RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title:	lumacaftor/ivacaftor
Policy Number:	RxA.435
Drug(s) Applied:	Orkambi®
Original Policy Date:	03/06/2020
Last Review Date:	09/14/2020
Line of Business Policy Applies to:	All lines of business

Background

Lumacaftor/ivacaftor (Orkambi®) is a combination drug for cystic fibrosis (CF). Lumacaftor improves the conformational stability of F508del-cystic fibrosis transmembrane conductance regulator (CFTR), while ivacaftor is a CFTR potentiator.

Orkambi is indicated for the treatment of CF in patients age 2 years and older who are homozygous for the F508del mutation in the CFTR gene.

If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of the F508del mutation on both alleles of the CFTR gene.

Limitation(s) of use: The efficacy and safety of Orkambi® have not been established in patients with CF other than those homozygous for the F508del mutation.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
Lumacaftor/Ivacaftor (Orkambi®)	CF	Adults and pediatric patients age 12 years and older: two tablets (each containing lumacaftor 200 mg/ivacaftor 125 mg) PO Q12H Pediatric patients age 6 through 11 years: two tablets (each containing lumacaftor 100 mg/ivacaftor 125 mg) PO Q12H Pediatric patients age 2 through 5 years and weighing < 14 kg: one packet of granules (each containing lumacaftor 100 mg/ivacaftor 125 mg) PO Q12H	Adults and pediatric patients age 12 years and older: lumacaftor 800 mg/ivacaftor 500 mg per day Pediatric patients age 6 through 11 years: lumacaftor 400 mg/ivacaftor 500 mg per day Pediatric patients age 2 through 5: <14 kg - lumacaftor 200 mg/ivacaftor 250 mg per day

		Pediatric patients age 2 through 5 years and weighing ≥ 14 kg: one packet of granules (each containing lumacaftor 150 mg/ivacaftor 188 mg) PO Q12H	≥ 14 kg - lumacaftor 300 mg/ivacaftor 376 mg per day

Dosage Forms

- Tablets: lumacaftor 100 mg and ivacaftor 125 mg, lumacaftor 200 mg and ivacaftor 125 mg.
- Oral granules: Unit-dose packets of lumacaftor 100 mg and ivacaftor 125 mg, lumacaftor 150 mg and ivacaftor 188 mg.

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

I. Initial Approval Criteria

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

1. Diagnosis of CF;
2. Age ≥ 2 years;
3. Member is homozygous for the F508del mutation in the CFTR gene;
4. Dose does not exceed one of the following (a, b, c, or d):
   a. Age 2 to 5 years weighing < 14 kg: lumacaftor 200 mg/ivacaftor 250 mg per day (2 packets per day);
   b. Age 2 to 5 years weighing ≥ 14 kg: lumacaftor 300 mg/ivacaftor 376 mg per day (2 packets per day);
   c. Age 6 to 11 years: lumacaftor 400 mg/ivacaftor 500 mg per day (4 tablets per day);
   d. Age ≥ 12 years: lumacaftor 800 mg/ivacaftor 500 mg per day (4 tablets per day).

Approval Duration
Commercial: 6 months
Medicaid/HIM: 6 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is responding positively to therapy;
3. If request is for a dose increase, new dose does not exceed one of the following (a, b, c, or d):
   a. Age 2 to 5 years weighing < 14 kg: lumacaftor 200 mg/ivacaftor 250 mg per day (2 packets per day);
   b. Age 2 to 5 years weighing ≥ 14 kg: lumacaftor 300 mg/ivacaftor 376 mg per day (2 packets per day);
   c. Age 6 to 11 years: lumacaftor 400 mg/ivacaftor 500 mg per day (4 tablets per day);
   d. Age ≥ 12 years: lumacaftor 800 mg/ivacaftor 500 mg per day (4 tablets per day).

Approval Duration
Commercial: 12 months
Medicaid/HIM: 12 months

III. Appendices

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

- Contraindication(s):
  - None
- Boxed Warning(s):
  - None

APPENDIX D: General Information

- 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. 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.

References

1. Orkambi Prescribing Information. Boston, MA: Vertex Pharmaceuticals, Inc. July 2019. Available at http://www.orkambi.com. Accessed July 24, 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. Accessed July 24, 2020.
3. 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. Accessed July 24, 2020.
4. 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. Accessed July 24, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/2020	03/06/2020
Policy was reviewed: 1) Policy title was updated. 2) Continued Therapy Approval criteria II.A.1 was rephrased. 3) Appendices updated. 4) References were updated.	03/06/2020	09/14/2020