation with a pulmonologist.
E. Alyftrek will not be used in combination with other CFTR modulator containing medications (e.g. Trikafta, Kalydeco).

III. CONTINUATION OF THERAPY

Authorization of 6 months may be granted for continued treatment in members requesting reauthorization for an indication listed in Section II who are experiencing benefit from therapy as evidenced by disease stability or disease improvement (e.g., improvement in FEV1 from baseline).

IV. QUANTITY LIMIT

Alyftrek 10 mg-50 mg-125 mg tablets have a quantity limit of 56 tablets every 28 days (2 tablets per day)
Alyftrek 4 mg-20 mg-50 mg tablets have a quantity limit of 84 tablets every 28 days (3 tablets per day)

Table 1: Recommended Dosage of ALYFTREK in Adult and Pediatric Patients Aged 6 Years and Older

Age	Weight	Once Daily Oral Dosage
6 to less than 12 years old	Less than 40 kg	Three tablets of vanzacaftor 4 mg/tezacaftor 20 mg/deutivacaftor 50 mg (total dose of vanzacaftor 12 mg/tezacaftor 60 mg/ deutivacaftor 150 mg)
	Greater than or equal to 40 kg	Two tablets of vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg (total dose of vanzacaftor 20 mg/tezacaftor 100 mg/ deutivacaftor 250 mg)
12 years and older	Any weight	Two tablets of vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg (total dose of vanzacaftor 20 mg/tezacaftor 100 mg/ deutivacaftor 250 mg)

V. REFERENCES

1. Alyftrek [package insert]. Boston, MA: Vertex Pharmaceuticals Inc; January 2025.