UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2025 P 2061-12
Program	Prior Authorization/Medical Necessity
Medication	Kalydeco® (ivacaftor)
P&T Approval Date	5/2015, 7/2016, 11/2016, 8/2017, 8/2018, 8/2019, 8/2020, 8/2021, 8/2022, 6/2023, 6/2024, 6/2025
Effective Date	9/1/2025

1. Background:

Kalydeco® (ivacaftor) is a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator indicated for the treatment of cystic fibrosis (CF) in patients aged 1 months and older who have at least one mutation in the CFTR gene that is responsive to ivacaftor based on clinical and/or in vitro assay data.

If the patient'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. [1]

Members will be required to meet the coverage criteria below.

2. Coverage Criteria[a]:

A. <u>Initial Authorization</u>

1. **Kalydeco** will be approved based upon **<u>all</u>** of the following criteria:

   a. Diagnosis of cystic fibrosis (CF)

   -AND-

   b. Submission of laboratory results confirming that patient has at least **<u>one</u>** of the following mutations in the CFTR gene that is responsive to Kalydeco^:

^List of CFTR gene mutations responsive to Kalydeco. A complete up to date list of responsive mutations can be referenced in the Kalydeco Prescribing Information.

711+3A→G *	F311del	I148T	R75Q	S589N
2789+5G→A *	F311L	I175V	R117C *	S737F
3272-26A→G *	F508C	I807M	R117G	S945L *
3849+10kbC→T *	F508C;S1251N †	I1027T	R117H *	S977F *
A120T	F1052V	I1139V	R117L	S1159F

A234D	F1074L	K1060T	R117P	S1159P
A349V	G178E	L206W *	R170H	S1251N *
A455E *	G178R *	L320V	R347H *	S1255P *
A1067T	G194R	L967S	R347L	T338I
D110E	G314E	L997F	R352Q *	T1053I
D110H	G551D *	L1480P	R553Q	V232D
D192G	G551S *	M152V	R668C	V562I
D579G *	G576A	M952I	R792G	V754M
D924N	G970D	M952T	R933G	V1293G
D1152H *	G1069R	P67L *	R1070Q	W1282R
D1270N	G1244E *	Q237E	R1070W *	Y1014C
E56K	G1249R	Q237H	R1162L	Y1032C
E193K	G1349D *	Q359R	R1283M	
E822K	H939R	Q1291R	S549N *	
E831X *	H1375P	R74W	S549R *	

* Clinical data exist for these mutations.
† Complex/compound mutations where a single allele of the CFTR gene has multiple mutations; these exist independent of the presence of mutations on the other allele.

-AND-

c. Prescribed by or in consultation with a provider who specializes in the treatment of CF

Authorization will be issued for 12 months.

B. <u>Reauthorization</u>

1. **Kalydeco** will be approved based on the following criterion:

   a. Documentation of positive clinical response to Kalydeco therapy (e.g., improved lung function, stable lung function)

Authorization will be issued for 12 months.

[a] State mandates may apply. Any federal regulatory requirements and the member specific benefit

plan coverage may also impact coverage criteria. Other policies and utilization management programs may apply.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class
- Supply limits may be in place.

4. References:

1. Kalydeco [Package Insert]. Boston, MA: Vertex Pharmaceuticals, Inc.; August 2023.

Program	Prior Authorization/Medical Necessity - Kalydeco (ivacaftor)
Change Control	
5/2015	New Program
7/2016	Annual Review. Updated indication for those 2 years and older in background section. Updated reference.
11/2016	Revised prescriber criterion.
8/2017	Added 28 additional CFTR mutations based on labeling change.
8/2018	Annual review. No changes.
8/2019	Annual review. Updated background and references.
8/2020	Annual review with no changes to clinical coverage criteria.
8/2021	Annual review. Updated background to reflect approval of 4 months and older. Updated with most recent approved mutation table. Decreased re-authorization to 12 months. Updated reference.
8/2022	Annual review with no change to coverage criteria.
6/2023	Updated background to reflect approval for patients one month and older. Updated prescriber requirement, simplified reauthorization criteria, and updated reference.
6/2024	Annual review. Increased initial authorization approval duration to 12 months. Removed prescriber requirement from reauthorization criteria. Updated reference.
6/2025	Annual review. Added notation in the CFTR gene mutations table. No changes to clinical criteria.