GUIDELINES FOR USE (NOTE: FOR RENEWAL CRITERIA SEE BELOW)

INITIAL CRITERIA

1. Does the patient have a diagnosis of cystic fibrosis (CF) and meets all the following criteria?
   - Patient has one of the following mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R or R117H (documentation required)
   - Patient is ≥ 2 years old
   - Patient is NOT homozygous for the F508del-CFTR mutation
   - Prescribed by or in consultation with a pulmonologist or CF expert
   - Previously treated or currently treated with another agent for CF (examples include oral inhaled corticosteroid, bronchodilator, inhaled antibiotics, dornase alfa, or acetylcysteine)
   - Baseline FEV1 of at least 40% for patients age 6 years and older as documented by lab report or chart notes (baseline FEV1 not required for patients younger than 6 years of age)
   - Patient is not on concurrent therapy with Orkambi
   - Patient is not currently pregnant

   If yes, continue to #2.
   If no, do not approve.

   DENIAL TEXT: See the initial denial text at the end of the guideline.

2. Is the patient of age 6 years or older?

   If yes, approve for 12 months by HICL with a quantity limit of #2 tablets per day.
   If no, continue to #3.

3. Does the patient weigh less than 14kg (documentation of weight required)?

   If yes, approve for 12 months by HICL with a quantity limit of two 50mg packets per day.
   If no, approve for 12 months by HICL with a quantity limit of two 75mg packets per day.

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IVACAFTOR

INITIAL CRITERIA (CONTINUED)

INITIAL DENIAL TEXT: Our guideline for IVACAFTOR requires a diagnosis of cystic fibrosis. For patients who are between 2 to 5 years of age, Ivacaftor packets will be approved. Documentation of patient's weight is required.

In addition, the following criteria must also be met:
- Patient has one of the following mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R or R117H (documentation required)
- Patient is ≥ 2 years old
- Patient is NOT homozygous for the F508del-CFTR mutation
- Prescribed by or in consultation with a pulmonologist or CF expert
- Previously treated or currently treated with another agent for CF (examples include oral inhaled corticosteroid, bronchodilator, inhaled antibiotics, dornase alfa, or acetylcysteine)
- Baseline FEV1 of at least 40% for patients age 6 years and older as documented by lab report or chart notes (baseline FEV1 not required for patients younger than 6 years of age)
- Patient is not on concurrent therapy with Orkambi
- Patient is not currently pregnant

RENEWAL CRITERIA

1. Does the patient have a diagnosis of cystic fibrosis (CF) and meets all the following criteria?
   - Improvement in CF as indicated by one of the following: maintained or improvement in FEV1 or BMI or reductions in pulmonary exacerbations (documentation must be provided)

   If yes, approve for 12 months by HICL with a quantity limit of #4 tablets per day.
   If no, do not approve.

RENEWAL DENIAL TEXT: Our guideline for IVACAFTOR renewal requires a diagnosis of cystic fibrosis. In addition, the following criteria must also be met:
- Improvement in CF as indicated by one of the following: maintained or improvement in FEV1 or BMI or reductions in pulmonary exacerbations (documentation must be provided)

RATIONALE
Promote appropriate utilization of Kalydeco based on FDA approved indication.

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IVACAFTOR

RATIONALE (CONTINUED)
CF is an inherited chronic disease that affects about 30,000 patients in the US. A defective cystic fibrosis transmembrane conductance regulator (CFTR) protein leads to production of unusually thick, sticky mucus that clogs the lungs and prevents the body from breaking down and absorbing food. Ivacaftor increases chloride transport by potentiating the channel open probability of G551D-CFTR protein resulting in more fluid mucus. About 4-5% of CF patients have a G551D mutation. There is no cure for this disease however current treatments that offer symptomatic relief include the single source brands: Cayston, Pulmozyme, and Tobi. Two double-blind trials randomized clinically stable patients with CF who have a G551D mutation to ivacaftor 150mg twice daily (n=109) or placebo (n=104) for 48 weeks. Patients could receive other CF treatments. Trial 1 involved patients 12 years of age and older while trial 2 involved patients who were 6 to 11 years of age. In both trials change from baseline in percent predicted pre-dose FEV1 through 24 weeks of treatment significantly increased: 10.6% in trial 1 and 12.5% in trial 2.

Common adverse reactions include headache, oropharyngeal pain, upper respiratory tract infection, nasal congestion, abdominal pain, nasopharyngitis, diarrhea, rash, nausea, and dizziness. Transaminases (ALT and AST) should be assessed prior to initiation of therapy, every 3 month during first year of treatment and annually thereafter.

DOSAGE
Adults and pediatric patients age 6 years and older: one 150mg tablet every 12 hours with fat-containing food. Reduce dose to 150mg twice weekly when co-administered with strong CYP3A inhibitors and reduce dose to 150mg once daily when co-administered with moderate CYP3A inhibitors. Avoid food containing grapefruit or Seville oranges.

Pediatric patients 2 to less than 6 years of age and less than 14kg: one 50mg packet mixed with 1 teaspoon of soft food or liquid and administered orally every 12 hours with fat-containing food.

Pediatric patients 2 to less than 6 years of age and 14kg or greater: one 75mg packet mixed with 1 teaspoon of soft food or liquid and administered orally every 12 hours with fat-containing food.

FDA APPROVED INDICATIONS
Kalydeco is a cystic fibrosis transmembrane conductance regulator (CFTR) potentiator indicated for the treatment of cystic fibrosis (CF) in patients age 2 years and older who have one of the following mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, or S549R. Kalydeco is also indicated for the treatment of CF in patients age 2 years and older who have an R117H 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 a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

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LIMITATIONS OF USE
Not effective in patients with CF who are homozygous for the F508del mutation in the CFTR gene.
Kalydeco has not been studied in other populations of patients with CF.

REFERENCES