Clinical Policy: Ivacaftor (Kalydeco)
Reference Number: CP.CPA.95
Effective Date: 11.16.16
Last Review Date: 11.17
Line of Business: Commercial

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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

FDA approved indication
Kalydeco is indicated for the treatment of cystic fibrosis (CF) in patients age 2 years 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
Provider must submit documentation (which may include office chart notes and lab results) supporting that member has met all approval criteria

It is the policy of health plans affiliated with Centene Corporation® that Kalydeco is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Cystic Fibrosis (must meet all)**:**

1. Diagnosis of cystic fibrosis (CF);
2. Age ≥ 2 years;
3. Presence of one mutation in the CFTR gene responsive to ivacaftor based on clinical and/or in vitro assay data *(Refer to Appendix B)*;
4. Confirmation that a homozygous F508del mutation in the CFTR gene is not present;
5. Dose does not exceed one of the following (a, b, or c):
   a. Age ≥ 6 years: 300 mg/day (2 tablets/day);
   b. Age 2 to < 6 years and < 14 kg: 100 mg/day (2 packets/day);
   c. Age 2 to < 6 years and ≥ 14 kg: 150 mg/day (2 packets/day).

Approval duration: Length of Benefit

B. Other diagnoses/indications

1. Refer to CP.CPA.09 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

II. Continued Therapy

A. Cystic Fibrosis (must meet all)**:**
1. Currently receiving medication via a health plan affiliated with Centene Corporation or member has previously met initial approval criteria;
2. Member is responding positively to therapy (e.g., stable or improved pulmonary function, improved quality of life, reduced hospitalization);
3. If request is for a dose increase, new dose does not exceed one of the following:
   a. Age ≥ 6 years: 300 mg/day (2 tablets/day);
   b. Age 2 to < 6 years and < 14 kg: 100 mg/day (2 packets/day);
   c. Age 2 to < 6 years and ≥ 14 kg: 150 mg/day (2 packets/day).

Approval duration: Length of Benefit

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via a health plan affiliated with Centene Corporation and documentation supports positive response to therapy.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to CP.CPA.09 if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized).

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off-label use policy – CP.CPA.09 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

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

Appendix B: 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	

Appendix C: Therapeutic Alternatives

N/A

Appendix D: General Information

- 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.
- The Cystic Fibrosis Foundation's Mutation Analysis Program (MAP) offers free and confidential genetic testing to patients with a confirmed diagnosis of cystic fibrosis. It can take up to 60 days to receive genotyping results and additional time if further testing is needed. http://www.cfpaf.org/ResourceCenter/MutationAnalysisProgram/
- Kalydeco is not effective in patients with CF who are homozygous for the F508del mutation in the CFTR gene.
- It is recommended that 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 (ULN).

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Cystic fibrosis	Adults and pediatric patients age 6 years and older: one 150 mg tablet taken orally every 12 hours with fat-containing food.	Age ≥ 6 years: 300 mg/day
	Pediatric patients 2 to less than 6 years of age and less than 14 kg: one 50 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours with fat containing food.	Age 2 to < 6 years and < 14 kg: 100 mg/day
	Pediatric patients 2 to less than 6 years of age and 14 kg or greater: one 75 mg packet mixed with 1 teaspoon (5 mL) of soft food or liquid and administered orally every 12 hours with fat-containing food.	Age 2 to < 6 years and ≥ 14 kg: 150 mg/day

VI. Product Availability

- Tablets: 150 mg
- Oral granules: Unit-dose packets of 50 mg and 75 mg

VII. References

1. Kalydeco Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc.; May 2017. Available at https://www.kalydeco.com/ Accessed June 5, 2017.
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. April 1, 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. Data on file. Vertex Pharmaceuticals Incorporated, Boston, MA.

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Converted to new template; minor changes to verbiage and grammar. References updated.	01.17	08.17
Policy updated with additional gene mutations. Appendix B added. Added age restriction per prescribing information. Added maximum dose for pediatric patients.	06.17	11.17

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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