Prior Authorization Review Panel

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CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 02/01/2021**
Policy Number: PA.CP.PHAR.210	**Effective Date: 01/2018** **Revision Date: 01/2021**
Policy Name: Ivacaftor (Kalydeco)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

1Q 2021 annual review: FDA approved pediatric age extension added from 6 months to 4 months with updated dosing;.references reviewed and updated.

Name of Authorized Individual (Please type or print): **Auren Weinberg, MD**	**Signature of Authorized Individual:** 

Clinical Policy: Ivacaftor (Kalydeco)

Reference Number: PA.CP.PHAR.210
Effective Date: 01/2018
Last Review Date: 01/2021

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 4 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. 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 ≥ 4 months;
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., Orkambi, Symdeko, Trikafta);
8. Dose does not exceed one of the following (a, b, c, d, or e):
   a. Age ≥ 6 years: 300 mg (2 tablets) per day;
   b. Age 4 months to < 6 months and weight ≥ 5 kg: 50 mg (2 packets) per day;
   c. Age 6 months to < 6 years and weight 5 kg to < 7 kg: 50 mg (2 packets) per day;
   d. Age 6 months to < 6 years and weight 7 kg to < 14 kg: 100 mg (2 packets) per day;
   e. Age 6 months to < 6 years and weight ≥ 14 kg: 150 mg (2 packets) 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 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. Kalydeco is not prescribed concurrently with other ivacaftor-containing CFTR modulator combination products (e.g., Orkambi, Symdeko, Trikafta);
4. If request is for a dose increase, new dose does not exceed one of the following (a, b, c, d, or e):
    a. Age ≥ 6 years: 300 mg (2 tablets) per day;
    b. Age 4 months to < 6 months and weight ≥ 5 kg: 50 mg (2 packets) per day;
    c. Age 6 months to < 6 years and weight 5 kg to < 7 kg: 50 mg (2 packets) per day;
    d. Age 6 months to < 6 years and weight 7 kg to < 14 kg: 100 mg (2 packets) per day;
    e. Age 6 months to < 6 years and weight ≥ 14 kg: 150 mg (2 packets) per day.

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

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

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
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: 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.
- 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. Forced oscillometry is another way to test lung function in young children. This test measures how easily air flows in the lungs (resistance and compliance) with the use of a machine.
- NHS Clinical Guidelines: Care of Children with Cystic Fibrosis: Normal ranges for LCI are device specific and still being established, but in general a value > 8.0 is above the normal range and > 10.0 is significantly abnormal.
- CFF 2020 guidelines for advanced cystic fibrosis lung disease (ACFLD):
  - Define ACFLD as ppFEV1 < 40% when stable or referred for lung transplantation evaluation or previous intensive care unit (ICU) admission for respiratory failure, hypercarbia, daytime oxygen requirement at rest (excluding nocturnal use only), pulmonary hypertension, severe functional impairment from respiratory disease (New York Heart Association Class IV), six-minute walk test distance < 400m.
  - No recommendations on the start or continuation of CFTR modulator therapy with ACFLD guidelines.
  - Treatment recommendations included: lung transplantation, supplemental oxygen, continuous alternating inhaled antibiotics, and systemic corticosteroids.

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)

CFTR Gene Mutations that are Responsive to Kalydeco				
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 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 soft food or liquid and PO every 12 hours with fat containing food.	Age 4 months to < 6 months and weight ≥ 5 kg: 50 mg/day
	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 soft food or liquid and PO every 12 hours with fat containing food.	Age 6 months to < 6 years and weight 5 kg to < 7 kg: 50 mg/day
	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 soft food or liquid and PO every 12 hours with fat containing food.	Age 6 months to < 6 years and weight 7 kg to < 14 kg: 100 mg/day
	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 soft food or liquid and PO every 12 hours with fat-containing food.	Age 6 months to < 6 years and weight ≥ 14 kg: 150 mg/day

V. Product Availability

- Tablets: 150 mg
- Unit-dose packets containing oral granules: 25 mg, 50 mg, 75 mg

VI. References

1. Kalydeco Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc.; September 2020. Available at https://www.kalydeco.com/. Accessed November 9, 2020.
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. Davies J, Sheridan P, Lee P, et al. Effect of ivacaftor on lung function in subjects with CF who have the G551D-CFTR mutation and mild lung disease: a comparison of lung clearance index (LCI) vs. spirometry. Journal of Cystic Fibrosis. 2012;11(1):S15.
6. 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.
7. 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.

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