



Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Potentiators:
Kalydeco (ivacaftor)
Orkambi (lumacaftor/ivacaftor)
Symdeko (tezacaftor/ivacaftor)
Trikafta (elexacaftor/tezacaftor/ivacaftor)
Effective 06/01/2022

Plan	<input type="checkbox"/> MassHealth <input checked="" type="checkbox"/> MH UPPL <input type="checkbox"/> Commercial/Exchange	Program Type	<input checked="" type="checkbox"/> Prior Authorization <input checked="" type="checkbox"/> Quantity Limit <input type="checkbox"/> Step Therapy
Benefit	<input checked="" type="checkbox"/> Pharmacy Benefit <input type="checkbox"/> Medical Benefit (NLX)		
Specialty Limitations	This medication has been designated specialty and must be filled at a contracted specialty pharmacy.		
Contact Information	Specialty Medications		
	All Plans	Phone: 866-814-5506	Fax: 866-249-6155
	Non-Specialty Medications		
	MassHealth	Phone: 877-433-7643	Fax: 866-255-7569
	Commercial	Phone: 800-294-5979	Fax: 888-836-0730
	Exchange	Phone: 855-582-2022	Fax: 855-245-2134
	Medical Specialty Medications (NLX)		
	All Plans	Phone: 844-345-2803	Fax: 844-851-0882
Exceptions			

Overview

CF is caused by genetic mutations in the CFTR protein. The CFTR protein is present in the respiratory epithelium and plays an important role in the regulation of airway surface liquid. Genetic mutations in the protein result in abnormal airway secretions, chronic endobronchial infection, and progressive airway obstruction. The CFTR potentiators treat the underlying cause of CF by targeting the defective CFTR protein to help facilitate increased chloride transport.

No PA	Drugs That Require PA
	Kalydeco [®] (ivacaftor) ^{PD}
	Orkambi [®] (lumacaftor/ivacaftor) ^{PD}
	Symdeko [®] (tezacaftor/ivacaftor) ^{PD}
	Trikafta [®] (elexacaftor/tezacaftor/ivacaftor) ^{PD}

PD = preferred drug. In general, a trial of the preferred drug or clinical rationale for prescribing a non-preferred drug within a therapeutic class.

Coverage Guidelines:



Kalydeco (ivacaftor)

Authorization may be reviewed on a case by case basis for members new to AllWays Health Partners are currently receiving treatment with Kalydeco for an FDA approved indication excluding when the product is obtained as samples or via manufacturer's patient assistance programs.

OR

Authorization may be granted when documentation is of ALL the following is provided:

1. The member has a diagnosis of Cystic Fibrosis with one mutation in the CFTR gene that is responsive to ivacaftor. (specific gene mutation MUST be documented) (see Appendix A)
2. The member is ≥ 4 months of age
3. Baseline body mass index (BMI) and percent predicted forced expiratory volume in one second (ppFEV₁) †
4. Request does not exceed 2 units per day
5. Kalydeco will not be used in combination with Symdeko, Orkambi, or Trikafta

Orkambi (lumacaftor/ivacaftor)

Authorization may be reviewed on a case by case basis for members new to AllWays Health Partners are currently receiving treatment with Orkambi for an FDA approved indication excluding when the product is obtained as samples or via manufacturer's patient assistance programs.

OR

Authorization may be granted when documentation is of ALL the following is provided:

1. The member has a diagnosis of Cystic Fibrosis with two copies (homozygous) of the F508del-CFTR mutation (specific gene mutation MUST be documented)
2. The member is ≥ 2 years of age.
3. Request does not exceed 4 tablets per day or 2 packets per day
4. Baseline BMI and ppFEV₁ †
5. Orkambi will not be used in combination with Kalydeco, Symdeko, or Trikafta.

Symdeko (tezacaftor/ivacaftor)

Authorization may be reviewed on a case by case basis for members new to AllWays Health Partners are currently receiving treatment with Symdeko for an FDA approved indication excluding when the product is obtained as samples or via manufacturer's patient assistance programs.

OR

Authorization may be granted when documentation is of ALL the following is provided:

1. The member has a diagnosis of Cystic Fibrosis with two copies (homozygous) of the F508del-CFTR mutation or at least one mutation in the CFTR gene that is responsive to tezacaftor/ivacaftor (specific gene mutation MUST be documented) (Appendix B)
2. The member ≥ 6 years of age
3. Request does not exceed 2 tablets per day
4. Baseline BMI and ppFEV₁ †
5. Symdeko will not be used in combination with Kalydeco, Orkambi, or Trikafta

Trikafta (elaxacaftor/tezacaftor/ivacaftor)

Authorization may be reviewed on a case by case basis for members new to AllWays Health Partners are currently receiving treatment with Trikafta for an FDA approved indication excluding when the product is obtained as samples or via manufacturer's patient assistance programs.

