

Clinical Policy: Ivacaftor (Kalydeco)

Reference Number: PA.CP.PHAR.210

Effective Date: 01/2018

Last Review Date: 07/2025

Description

Ivacaftor (Kalydeco®) is a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator.

FDA Approved Indication(s)

Kalydeco is indicated for the treatment of cystic fibrosis (CF) in patients age 1 month and older who have 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.

Policy/Criteria

It is the policy of PA Health & Wellness that Kalydeco is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cystic Fibrosis (must meet all):

1. Diagnosis of CF;
2. Presence of one mutation in the CFTR gene responsive to ivacaftor based on clinical and/or *in vitro* assay data (*see Appendix E*);
3. Confirmation that a homozygous *F508del* mutation in the CFTR gene is not present;
4. Age $\geq$ 1 month;
5. Prescribed by or in consultation with a pulmonologist or cystic fibrosis specialist;
6. Documentation indicates member has baseline forced expiratory volume in 1 second (FEV1), unless member is unable to perform spirometry testing;
7. Kalydeco is not prescribed concurrently with other ivacaftor-containing CFTR modulator combination products (e.g., Alyftrek, Orkambi, Symdeko, Trikafta);
8. Dose does not exceed one of the following (a-g):
 - a. Age 1 month to < 2 months and weight $\geq$ 3 kg (both i and ii):
 - i. 11.6 mg per day;
 - ii. 2 packets per day;
 - b. Age 2 months to < 4 months and weight $\geq$ 3 kg (both i and ii):
 - i. 26.8 mg per day;
 - ii. 2 packets per day;
 - c. Age 4 months to < 6 months and weight $\geq$ 5 kg (both i and ii):
 - i. 50 mg per day;
 - ii. 2 packets per day;
 - d. Age 6 months to < 6 years and weight 5 kg to < 7 kg (both i and ii):
 - i. 50 mg per day;
 - ii. 2 packets per day;

- e. Age 6 months to < 6 years and weight 7 kg to < 14 kg (both i and ii):
 - i. 100 mg per day;
 - ii. 2 packets per day;
- f. Age 6 months to < 6 years and weight $\geq$ 14 kg (both i and ii):
 - i. 150 mg (2 packets) per day.
 - ii. 2 packets per day.
- g. Age $\geq$ 6 years (both i and ii):
 - i. 300 mg per day;
 - ii. 2 tablets per day

Approval duration: 6 months

B. Other diagnoses/indications: Refer to PA.CP.PMN.53 for Medicaid.

II. Continued Approval

A. Cystic Fibrosis (must meet all):

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy (e.g.: stable or improved pulmonary function, improved quality of life, reduced hospitalization) OR the member continues to benefit from therapy based on the prescriber's assessment;
3. Kalydeco is not prescribed concurrently with other ivacaftor-containing CFTR modulator combination products (e.g., Alyftrek, Orkambi, Symdeko, Trikafta);
4. If request is for a dose increase, new dose does not exceed one of the following (a-g):
 - a. Age 1 month to < 2 months and $\geq$ 3 kg (both i and ii):
 - i. 11.6 mg per day;
 - ii. 2 packets per day;
 - b. Age 2 months to < 4 months and $\geq$ 3 kg (both i and ii):
 - i. 26.8 mg per day;
 - ii. 2 packets per day;
 - c. Age 4 months to < 6 months and weight $\geq$ 5 kg (both i and ii):
 - i. 50 mg per day;
 - ii. 2 packets per day;
 - d. Age 6 months to < 6 years and weight 5 kg to < 7 kg (both i and ii):
 - i. 50 mg per day;
 - ii. 2 packets per day;
 - e. Age 6 months to < 6 years and weight 7 kg to < 14 kg (both i and ii):
 - i. 100 mg per day;
 - ii. 2 packets per day;
 - f. Age 6 months to < 6 years and weight $\geq$ 14 kg (both i and ii):
 - i. 150 mg per day;
 - ii. 2 packets per day;
 - g. Age $\geq$ 6 years (both i and ii):
 - i. 300 mg per day;
 - ii. 2 tablets per day.

Approval duration: 12 months

B. Other diagnoses/indications (1 or 2):

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.

Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to PA.CP.PMN.53

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ACFLD: advanced cystic fibrosis lung disease

CF: cystic fibrosis

CFF: Cystic Fibrosis Foundation

CFTR: cystic fibrosis transmembrane conductance regulator

FDA: Food and Drug Administration

LCI: lung clearance index

MAP: Mutation Analysis Program

MBW: multiple-breath washout

ppFEV1: percent predicted forced expiratory volume in 1 second

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- The Cystic Fibrosis Foundation (CFF) Mutation Analysis Program (MAP; available here: <https://www.cff.org/medical-professionals/mutation-analysis-program>). The MAP is a free and confidential genetic testing program for people with a strongly suspected or confirmed diagnosis of CF.
- Kalydeco is not effective in patients with CF who are homozygous for the F508del mutation in the CFTR gene.
- It is recommended that transaminases (ALT and AST) be assessed prior to initiating Kalydeco, every 3 months during the first year of treatment, and annually thereafter. Dosing should be interrupted in patients with ALT or AST of greater than 5 times the upper limit of normal.
- Data from the study of CF patients with nine *CFTR* mutations did not support approval of the drug in patients with the G970R mutation. As of 2014, it is estimated that there are about 10 people worldwide who have this mutation, including two in the United States.
- Regarding the diagnostic criteria for CF of “genetic testing confirming the presence of two disease-causing mutations in *CFTR* gene,” this is to ensure that whether heterozygous or homozygous, there are two disease-causing mutations in the *CFTR* gene, one from each parental allele.
- Most children can do spirometry by age 6, though some preschoolers are able to perform the test at a younger age. Some young children aren’t able to take a deep enough breath and blow out hard and long enough for spirometry.

