



## MASSACHUSETTS

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# Pharmacy Medical Policy Drugs for Cystic Fibrosis

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## Policy Number: 408

BCBSA Reference Number: None

## Policy

### Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

**Note:** All requests for outpatient retail pharmacy for indications listed and not listed on the medical policy guidelines may be submitted to BCBSMA Clinical Pharmacy Operations by completing the Prior Authorization Form on the last page of this document. Physicians may also call BCBSMA Pharmacy Operations department at (800)366-7778 to request a prior authorization/formulary exception verbally. Physicians may also submit requests for retail pharmacy exceptions via the web using Express Path which can be found on the BCBSMA provider website or directly on the web at <https://provider.express-path.com>. Patients must have pharmacy benefits under their subscriber certificates.

## Prior Authorization Information

<input checked="" type="checkbox"/> <b>Prior Authorization</b> <input type="checkbox"/> <b>Step Therapy</b> <input type="checkbox"/> <b>Quality Care Dosing</b>		<b>Pharmacy Operations:</b> Tel: 1-800-366-7778 Fax: 1-800-583-6289	
		Policy last updated	<b>7/1/2023</b>
Pharmacy (Rx) or Medical (MED) benefit coverage	<input checked="" type="checkbox"/> <b>Rx</b> <input type="checkbox"/> <b>MED</b>	<b>To request for coverage:</b> Physicians may call, fax, or mail the attached form ( <a href="#">Formulary Exception/Prior Authorization form</a> ) to the address below.	
<b>Policy applies to Commercial Members:</b> <ul style="list-style-type: none"> <li>• Managed Care (HMO and POS),</li> <li>• PPO and Indemnity</li> <li>• MEDEX with Rx plan</li> <li>• Managed Major Medical with Custom BCBSMA Formulary</li> <li>• Comprehensive Managed Major Medical with Custom BCBSMA Formulary</li> <li>• Managed Blue for Seniors with Custom BCBSMA Formulary</li> </ul>		<b>Blue Cross Blue Shield of Massachusetts Pharmacy Operations Department</b> 25 Technology Place Hingham, MA 02043  <b>Individual Consideration:</b> Policy for requests that do not meet clinical criteria of this policy, see section labeled <a href="#">Individual Consideration</a>	

Please refer to the chart below for the formulary and step status of the medications affected by this policy.

Drug	Formulary Information
	Standard
	Formulary Status
<b>Kalydeco</b> ™ (ivacaftor)	PA Required
<b>Orkambi</b> ™ (lumacaftor / ivacaftor)	PA Required
<b>Symdeko</b> ™ (tezacaftor / ivacaftor)	PA Required
<b>Trikafta</b> ™ (elexacaftor / tezacaftor / ivacaftor)	PA Required

**We may cover Kalydeco**™ (ivacaftor) for the treatment of cystic fibrosis when **all** of the following criteria are met<sup>1</sup>:

- Age 4 months of age or older
- Documentation of a mutation of the CFTR gene as confirmed by an FDA- cleared cystic fibrosis mutation test. In Table 2 below.

Table 2 (Kalydeco Mutations)

711+3A→G <sub>-</sub> *	F311del	I148T	R75Q	S589N
2789+5G→A <sub>-</sub> *	F311L	I175V	R117C <sub>-</sub> *	S737F
3272-26A→G <sub>-</sub> *	F508C	I807M	R117G	S945L <sub>-</sub> *
3849+10kbC→T <sub>-</sub> *	F508C;S1251N <sub>±</sub>	I1027T	R117H <sub>-</sub> *	S977F <sub>-</sub> *
A120T	F1052V	I1139V	R117L	S1159F
A234D	F1074L	K1060T	R117P	S1159P
A349V	G178E	L206W <sub>-</sub> *	R170H	S1251N <sub>-</sub> *
A455E <sub>-</sub> *	G178R <sub>-</sub> *	L320V	R347H <sub>-</sub> *	S1255P <sub>-</sub> *
A1067T	G194R	L967S	R347L	T338I
D110E	G314E	L997F	R352Q <sub>-</sub> *	T1053I
D110H	G551D <sub>-</sub> *	L1480P	R553Q	V232D
D192G	G551S <sub>-</sub> *	M152V	R668C	V562I
D579G <sub>-</sub> *	G576A	M952I	R792G	V754M
D924N	G970D	M952T	R933G	V1293G
D1152H <sub>-</sub> *	G1069R	P67L <sub>-</sub> *	R1070Q	W1282R
D1270N	G1244E <sub>-</sub> *	Q237E	R1070W <sub>-</sub> *	Y1014C
E56K	G1249R	Q237H	R1162L	Y1032C
E193K	G1349D <sub>-</sub> *	Q359R	R1283M	
E822K	H939R	Q1291R	S549N <sub>-</sub> *	
E831X <sub>-</sub> *	H1375P	R74W	S549R <sub>-</sub> *	

\*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.

**We may cover Orkambi™** (lumacaftor and ivacaftor) for the treatment of cystic fibrosis when **all** of the following criteria are met<sup>1</sup>:

- Age 1 years of age or older
- Documentation of **TWO** copies of the F508del mutation in the CFTR gene as confirmed by an FDA-cleared cystic fibrosis mutation test
- Concurrent use of **Kalydeco™** must be discontinued.

**We may cover Symdeko™** (tezacaftor and ivacaftor) for the treatment of cystic fibrosis when **all** of the following criteria are met<sup>1</sup>:

- Age 6 years of age or older, **AND**
- Documentation of Homozygous for the F508del mutation in the CFTR gene as confirmed by an FDA-cleared cystic fibrosis mutation test

**OR**

- Documentation of one mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene that is responsive to tezacaftor/ivacaftor based on in vitro data and/or clinical evidence as noted in table 6 below:

**AND**

- Concurrent use of **Kalydeco™** or **Orkambi™** must be discontinued.