OR

Authorization may be granted when documentation is of ALL the following is provided:



1. The member has a diagnosis of Cystic Fibrosis with at least one F508del mutation in the CFTR gene or a mutation in the CFTR gene that is responsive to elexacaftor/tezacaftor/ivacaftor (specific gene mutation MUST be documented) (see Appendix C)
2. The member is ≥ 6 years of age
3. Request does not exceed 3 tablets per day
4. Baseline BMI and ppFEV₁ †
5. Trikafta will not be used in combination with Kalydeco, Symdeko, or Orkambi.

† If member is ≤ 6 years of age, ppFEV₁ does not have to be performed

Continuation of Therapy

Reauthorization requires physician documentation of ALL of the following:

1. Provider provides documentation of positive response to therapy (e.g., improvement in BMI, ppFEV₁, decrease in clinical exacerbations, etc.)
2. Provider documentations continuation OR pharmacy claims confirms adherence

Limitations

1. Initial approvals will be granted for 6 months
2. Reauthorizations will be granted for 12 months
3. The following quantity limits apply:

Kalydeco 150mg tablets	56 tablets per 28 days
Kalydeco 25mg, 50mg, or 75mg packets	56 packets per 28 days
Orkambi 200-125mg tablets	112 tablets per 28 days
Orkambi 150-188mg granules	56 packets per 28 days
Symdeko 50-75mg tablets	56 tablets per 28 days
Symdeko 100-150mg tablets	56 tablets per 28 days
Trikafta 100-50-75mg tablets	84 tablets per 28 days

Appendix

Appendix A: List of CFTR gene that is responsive to Kalydeco

List of CFTR Gene Mutations that Produce CFTR Protein and are Responsive to Kalydeco				
<i>711+3A→G *</i>	<i>F311del</i>	<i>I148T</i>	<i>R75Q</i>	<i>S589N</i>
<i>2789+5G→A *</i>	<i>F311L</i>	<i>I175V</i>	<i>R117C*</i>	<i>S737F</i>
<i>3272-26A→G *</i>	<i>F508C</i>	<i>I807M</i>	<i>R117G</i>	<i>S945L*</i>
<i>3849+10kbC→T *</i>	<i>F508C;S1251N †</i>	<i>I1027T</i>	<i>R117H*</i>	<i>S997F *</i>
<i>A120T</i>	<i>F1052V</i>	<i>I1139V</i>	<i>R117L</i>	<i>S1159F</i>
<i>A234D</i>	<i>F1074L</i>	<i>K1060T</i>	<i>R117P</i>	<i>S1159P</i>
<i>A349V</i>	<i>G178E</i>	<i>L206W *</i>	<i>R170H</i>	<i>S1251N*</i>
<i>A455E *</i>	<i>G178R*</i>	<i>L320V</i>	<i>R347H*</i>	<i>S1255P*</i>
<i>A1067T</i>	<i>G194R</i>	<i>L967S</i>	<i>R347L</i>	<i>T338I</i>
<i>D110E</i>	<i>G314E</i>	<i>L997F</i>	<i>R352Q*</i>	<i>T1053I</i>
<i>D110H</i>	<i>G551D *</i>	<i>L1480P</i>	<i>R553Q</i>	<i>V232D</i>
<i>D192G</i>	<i>G551S *</i>	<i>M152V</i>	<i>R668C</i>	<i>V562I</i>
<i>D579G *</i>	<i>G576A</i>	<i>M952I</i>	<i>R792G</i>	<i>V754M</i>
<i>D924N</i>	<i>G970D</i>	<i>M952T</i>	<i>R993G</i>	<i>V1293G</i>
<i>D1152H *</i>	<i>G1069R</i>	<i>P67L*</i>	<i>R1070Q</i>	<i>W1282R</i>
<i>D1270N</i>	<i>G1244E *</i>	<i>Q237E</i>	<i>R1070W*</i>	<i>Y1014C</i>
<i>E56K</i>	<i>G1249R</i>	<i>Q237H</i>	<i>R1162L</i>	<i>Y1032C</i>
<i>E193K</i>	<i>G1349D*</i>	<i>Q359R</i>	<i>R1283M</i>	
<i>E822K</i>	<i>H939R</i>	<i>Q1291R</i>	<i>S549N*</i>	
<i>E831X*</i>	<i>H1375P</i>	<i>R74W</i>	<i>S549R*</i>	

* Clinical data exist for these mutations.
† Complex/compound mutations where a single allele of the CFTR gene has multiple mutations; these exist independent of the presence of mutations on the other allele.

