Clinical Policy: Ivacaftor (Kalydeco)

Reference Number: PA.CP.PHAR.210
Effective Date: 01/18
Last Review Date: 01/19

Coding Implications
Revision Log

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 12 months 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 Pennsylvania Health and Wellness that Kalydeco is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cystic Fibrosis (must meet all):

1. Age ≥ 12 months;
2. Diagnosis of cystic fibrosis (CF);
3. Presence of one mutation in the CFTR gene responsive to ivacaftor based on clinical and/or in vitro assay data *(see Appendix E)*;
4. Confirmation that a homozygous *F508del* mutation in the *CFTR* gene is not present;
5. Prescribed total daily dose of Kalydeco does not exceed the following:
   a. Age 12 months to < 6 years and < 14 kg: 100 mg (granules);
   b. Age 12 months to < 6 years and ≥ 14 kg: 150 mg (granules);
   c. Age ≥ 6 years: 300 mg (tablets).

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 Pennsylvania Health and Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.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. If request is for a dose increase, new dose does not exceed one of the following (a, b, or c):
   a. Age 12 months to < 6 years and < 14 kg: 100 mg (granules);
   b. Age 12 months to < 6 years and ≥ 14 kg: 150 mg (granules);
   c. Age ≥ 6 years: 300 mg (tablets).

Approval duration: 12 months

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

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

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

2. Refer to PA.CP.PMN.53 for Medicaid..

Background

Description/Mechanism of Action:

The CFTR protein is a chloride channel present on the surface of epithelial cells in multiple organs. Ivacaftor facilitates increased chloride transport by potentiating the channel-open probability (or gating) of the CFTR protein.

III. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

CF: cystic fibrosis
CFTR: cystic fibrosis transmembrane conductance regulator
FDA: Food and Drug Administration

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- The Cystic Fibrosis Foundation's Mutation Analysis Program (MAP; available here: http://www.cfpaf.org/ResourceCenter/MutationAnalysisProgram) offers free and confidential genetic testing to patients with a confirmed diagnosis of CF. It can take up to 60 days to receive genotyping results and additional time if further testing is needed.
- 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.

Appendix E: CFTR Gene Mutations that are Responsive to Kalydeco

CFTR Gene Mutations that are Responsive to Kalydeco				
A1067T	E56K	G551S	R347H	S977F
A455E	F1052V	K1060T	R352Q	2789+5G→A (28)
D110E	F1074L	L206W	R74W	3272-26A→G (23)
D110H	G1069R	P67L	S1251N	3849+10kBc→T (40)
D115H	G1244E	R1070Q	S1255P	711+3A→G (2)
D1270N	G1349D	R1070W	S459R	E831X (1)
D579G	G178R	R117C	S549N	
E193K	G551D	R117H	S945L	

IV. Dosage and Administration

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

V. Product Availability

- Tablets: 150 mg
- Unit-dose packets containing oral granules: 50 mg, 75 mg

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
N/A	

Reviews, Revisions, and Approvals	Date	Approval Date
References reviewed and updated.	02/18	
1Q 2019 annual review: references reviewed and updated.	01/19	

References

1. Kalydeco Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc.; August 2018. Available at https://www.kalydeco.com/. Accessed November 9, 2018.
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.