Table 6: 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>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>

A1006E	F508C	H1375P	P5L	R347P	T1036N
A1067T	F508C;S1251N ‡	I148T	P67L *	R352Q *	T1053I
D110E	F508del ‡	I175V	P205S	R352W	V201M
D110H *	F575Y	I336K	Q98R	R553Q	V232D
D192G	F1016S	I601F	Q237E	R668C	V562I
D443Y	F1052V	I618T	Q237H	R751L	V754M
D443Y;G576A;R668C †	F1074L	I807M	Q359R	R792G	V1153E
D579G *	F1099L	I980K	Q1291R	R933G	V1240G
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 [see [CLINICAL STUDIES \(14.1 and 14.2\)](#)].

† 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.

‡ 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.

**We may cover Trikafta™ (elexacaftor, tezacaftor and ivacaftor) for the treatment of cystic fibrosis when all of the following criteria are met<sup>1</sup>:**

- Age 2 years of age or older, **AND**
- Concurrent use of **Symdeko™** or **Kalydeco™** or **Orkambi™** must be discontinued, **AND**
- Documentation for at least one F508del mutation in the *CFTR* gene as confirmed by an FDA- cleared cystic fibrosis mutation test in table 4 below.

Table 4 (Trikafta Mutations)

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	

\*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.

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

We do not cover the above drugs for other conditions not listed above.

## Other Information

Blue Cross Blue Shield of Massachusetts (BCBSMA\*) members (other than Medex®; Blue MedicareRx, Medicare Advantage plans that include prescription drug coverage) will be required to fill their prescriptions for the above medications at one of the providers in our retail specialty pharmacy network, see link below:

[Link to Specialty Pharmacy List](#)

### Individual Consideration

All our medical policies are written for the majority of people with a given condition. Each policy is based on medical science. For many of our medical policies, each individual's unique clinical circumstances may be considered in light of current scientific literature. Physicians may send relevant clinical information for individual patients for consideration to:

Blue Cross Blue Shield of Massachusetts  
Pharmacy Operations Department  
25 Technology Place  
Hingham, MA 02043  
Tel: 1-800-366-7778  
Fax: 1-800-583-6289

### Policy History

Date	Action
7/2023	Updated Age for Trikafta.
11/2022	Updated new age for Orkambi™ for homozygous F508del mutation criteria.
7/2021	Updated to include age update for Trikafta™
2/2021	Updated to add New eligible mutations to the policy.
10/2020	Updated to include new age edit for Kalydeco™.
2/2020	Updated to add Trikafta™ to the policy.
8/2019	Updated to include new age range for Symdeko™.
9/2018	Updated to include new age range for Orkambi™ & Kalydeco™.
6/2018	Updated to include Symdeco™ and to add Specialty Pharmacy Link.
10/2017	Updated to change Walgreens Specialty Name.
7/2017	Updated to include additional genes and add AllCare to Specialty pharmacy list.
6/2017	Updated address for Pharmacy Operations.
11/2016	Updated to include new age indication for Orkambi™.
4/2016	Updated to include Orkambi™ & add Walgreens Specialty.
4/2015	Updated for new FDA approved ages.
2/2015	Updated new gene types which were FDA approved.
4/2014	Updated new gene types which were FDA approved.
2/2014	Removal of Curascript from Specialty Pharmacy section.
1/2014	Updated to remove Blue Value.
1/2013	New Policy, effective 1/1/2013.

### References

1. Kalydeco™ [package insert]. Cambridge, MA: Vertex Pharmaceuticals, Inc.: 2012.
2. Yu H, Burton B, Huang CJ, et al. Ivacaftor potentiation of multiple CFTR channels with gating mutations. *J Cyst Fibros.* Jan 30 2012.
3. Accurso FJ, Rowe SM, Clancy JP, et al. Effect of VX-770 in persons with cystic fibrosis and the G551D-CFTR mutation. *N Engl J Med.* Nov 18 2010;363(21):1991-2003.
4. Ramsey BW, Davies J, McElvaney NG, et al. A CFTR potentiator in patients with cystic fibrosis and the G551D mutation. *N Engl J Med.* Nov 3 2011;365(18):1663-1672.
5. Flume PA, Liou TG, Borowitz DS, et al. Ivacaftor in Subjects with Cystic Fibrosis who are Homozygous for the F508del-CFTR Mutation. *Chest.* Mar 1 2012.
6. Sanders DB, Farrell PM. Transformative mutation specific pharmacotherapy for cystic fibrosis. *BMJ.* 2012;344:e79.

7. Aherns R, Rodriguez S, Yen K, Davies JC. VX-770 in subjects 6 to 11 years with cystic fibrosis and the G551D-CFTR mutation. *Pediatric Pulmonology*. 2011;46:283.
8. Orkambi™ [package insert]. Cambridge, MA: Vertex Pharmaceuticals, Inc.: July 2015.
9. Symdeko™ [package insert]. Cambridge, MA: Vertex Pharmaceuticals, Inc.: Feb 2018.
10. Trikafta™ [package insert]. Cambridge, MA: Vertex Pharmaceuticals, Inc.: Oct 2019.

### **Endnotes**

1. 1. Based on BCBSA Technology Evaluation Center Specialty Pharmacy Combined Capacity (SPCC) Report #3-2012 Ivacaftor (Kalydeco™), reviewed March 2012.

**To request prior authorization using the Massachusetts Standard Form for Medication Prior Authorization Requests (eForm), click the link below:**

<http://www.bluecrossma.org/medical-policies/sites/g/files/csphws2091/files/acquiadam-assets/023%20E%20Form%20medication%20prior%20auth%20instruction%20pm.pdf>