Appendix B: List of CFTR Gene Mutations that are Responsive to Symdeko

List of CFTR Gene Mutations that Produce CFTR Protein and are Responsive to Symdeko					
<i>546insCTA</i>	<i>E92K</i>	<i>G576A</i>	<i>L346P</i>	<i>R117G</i>	<i>S589N</i>
<i>711+3A→G *</i>	<i>E116K</i>	<i>G576A;R668C †</i>	<i>L967S</i>	<i>R117H</i>	<i>S737F</i>
<i>2789+5G→A *</i>	<i>E193K</i>	<i>G622D</i>	<i>L997F</i>	<i>R117L</i>	<i>S912L</i>
<i>3272-26A→G *</i>	<i>E403D</i>	<i>G970D</i>	<i>L1324P</i>	<i>R117P</i>	<i>S945L *</i>
<i>3849+10kbC→T *</i>	<i>E588V</i>	<i>G1069R</i>	<i>L1335P</i>	<i>R170H</i>	<i>S977F *</i>
<i>A120T</i>	<i>E822K</i>	<i>G1244E</i>	<i>L1480P</i>	<i>R258G</i>	<i>S1159F</i>
<i>A234D</i>	<i>E831X</i>	<i>G1249R</i>	<i>M152V</i>	<i>R334L</i>	<i>S1159P</i>
<i>A349V</i>	<i>F191V</i>	<i>G1349D</i>	<i>M265R</i>	<i>R334Q</i>	<i>S1251N</i>
<i>A455E *</i>	<i>F311del</i>	<i>H939R</i>	<i>M952I</i>	<i>R347H *</i>	<i>S1255P</i>
<i>A554E</i>	<i>F311L</i>	<i>H1054D</i>	<i>M952T</i>	<i>R347L</i>	<i>T338I</i>
<i>A1006E</i>	<i>F508C</i>	<i>H1375P</i>	<i>P5L</i>	<i>R347P</i>	<i>T1036N</i>
<i>A1067T</i>	<i>F508C;S1251N †</i>	<i>I148T</i>	<i>P67L *</i>	<i>R352Q *</i>	<i>T1053I</i>
<i>D110E</i>	<i>F508del ^</i>	<i>I175V</i>	<i>P205S</i>	<i>R352W</i>	<i>V201M</i>
<i>D110H *</i>	<i>F575Y</i>	<i>I336K</i>	<i>Q98R</i>	<i>R553Q</i>	<i>V232D</i>
<i>D192G</i>	<i>F1016S</i>	<i>I601F</i>	<i>Q237E</i>	<i>R668C</i>	<i>V562I</i>
<i>D443Y</i>	<i>F1052V</i>	<i>I618T</i>	<i>Q237H</i>	<i>R751L</i>	<i>V754M</i>
<i>D443Y;G576A;R668C †</i>	<i>F1074L</i>	<i>I807M</i>	<i>Q359R</i>	<i>R792G</i>	<i>V1153E</i>
<i>D579G *</i>	<i>F1099L</i>	<i>I980K</i>	<i>Q1291R</i>	<i>R933G</i>	<i>V1240G</i>

D614G	G126D	I1027T	R31L	R1066H	V1293G
D836Y	G178E	I1139V	R74Q	R1070Q	W1282R
D924N	G178R	I1269N	R74W	R1070W*	Y109N
D979V	G194R	I1366N	R74W;D1270N†	R1162L	Y161S
D1152H*	G194V	K1060T	R74W;V201M†	R1283M	Y1014C
D1270N	G314E	L15P	R74W;V201M;D1270N†	R1283S	Y1032C
E56K	G551D	L206W*	R75Q	S549N	
E60K	G551S	L320V	R117C*	S549R	

* Clinical data for these mutations in Clinical Studies.

^ A patient must have two copies of the *F508del* mutation or at least one copy of a responsive mutation presented in Table 6 to be indicated.