Appendix E: CFTR Gene Mutations that are Responsive to Kalydeco

CFTR Gene Mutations that are Responsive to Kalydeco				
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	

[†] 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.

IV. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
CF	<i>Pediatric patients 1 month to less than 2 months of age and weighing at least 3 kg: one 5.8 mg packet mixed with 1 teaspoon (5 mL) of age-appropriate soft food or liquid and PO every 12 hours with fat containing food.</i>	Age 1 month to < 2 months and weight ≥ 3 kg: 11.8 mg/day
	<i>Pediatric patients 2 months to less than 4 months of age and weighing at least 3 kg: one 13.4 mg packet mixed with 1 teaspoon (5 mL) of age-appropriate soft food or liquid and PO every 12 hours with fat containing food.</i>	Age 2 months to < 4 months and weight ≥ 3 kg: 26.8 mg/day
	<i>Pediatric patients 4 months to less than 6 months of age and weighing at least 5 kg: one 25 mg packet mixed with 1 teaspoon (5 mL) of age-appropriate soft food or liquid and PO every 12 hours with fat containing food.</i>	Age 4 months to < 6 months and weight ≥ 5 kg: 50 mg/day

Indication	Dosing Regimen	Maximum Dose
	<i>Pediatric patients 6 months to less than 6 years of age weighing 5 kg to less than 7 kg: one 25 mg packet mixed with 1 teaspoon (5 mL) of age-appropriate soft food or liquid and PO every 12 hours with fat containing food.</i>	Age 6 months to < 6 years and weight 5 kg to < 7 kg: 50 mg/day
	<i>Pediatric patients 6 months to less than 6 years of age weighing 7 kg to less than 14 kg: one 50 mg packet mixed with 1 teaspoon (5 mL) of age-appropriate soft food or liquid and PO every 12 hours with fat containing food.</i>	Age 6 months to < 6 years and weight 7 kg to < 14 kg: 100 mg/day
	<i>Pediatric patients 6 months to less than 6 years of age weighing 14 kg or greater: one 75 mg packet mixed with 1 teaspoon (5 mL) of age-appropriate soft food or liquid and PO every 12 hours with fat-containing food.</i>	Age 6 months to < 6 years and weight $\geq$ 14 kg: 150 mg/day
	<i>Adults and pediatric patients age 6 years and older: one 150 mg tablet PO every 12 hours with fat-containing food.</i>	Age $\geq$ 6 years: 300 mg/day

V. Product Availability

- Tablet: 150 mg
- Unit-dose packets (56 packets per carton) containing oral granules: 5.8 mg, 13.4 mg, 25 mg, 50 mg, 75 mg

VI. References

1. Kalydeco Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc.; August 2023. Available at: https://pi.vrtx.com/files/uspi_ivacaftor.pdf. Accessed April 14, 2025.
2. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines: Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med*. 2013; 187(7): 680-689.
3. Farrell PM, White TB, Ren CL et al. Diagnosis of cystic fibrosis: Consensus guidelines from the Cystic Fibrosis Foundation. *J Pediatr*. 2017; 181S: S4-15.
4. Ren CL, Morgan RL, Oermann C, et al. Cystic Fibrosis Foundation pulmonary guidelines: Use of cystic fibrosis transmembrane conductance regulator modulator therapy in patients with cystic fibrosis. *Ann Am Thorac Soc*. 2018; 15(3): 271-280.
5. Alexander S, Alshafi K, Al-Yaghchi C, et al. Clinical Guidelines: Care of Children with Cystic Fibrosis. Royal Brompton and Harefield NHS. 2020;(8):22-23.
6. Kapnadak SG, Dimango E, Hadjiliadis D, et al. Cystic Fibrosis Foundation consensus guidelines for the care of individuals with advanced cystic fibrosis lung disease. *J Cyst Fibros*. 2020 May;19(3):344-354.
7. Cystic Fibrosis Foundation: Clinical Care Guidelines. Available at: <https://www.cff.org/medical-professionals/clinical-care-guidelines>. Accessed April 15, 2025.

Reviews, Revisions, and Approvals	Date
References reviewed and updated.	02/2018
1Q 2019 annual review: references reviewed and updated.	01/2019
1Q 2020 annual review: added the following criteria to initial approval: prescriber requirement of pulmonologist or cystic fibrosis specialist, requirement for baseline FEV1 unless unable to perform spirometry, requirement that Kalydeco not be prescribed concurrently with other ivacaftor-containing CFTR modulator combination products; added the following to continued therapy criteria: not prescribed concurrently with other CFTR modulators; references reviewed and updated.	01/2020
1Q 2021 annual review: FDA approved pediatric age extension added from 6 months to 4 months with updated dosing; references reviewed and updated.	01/2021
1Q 2022 annual review: updated Appendix E with CFTR mutations that are responsive to Kalydeco based on the updated Prescribing Information; references reviewed and updated.	01/2022
1Q 2023 annual review: no significant changes; updated Appendix D; references reviewed and updated.	01/2023
3Q 2023 annual review: revised criteria to include pediatric expansion and new 5.8 mg and 13.4 mg granule strengths; references reviewed and updated.	07/2023
3Q 2024 annual review: no significant changes; references reviewed and updated.	07/2024
3Q 2025 annual review: added Alyftrek to list of CFTR modulator concurrent exclusion criteria; references reviewed and updated.	07/2025