UnitedHealthcare Pharmacy
Clinical Pharmacy Programs

Program Number	2026 P 1054-16
Program	Prior Authorization/Notification
Medication	Kalydeco® (ivacaftor)
P&T Approval Date	2/2012, 2/2013, 2/2014, 4/2014, 2/2015, 2/2016, 2/2017, 8/2017, 8/2018, 8/2019, 8/2020, 8/2021, 8/2022, 6/2023, 6/2024, 6/2025, 6/2026
Effective Date	9/1/2026

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. Initial Authorization

1. **Kalydeco** will be approved based upon **both** of the following criteria:

   a. Diagnosis of cystic fibrosis (CF)

   -AND-

   b. Documentation confirming that patient has at least **one** 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

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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.

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.

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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.
- Medical Necessity and/or Supply limits may be in place.

4. References:

1. Kalydeco [Package Insert]. Boston, MA: Vertex Pharmaceuticals, Inc.; March 2026.

Program	Prior Authorization/Notification - Kalydeco (ivacaftor)
Change Control	
2/2014	Annual review. Increased re-authorization from 6 months to 24 months.
4/2014	Added eight additional CFTR mutations based on label change.
2/2015	Annual review. Expanded coverage to include *R117H* mutation. Updated Background and References.
2/2016	Annual review. Updated reference.
2/2017	Annual review. Updated background information to include indication in those 2 years and older
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. Added state mandate footnote.
6/2023	Updated background to reflect approval for patients one month and older. Simplified reauthorization criteria and updated reference.
6/2024	Annual review. Increased initial authorization approval duration to 12 months. Updated reference.
6/2025	Annual review. Added notation in the CFTR gene mutations table. No changes to coverage criteria.
6/2026	Annual review. No changes to coverage criteria. Updated references.

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