



Cystic Fibrosis Agents (Oral)

WA.PHAR.48 Cystic Fibrosis Agents (Oral)

Background:

Cystic fibrosis is a condition that causes thick, sticky mucus to build up in the lungs, digestive tract, and other areas of the body and is caused by change(s) to the CFTR gene. A child inherits one CFTR gene from each parent. If two faulty CFTR genes are inherited, it leads to cystic fibrosis. (If children inherit one problematic CFTR gene, they usually will not have symptoms of cystic fibrosis but can pass the changed gene to their children.) The change(s) in the CFTR gene results in problems with how salt moves in and out of cells. The result is a buildup of sticky, thick mucus. Drugs have been developed that target specific changes on the CFTR gene.

Medical necessity

Drug	Medical Necessity
ivacaftor (KALYDECO®)	KALYDECO® may be considered medically necessary when: Used for the treatment of cystic fibrosis (CF) in patients age 2 years and older who have at least one mutation in the CFTR gene that is responsive to ivacaftor potentiation.
lumacaftor/ivacaftor (ORKAMBI®)	ORKAMBI® may be considered medically necessary when: Used for the treatment of cystic fibrosis (CF) in patients age 6 years and older who are homozygous for the <i>F508del</i> mutation in the cystic fibrosis transmembrane conductance regulator (<i>CFTR</i>) gene.
Tezacaftor/ivacaftor and ivacaftor (SYMDEKO™)	SYMDEKO™ may be considered medically necessary when: Used for the treatment of cystic fibrosis (CF) in patients age 12 years and older who are homozygous for the <i>F508del</i> mutation or who have at least one mutation in the cystic fibrosis transmembrane conductance regulator (<i>CFTR</i>) gene that is responsive to tezacaftor/ivacaftor.

Clinical policy:

Drug	Clinical Criteria (Initial Approval)
ivacaftor (KALYDECO®)	KALYDECO® may be covered when ALL of the following are met: <ol style="list-style-type: none"> 1. Diagnosis of cystic fibrosis 2. Documentation of at least ONE mutation in the CFTR gene that is responsive to ivacaftor potentiation (Table 1) 3. Greater than or equal to (\geq) 2 years of age <p>Approve for 6 months</p>

	<p>Criteria (Reauthorization)</p> <p>FEV₁ has significantly improved from baseline or stabilization of disease</p> <p>Approve for 12 months</p>
lumacaftor/ivacaftor (ORKAMBI®)	<p>ORKAMBI® may be covered when ALL of the following are met:</p> <ol style="list-style-type: none"> 1. Diagnosis of cystic fibrosis 2. Confirmation of 2 copies of the <i>F508del</i> mutation in the CFTR gene (i.e. the patient is homozygous for the <i>F508del</i> mutation) 3. Greater than or equal to (≥) 6 years of age <p>Approve for 6 months</p> <p>Criteria (Reauthorization)</p> <p>FEV₁ has significantly improved from baseline or stabilization of disease</p> <p>Approve for 12 months</p>
Tezacaftor/ivacaftor and ivacaftor (SYMDEKO™)	<p>SYMDEKO™ may be covered when ALL of the following are met:</p> <ol style="list-style-type: none"> 1. Diagnosis of cystic fibrosis 2. ONE of the following: <ol style="list-style-type: none"> a. Confirmation of 2 copies of the <i>F508del</i> mutation in the CFTR gene (i.e. the patient is homozygous for the <i>F508del</i> mutation) b. Documentation of at least ONE mutation in the CFTR gene that is responsive to tezacaftor/ivacaftor (Table 1) 3. Greater than or equal to (≥) 12 years of age <p>Approve for 6 months</p> <p>Criteria (Reauthorization)</p> <p>FEV₁ has significantly improved from baseline or stabilization of disease</p> <p>Approve for 12 months</p>

Dosage and quantity limits

Drug Name	Dose and Quantity Limits
ivacaftor (KALYDECO®)	Tablets: #60 tablets per 30-days Granules: #56 per 28-days
lumacaftor/ivacaftor (ORKAMBI®)	#112 tablets per 28-days
Tezacaftor/ivacaftor and ivacaftor (SYMDEKO™)	#56 tablets per 28-days

Appendix

Table 1:

KALYDECO® (ivacaftor) 2 years of age and older			ORKAMBI® (lumacaftor/ivacaftor) 6 years of age and older	SYMDEKO™ (tezacaftor/ivacaftor and ivacaftor) 12 years of age and older		
A1067T c.3199G>A	G1244E c.3731G>A	R352Q c.1055G>A	F508del/F508del c.1521_1523delCTT	F508del/F508del c.1521_1523delCTT	K1060T c.3179A>C	711+3A→G c.579+3A>G
A455E c.1364C>A	G1349D c.4046G>A	R74W c.220C>T		A1067T c.3199G>A	L206W c.617T>G	
D110E c.330C>A	G178R c.532G>A	S1251N c.3752G>A		A455E c.1364C>A	P67L c.200C>T	
D110H c.328G>C	G551D c.1652G>A	S1255P c.3763T>C		D110E c.330C>A	R1070W c.3208C>T	
D1152H c.3454G>C	G551S c.1651G>A	S549N c.1646G>A		D110H c.328G>C	R117C c.349C>T	
D1270N c.3808G>A	K1060T c.3179A>C	S549R c.1645A>C, c.1647T>G		D1152H c.3454G>C	R347H c.1040G>A	
D579G c.1736A>G	L206W c.617T>G	S945L c.2834C>T		D1270N c.3808G>A	R352Q c.1055G>A	
E193K c.577G>A	P67L c.200C>T	S977F c.2930C>T		D579G c.1736A>G	R74W c.220C>T	
E56K c.166G>A	R1070Q c.3209G>A	2789+5G→A c.2657+5G>A		E193K c.577G>A	S945L c.2834C>T	
E831X c.2491G>T	R1070W c.3208C>T	3272-26A→G c.3140-26A>G		E56K c.166G>A	S977F c.2930C>T	
F1052V c.3154T>G	R117C c.349C>T	3849+10kbC→T c.3718- 2477C>T		E831X c.2491G>T	2789+5G→A c.2657+5G>A	
F1074L c.3222T>A	R117H c.350G>A	711+3A→G c.579+3A>G		F1052V c.3154T>G	3272-26A→G c.3140-26A>G	
G1069R c.3205G>A	R347H c.1040G>A			F1074L c.3222T>A	3849+10kbC→T c.3718- 2477C>T	

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