NC Medicaid **Effective Date: November 14, 2012**
Outpatient Pharmacy
Prior Approval Criteria
Cystic Fibrosis **Amended Date: January 5, 2026**

Therapeutic Class Code: B0B, B0F

Therapeutic Class Description: CFTR (Cystic Fibrosis Transmembrane Conductance Regulator) Potentiator, and CFTR Potentiator and Corrector Combination

Medication
Kalydeco 150mg tablets Kalydeco 50mg granules Kalydeco 75mg granules Kalydeco 25mg granules Kalydeco 13.4mg granules Kalydeco 5.8mg granules
Orkambi 200mg/125mg tablets Orkambi 100mg/125mg tablets Orkambi 150/188mg granules Orkambi 100/125mg granules Orkambi 75/94mg granules
Symdeko 50mg/75mg -75 mg tablets Symdeko 100/150 mg - 150 mg tablets
Trikafta 100-50-75/75mg packet Trikafta 100-50-75/150mg Trikafta 50-25-37.5mg/75mg Trikafta 80-40-60mg/59.5mg packet
Alyftrek 4-20-50 tablets Alyftrek 10-50-15 tablets

Eligible Beneficiaries
NC Medicaid (Medicaid) beneficiaries shall be enrolled on the date of service and may have service restrictions due to their eligibility category that would make them ineligible for this service.

EPSDT does not apply to NCHC beneficiaries.

EPSDT Special Provision: Exception to Policy Limitations for Beneficiaries under 21 Years of Age

42 U.S.C. § 1396d(r) [1905(r) of the Social Security Act]

Early and Periodic Screening, Diagnostic, and Treatment (EPSDT) is a federal Medicaid requirement that requires the state Medicaid agency to cover services, products, or procedures for Medicaid beneficiaries under 21 years of age **if** the service is **medically necessary health care** to correct or ameliorate a defect, physical or mental illness, or a condition [health problem] identified through a screening examination (includes any evaluation by a physician or other licensed clinician). This means EPSDT covers most of the medical or remedial care a child needs to improve or maintain his/her health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems. Medically necessary services will be provided in the most economic mode, as long as the treatment made available is similarly efficacious to the service requested by the beneficiary's physician, therapist, or other licensed practitioner; the determination process does not delay the delivery

of the needed service; and the determination does not limit the beneficiary's right to a free choice of providers.

EPSDT does not require the state Medicaid agency to provide any service, product, or procedure
a. that is unsafe, ineffective, or experimental/investigational.
b. that is not medical in nature or not generally recognized as an accepted method of medical practice or treatment.

Service limitations on scope, amount, duration, frequency, location of service, and/or other specific criteria described in clinical coverage policies may be exceeded or may not apply as long as the provider's documentation shows that the requested service is medically necessary "to correct or ameliorate a defect, physical or mental illness, or a condition" [health problem]; that is, provider documentation shows how the service, product, or procedure meets all EPSDT criteria, including to correct or improve or maintain the beneficiary's health in the best condition possible, compensate for a health problem, prevent it from worsening, or prevent the development of additional health problems.

EPSDT and Prior Approval Requirements
a. If the service, product, or procedure requires prior approval, the fact that the beneficiary is under 21 years of age does **NOT** eliminate the requirement for prior approval.
b. IMPORTANT ADDITIONAL INFORMATION about EPSDT and prior approval is found in the NCTracks Provider Claims and Billing Assistance Guide, and on the EPSDT provider page. The Web addresses are specified below.

NCTracks Provider Claims and Billing Assistance Guide:
https://www.nctracks.nc.gov/content/public/providers/provider-manuals.html

EPSDT provider page:
https://medicaid.ncdhhs.gov/medicaid/get-started/find-programs-and-services-right-you/medicaid-benefit-children-and-adolescents

Criteria for Coverage- Kalydeco:

- Beneficiary has been diagnosed with Cystic Fibrosis
  and
- Beneficiary is age 1 month or greater
  and
- Beneficiary has a documented mutation in the CFTR gene that is responsive to ivacaftor. If the beneficiary's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use. (KALYDECO is not effective in beneficiaries with CF who are homozygous for the F508del mutation in the CFTR gene)
  and
- Dosing is 150mg taken every 12 hours (300mg/day total) or less
  and

- A baseline ALT and AST assessed prior to beginning therapy

Criteria for Coverage- Orkambi:

- Beneficiary has been diagnosed with Cystic Fibrosis

and

- Beneficiary is age 1 or greater

and

- Beneficiary is documented as homozygous for the *F508del* mutation in the *CFTR* gene. If the beneficiary's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the *F508del* mutation on both alleles of the *CFTR* gene.

and

- Dosing is two tablets (each containing lumacaftor 200 mg/ivacaftor 125 mg) or less taken orally every 12 hours with fat-containing food

and

- A baseline ALT and AST assessed prior to beginning therapy

Criteria for Coverage- Symdeko:

- Beneficiary has been diagnosed with Cystic Fibrosis

and

- Beneficiary is 6 years of age or greater

and

- Beneficiary is documented as homozygous for the F508del mutation in the CFTR gene or beneficiary has one mutation in the CFTR gene that is responsive to tezacaftor/ivacaftor. If the beneficiary's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the F508del mutation on both alleles of the CFTR gene.