† Complex/compound mutations where a single allele of the *CFTR* gene has multiple mutations; these exist independent of the presence of mutations on the other allele.

Appendix C: List of CFTR Gene Mutations that are Responsive to Trikafta

CFTR Gene Mutations Responsive to Trikafta					
3141del9	E822K	G1069R	L967S	R117L	S912L
546insCTA	F191V	G1244E	L997F	R117P	S945L
A46D	F311del	G1249R	L1077P	R170H	S977F
A120T	F311L	G1349D	L1324P	R258G	S1159F
A234D	F508C	H139R	L1335P	R334L	S1159P
A349V	F508C;S1251N†	H199Y	L1480P	R334Q	S1251N
A455E	F508del*	H939R	M152V	R347H	S1255P
A554E	F575Y	H1054D	M265R	R347L	T338I
A1006E	F1016S	H1085P	M952I	R347P	T1036N
A1067T	F1052V	H1085R	M952T	R352Q	T1053I
D110E	F1074L	H1375P	M1101K	R352W	V201M
D110H	F1099L	I148T	P5L	R553Q	V232D
D192G	G27R	I175V	P67L	R668C	V456A
D443Y	G85E	I336K	P205S	R751L	V456F
D443Y;G576A;R668C†	G126D	I502T	P574H	R792G	V562I
D579G	G178E	I601F	Q98R	R933G	V754M
D614G	G178R	I618T	Q237E	R1066H	V1153E
D836Y	G194R	I807M	Q237H	R1070Q	V1240G
D924N	G194V	I980K	Q359R	R1070W	V1293G
D979V	G314E	I1027T	Q1291R	R1162L	W361R
D1152H	G463V	I1139V	R31L	R1283M	W1098C
D1270N	G480C	I1269N	R74Q	R1283S	W1282R
E56K	G551D	I1366N	R74W	S13F	Y109N
E60K	G551S	K1060T	R74W;D1270N†	S341P	Y161D
E92K	G576A	L15P	R74W;V201M†	S364P	Y161S
E116K	G576A;R668C†	L165S	R74W;V201M;D1270N†	S492F	Y563N
E193K	G622D	L206W	R75Q	S549N	Y1014C
E403D	G628R	L320V	R117C	S549R	Y1032C
E474K	G970D	L346P	R117G	S589N	
E588V	G1061R	L453S	R117H	S737F	

* *F508del* is a responsive *CFTR* mutation based on both clinical and *in vitro* data.

† Complex/compound mutations where a single allele of the *CFTR* gene has multiple mutations; these exist independent of the presence of mutations on the other allele.

References

1. Kalydeco [package insert]. Boston, MA: Vertex Pharmaceuticals Inc.; April 2019.
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;187:680-689.



3. Orkambi [package insert]. Boston, MA: Vertex Pharmaceuticals Inc.; August 2018.
4. Symdeko [package insert]. Boston, MA: Vertex Pharmaceuticals Inc.; June 2019.
5. Rowe SM, Daines C, Ringshausen FC, Kerem E, Wilson J, Tullis E, Nair N, Simard C, Han L, Ingenito EP, McKee C, Lekstrom-Himes J, Davies JC. Tezacaftor-Ivacaftor in Residual Function Heterozygotes with Cystic Fibrosis. *N Engl J Med.* 2017; 377:2024-2035
6. Taylor-Cousar JL, Munck A, McKone EF, et al. Tezacaftor-ivacaftor in patients with cystic fibrosis homozygous for Phe508del *N Engl J Med* 2017; 377:2013-2023
7. Trikafta (elixacaftor/tezacaftor/ivacaftor) [prescribing information]. Boston, MA: Vertex Pharmaceuticals Inc., January 2020.

Review History

05/19/2021 – Created and Reviewed May P&T Mtg; Matched MH UPPL; previously on same criteria with Comm/exch. Removed Kalydeco, Orkambi, and Symdeko use prior to Trikafta. Added all 4 drugs as preferred. Effective 7/1/2021

05/18/2022 – Reviewed and updated for May P&T; note added to Symdeko and Trikafta (similar to other CFTR modulators that if member is ≤ 6 years of age, ppFEV1 does not have to be performed); guideline updated to include FDA-expanded age indication for Trikafta to ≥ 6 years; matched MH UPPL; Effective 6/1/22.

Disclaimer

AllWays Health Partners complies with applicable federal civil rights laws and does not discriminate or exclude people on the basis of race, color, national origin, age, disability, or sex.