MASSACHUSETTS

Blue Cross Blue Shield of Massachusetts is an Independent Licensee of the Blue Cross and Blue Shield Association

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.

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
Kalydeco™ (ivacaftor)	PA Required
Orkambi™ (lumacaftor / ivacaftor**)**	PA Required
Symdeko™ (tezacaftor / ivacaftor)	PA Required
Trikafta™ (elexacaftor / tezacaftor / ivacaftor)	PA Required

We may cover Kalydeco™ (ivacaftor) for the treatment of cystic fibrosis when **all** of the following criteria are met[1]:

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

*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[1]:

- Age 2 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[1]:

- 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 3 below:

Table 3 (Orkambi Mutations)

546insCTA	*E92K*	*G576A*	*L346P*	*R117G*	*S589N*
711+3A→G *	*E116K*	*G576A;R668C* †	*L967S*	*R117H*	*S737F*
2789+5G→A *	*E193K*	*G622D*	*L997F*	*R117L*	*S912L*
3272-26A→G *	*E403D*	*G970D*	*L1324P*	*R117P*	*S945L* *
3849+10kbC→T *	*E588V*	*G1069R*	*L1335P*	*R170H*	*S977F* *
A120T	*E822K*	*G1244E*	*L1480P*	*R258G*	*S1159F*
A234D	*E831X*	*G1249R*	*M152V*	*R334L*	*S1159P*
A349V	*F191V*	*G1349D*	*M265R*	*R334Q*	*S1251N*
A455E *	*F311del*	*H939R*	*M952I*	*R347H* *	*S1255P*
A554E	*F311L*	*H1054D*	*M952T*	*R347L*	*T338I*
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.

† 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

AND

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

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

- Age 6 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

Prior Authorization Information

Outpatient

For services described in this policy, see below for products where prior authorization **IS REQUIRED** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **required**.
Commercial PPO and Indemnity	Prior authorization is **required**.

Policy History

Date	Action
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 Symdeko™ 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%20prn.pdf