and

- Dosing is one tablet in the morning and one tablet in the evening

and

- A baseline ALT and AST assessed prior to beginning therapy

Criteria for Coverage- Trikafta:

- Beneficiary has been diagnosed with Cystic Fibrosis

and

- Beneficiary is 2 years of age or greater

and

- Beneficiary is documented to have at least one copy of the F508del mutation in the CFTR gene or beneficiary has one mutation in the CFTR gene that is responsive to tezacaftor/ivacaftor. If the beneficiary's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one F508del mutation.

and

- Dosing does not exceed: two tablets (elexacaftor 100 mg, tezacaftor 50 mg and ivacaftor 75 mg) in the morning and one tablet (ivacaftor 150 mg) in the evening

and

- Baseline ALT, AST, and bilirubin have been assessed prior to beginning therapy

and

- If beneficiary less than 18 year of age: baseline ophthalmic examination has been performed

Criteria for Coverage- Alyftrek:

- Beneficiary has been diagnosed with Cystic Fibrosis

and

- Beneficiary is 6 years of age or greater

and

- Beneficiary is documented to have at least one copy of the F508del mutation in the CFTR gene or beneficiary has one mutation in the CFTR gene that is responsive to vanzacaftor/tezacaftor/deutivacaftor. If the beneficiary's genotype is unknown, an FDA-cleared CF mutation test should be used to confirm the presence of at least one F508del mutation.

and

- Dosing does not exceed: two tablets (vanzacaftor 10 mg, tezacaftor 50 mg and deutivacaftor 125 mg) OR three tablets daily (vanzacaftor 4 mg, tezacaftor 20 mg and deutivacaftor 50mg)

and

- Baseline ALT, AST, and bilirubin have been assessed prior to beginning therapy

and

- If beneficiary is less than 18 year of age: baseline ophthalmic examination has been performed

Procedures:

Length of therapy may be approved for up to 12 months.

Renewal Criteria: (Kalydeco, Orkambi, Symdeko, Trikafta, and Alyftrek)

• Must continue to meet all prior criteria

• Documentation of ongoing Liver Function Testing

References

1. Prescribing Information Orkambi®. Vertex Pharmaceuticals Incorporated Boston, MA; Revised April 2015. September 2016. Revised July 2019. Revised September 2025.

2. Prescribing Information Kalydeco®. Vertex Pharmaceuticals Incorporated Cambridge, MA; May 2017. Revised April 2019. Revised September 2020. Revised April 2023.

3. Prescribing Information Symdeko. Vertex Pharmaceuticals, Inc. Cambridge, MA; February 2018. Revised June 2019.

4. Prescribing Information Trikafta. Vertex Pharmaceuticals, Inc. Cambridge, MA; December 2020. Revised April 2023.

5. Prescribing Information Alyftrek. Vertex Pharmaceuticals, Inc. Cambridge, MA; December 2024.

Criteria Change Log

11/14/2012	Criteria effective date-Kalydeco only
08/01/2014	Added G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R mutation in the CFTR gene. If the beneficiary's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use. (KALYDECO is not effective in beneficiaries with CF who are homozygous for the F508del mutation in the CFTR gene)
04/01/2015	Added R117H mutation
11/05/2015	Added Kalydeco gcn's 38138, 38139
03/09/2016	Added coverage for Orkambi
04/06/2017	Changed age for Kalydeco to 2 yrs and older and for Orkambi to 6 yrs and older
10/03/2017	Added genetic mutations E56K, K1060T, P67L, E193K, A1067T, R74W, L206W, G1069R, D110E, R347H, D579G, R1070Q, D1270N, D110H, R352Q, S945L, R1070W, R117C, A455E, S977F, F1074L, F1052V,or D1152H for Kalydeco
06/11/2018	Added information about Symdeko
02/26/2019	Age for Kalydeco changed from 2 or greater to 1 or greater
	Age for Symdeko changed from 12 or greater to 6 or greater. Updated GCN's with new products
11/03/2020	Removed GCN's Age for Kalydeco changed from 1 or greater to 6 months or greater. Age for Orkambi changed from 6 or greater to 2 or greater. Removed GCNs. Removed G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R, R117H, E56K, K1060T, P67L, E193K, A1067T, R74W, L206W, G1069R, D110E, R347H, D579G, R1070Q, D1270N, D110H, R352Q, S945L, R1070W, R117C, A455E, S977F, F1074L, F1052V, or D1152H and replaced with mutation in the CFTR gene that is responsive to ivacaftor. Updated EPSDT web addresses and info
11/03/2020	Added Trikafta
03/15/2021	Age for Kalydeco changed from 6 months or greater to 4 months or greater.
10/01/2021	add the wording "or mutation in the CFTR gene that is responsive" for Trikafta based on a change to the FDA labelling.
02/01/2022	Age for Trikafta changed from 12 years to 6 years or greater
03/01/2024	Age for Trikafta changed to 2 and up and added strengths Age for Kalydeco changed to 1 month and older
01/05/2026	Added Alyftrek and changing age on Orkambi to age 1 and under and clarify continuation criteria