Updated: 10/2017
PARP Approved: 11/2017

Gateway Health
Prior Authorization Criteria

Kalydeco (ivacafor) or Orkambi (lumacaftor/ivacaftor)

All requests for Kalydeco (ivacafor) or Orkambi (lumacaftor/ivacaftor) require a prior authorization and will be screened for medical necessity and appropriateness using the criteria listed below.

Kalydeco (ivacafor) or Orkambi (lumacaftor/ivacaftor) Prior Authorization Criteria:

Coverage is provided in the following situations:

- Member is at least 6 years of age for Orkambi® and 2 years of age for Kalydeco®
- Member must have a diagnosis of cystic fibrosis
- The prescriber is a cystic fibrosis specialist
- Documentation has been submitted with the request that the member has two copies of the *F508del* mutation in the CFTR gene for Orkambi®
- Documentation has been submitted with the request that the member has **one** of the listed mutations in the CFTR gene (See table below for all listed mutations as noted from the package labeling) for Kalydeco®
- Baseline liver function tests (ALT and AST) and lung function tests (FEV1) were completed.
- The member is not on strong CYP3A inducers (as they may decrease the effectiveness of Kalydeco and Orkambi) such as: rifampin, rifabutin, phenobarbital, carbamazepine, phenytoin or St. John's wort.
- Orkambi® dosing schedule of 2 tablets every 12 hours unless:
  - There is moderate hepatic impairment (Child Pugh class B as determined by table below or submitted by physician) where the dosing should be 2 tablets each morning and 1 tablet in the evening
  - There is severe hepatic impairment (Child Pugh class C as determined by table below or submitted by physician) where the dosing should be 1 tablet in the morning and 1 tablet in the evening, or less, after risks and benefits have been weighed for use
  - The member is currently on a CYP3A Inhibitor (such as ketoconazole, itraconazole, voriconazole, posaconazole, telithromycin, clarithromycin, erythromycin) where the dose should be initiated at 1 tablet daily for the first week and then increased to the recommended dose.
- Kalydeco® dosing schedule of 150mg twice daily for members 6 years of age and older; 75mg twice daily for members 2-5 years of age weighing 14kg or more; and 50mg twice daily for members 2-5 years of age weighing less than 14kg:
  - There is moderate hepatic impairment (Child Pugh class B as determined by table below or submitted by physician) where the dosing should be 150mg daily for members 6 years of age and older; 75mg daily for members 2-5 years of age weighing 14kg or more; and 50mg daily for members 2-5 years of age weighing less than 14kg

- There is severe hepatic impairment (Child Pugh class C as determined by table below or submitted by physician) where the dosing should be one tablet or packet of granules once daily or less frequently, after risks and benefits have been weighed for use
- The member is currently on a CYP3A Inhibitor (such as ketoconazole, itraconazole, voriconazole, posaconazole, telithromycin, clarithromycin, erythromycin) where the dose frequency should be cut to daily dosing such as in hepatic impairment dosing or even less frequent.

- Upon approval, coverage benefit will be 3 months.

Re-authorization Criteria

- The member remains not being on strong CYP3A inducers
- Documentation the member has not had worsened lung function (i.e. maintained or improved FEV1 from baseline)
- Liver function tests have been completed every 3 months during the first year of treatment. Annual liver function tests are required after the first year of therapy unless elevations are reported during therapy or the member has a history of elevated liver enzymes.
    - Authorization will not be approved if:
        - AST/ALT are 5 times the upper normal limit if bilirubin is within normal limits
        - AST/ALT are 3 times the upper normal limit if bilirubin is 2 times the upper normal limit (Orkambi only)
- Orkambi® dosing schedule of 2 tablets every 12 hours unless:
    - There is moderate hepatic impairment (Child Pugh class B as determined by table below or submitted by physician) where the dosing should be 2 tablets each morning and 1 tablet in the evening
- Kalydeco® dosing schedule of 150mg twice daily for members 6 years of age and older; 75mg twice daily for members 2-5 years of age weighing 14kg or more; and 50mg twice daily for members 2-5 years of age weighing less than 14kg:
    - There is moderate hepatic impairment (Child Pugh class B as determined by table below or submitted by physician) where the dosing should be 150mg daily for members 6 years of age and older; 75mg daily for members 2-5 years of age weighing 14kg or more; and 50mg daily for members 2-5 years of age weighing less than 14kg
    - The member is currently on a CYP3A Inhibitor (such as ketoconazole, itraconazole, voriconazole, posaconazole, telithromycin, clarithromycin, erythromycin) where the dose frequency should be cut to daily dosing such as in hepatic impairment dosing or even less frequent.
- Upon approval, coverage benefit will be 6 months.

Coverage may be provided for any non-FDA labeled indication if it is determined that the use is a medically accepted indication supported by nationally recognized pharmacy compendia or peer-reviewed medical literature for treatment of the diagnosis(es) for which it is prescribed. These requests will be reviewed on a case by case basis to determine medical necessity.

When criteria are not met, the request will be forwarded to a Medical Director for review. The physician reviewer must override criteria when, in their professional judgment, the requested medication is medically necessary.

List of *CFTR* Gene Mutations that Produce CFTR Protein and are Responsive to KALYDECO				
E56K	*G178R*	*S549R*	*K1060T*	*G1244E*
P67L	*E193K*	*G551D*	*A1067T*	*S1251N*
R74W	*L206W*	*G551S*	*G1069R*	*S1255P*
D110E	*R347H*	*D579G*	*R1070Q*	*D1270N*
D110H	*R352Q*	*S945L*	*R1070W*	*G1349D*
R117C	*A455E*	*S977F*	*F1074L*	*E831X*
R117H	*S549N*	*F1052V*	*D1152H*	*711+3A→G*
2789+5G→A	*3272-26A→G*	*3849+10kbC→T*		

Child Pugh Score Formula:			
	1 point	**2 points**	**3 points**
Total bilirubin	< 2	2-3	> 3
Serum albumin	> 3.5	2.8-3.5	< 2.8
INR	> 1.7	1.71-2.20	< 2.20
Ascites	None	Mild	Severe
Hepatic encephalopathy	None	Grade I-II	Grade III-IV
Explanation of Result :			
Class A: 5-6			
Class B: 7-9			
Class C: 10-15			
The prognosis worsens going from A to C and is evidenced by worsening decompensation			
The Child-Pugh Score is a scoring system used to determine the prognosis with cirrhosis and need for liver transplantation.			