

Drug Policy

Policy:	Kalydeco (ivacaftor)	Annual Review Date: 06/15/2023
		Last Revised Date: 06/15/2023

OVERVIEW

Kalydeco, a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator, is indicated for the treatment of cystic fibrosis (CF) in patients \geq 1 month of age who have who have one mutation in the CFTR gene that is responsive to Kalydeco potentiation based on clinical and/or *in vitro* assay data. Mutations with an increase in chloride transport of 10% or greater are considered responsive.¹ In patients with unknown genotype, a FDA-cleared CF mutation test should be used to detect the presence of the CFTR mutation followed by verification with bidirectional sequencing when recommended by the mutation test instructions for use. Kalydeco is not effective in patients with CF who are homozygous for the F508del mutation in the CFTR.¹ A patient must have at least one CFTR mutation responsive to ivacaftor to be indicated. Table 1 lists mutations that are responsive to Kalydeco.

Table 1. List of CFTR Gene Mutations that Produce CFTR Protein and are Responsive to Kalydeco.¹

2789+5G→A	F311del	I148T	R75Q	S549N
3272-26A→G	F311L	I175V	R1070Q	S549R
3849+10kbC→T	F508C	I807M	R1070W	S945L
711+3A→G	F508C;S1251N	I1027T	R117C	S977F
A120T	F1052V	I1139V	R117H	S589N
A234D	F1074L	K1060T	R347H	S737F
A349V	G1069R	L206W	R352Q	S1159F
A1067T	G1244E	L320V	R117G	S1159P
A455E	G1349D	L967S	R117L	T338I
D110E	G178R	L997F	R117P	T1053I
D1152H	G551D	L1480P	R170H	V232D
D110H	G551S	M152V	R347L	V562I
D192G	G194R	M952I	R553Q	V754M
D1270N	G314E	M952T	R668C	V1293G
D924N	G576A	P67L	R792G	W1282R
D579G	G970D	Q237E	R933G	Y1014C
E193K	Y1032C	Q237H	R1162L	G178E
E882K	G1249R	Q359R	R1283M	
E56K	H939R	Q1291R	S1251N	
E831X	H1375P	R74W	S1255P	

CFTR – Cystic fibrosis transmembrane regulator.

POLICY STATEMENT

This policy involves the use of Kalydeco. Prior authorization is recommended for pharmacy benefit coverage of Kalydeco. Approval is recommended for those who meet the conditions of coverage in the **Criteria and Initial/Extended Approval**

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for the diagnosis provided. **Conditions Not Recommended for Approval** are listed following the recommended authorization criteria. Requests for uses not listed in this policy will be reviewed for evidence of efficacy and for medical necessity on a case-by-case basis.

Because of the specialized skills required for evaluation and diagnosis of patients treated with Kalydeco as well as the monitoring required for adverse events and long-term efficacy, initial approval requires Kalydeco be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals for initial therapy are provided for the initial approval duration noted below; if reauthorization is allowed, a response to therapy is required for continuation of therapy unless otherwise noted below.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Kalydeco is recommended in those who meet the following criteria:

1. Cystic Fibrosis (CF); Initial Therapy

Criteria. *Patient must meet the following criteria (A, B, and C):*

- A) The patient has at least one mutation of the cystic fibrosis transmembrane conductance regulator (CFTR) gene that laboratory testing shows is susceptible to treatment with Kalydeco (Note: See Table 1 above for list of mutations); AND
- B) The patient is ≥ 1 month old; AND
- C) Kalydeco is prescribed by or in consultation with a pulmonologist or a physician who specializes in the treatment of CF.

2. Cystic Fibrosis; Continuation of Therapy

Criteria. *Patient must meet the following criteria (A and B):*

- A) Kalydeco is prescribed by or in consultation with a pulmonologist or a physician who specializes in the treatment of CF; AND
- B) The patient has experienced a beneficial response to therapy such as increase in weight; improvement in sweat chloride; improvement in predicted FEV1 or other lung function tests; decrease in amount/frequency of pulmonary exacerbations; decrease in amount/frequency of pulmonary infections; decrease in hospitalizations.

Initial Approval/ Extended Approval.

A) *Initial Approval:* 6 months

B) *Extended Approval:* 1 year

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Kalydeco has not been shown to be effective, or there are limited or preliminary data or potential safety concerns that are not supportive of general approval for the following conditions. (Note: This is not an exhaustive list of Conditions Not Recommended for Approval).

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- 1. Cystic Fibrosis (CF), Patients who are Homozygous for the phe508del (F508del) Mutation in the Cystic Fibrosis Transmembrane Regulator (CFTR) Gene.** Efficacy results from a double-blind, placebo controlled trial in patients with CF who were homozygous for the phe508del mutation in the CFTR gene showed no statistically significant difference in FEV₁ over 16 weeks of Kalydeco treatment compared with placebo. In a Phase II trial in patients homozygous for the F508del (n = 112) Kalydeco did not result in an improvement in FEV₁ relative to placebo.
- 2. Cystic Fibrosis (CF), Patients with Unknown Cystic Fibrosis Transmembrane Regulator (CFTR) Gene Mutation.** A Food and Drug Administration (FDA)-cleared CF mutation test should be used to detect the presence of the CFTR mutation prior to use of Kalydeco.
- 3. Combination Therapy with Orkambi, Symdeko, or Trikafta.** Orkambi, Symdeko, and Trikafta contain ivacaftor, the active agent in Kalydeco and therefore are not indicated in combination with Kalydeco.
- 4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria.** Criteria will be updated as new published data are available.

Documentation Requirements:

The Company reserves the right to request additional documentation as part of its coverage determination process. The Company may deny reimbursement when it has determined that the drug provided or services performed were not medically necessary, investigational or experimental, not within the scope of benefits afforded to the member and/or a pattern of billing or other practice has been found to be either inappropriate or excessive. Additional documentation supporting medical necessity for the services provided must be made available upon request to the Company. Documentation requested may include patient records, test results and/or credentials of the provider ordering or performing a service. The Company also reserves the right to modify, revise, change, apply and interpret this policy at its sole discretion, and the exercise of this discretion shall be final and binding.

REFERENCES

1. Kalydeco® tablets and oral granules [prescribing information]. Cambridge, MA: Vertex Pharmaceuticals, Inc; August 2018.
2. Farrell PM, Rosenstein BJ, White TB, et al. Guidelines for diagnosis of cystic fibrosis in newborns through older adults: Cystic Fibrosis Foundation consensus report. *J Pediatr.* 2008;153:S4-S14.
3. De Bock K, Munck A, Walker S, et al. Efficacy and safety of ivacaftor in patients with cystic fibrosis and a non-*G551D* gating mutation. *J Cyst Fibros.* 2014;13:674-680
4. Cystic Fibrosis Foundation Annual Report. Available at: <http://www.cff.org/UploadedFiles/aboutCFFoundation/AnnualReport/2013-Annual-Report.pdf>. Accessed on: August 7, 2017.
5. Ivacaftor. In: DRUGDEX [online database]. Truven Health Analytics; Greenwood Village, CO. Last updated 28 September 2020. Accessed on 7 October 2020.
6. Institute for Clinical and Economic Review (ICER). Modulator Treatments for Cystic Fibrosis: Effectiveness and Value. May 3, 2018.