BOSTON MEDICAL CENTER HEALTHNet PLAN

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Pharmacy Policy

Cystic Fibrosis Agents

Policy Number: 9.100
Version Number: 2
Version Effective Date: 1/1/2022

Product Applicability	☐ **All Plan[+] Products**
Well Sense Health Plan ☐ New Hampshire Medicaid	**Boston Medical Center HealthNet Plan** ☐ MassHealth – MCO ☐ MassHealth – ACO ☒ Qualified Health Plans/ConnectorCare/Employer Choice Direct ☐ Senior Care Options

Note: Disclaimer and audit information is located at the end of this document.

Prior Authorization Policy

Products Affected:

- **Kalydeco® (ivacaftor)**
- **Symdeko™ (tezacaftor/ivacaftor)**
- **Orkambi® (lumacaftor/ivacaftor)**
- **Trikafta™ (elexacaftor/tezacaftor/ivacaftor)**

The Plan may authorize coverage of the above products for members meeting the following criteria:

Covered Use	All FDA approved indications not otherwise excluded
Exclusion Criteria	Use of concurrent therapy Kalydeco®, Symdeko™, Trikafta or Orkambi®
Required Medical Information	**<u>Kalydeco®(ivacaftor)</u>** 1. Diagnosis of Cystic Fibrosis; ***AND*** 2. Genetic testing documenting a confirmed presence of one of the mutations listed in the FDA

[+] *Plan* refers to Boston Medical Center Health Plan, Inc. and its affiliates and subsidiaries offering health coverage plans to enrolled members. The Plan operates in Massachusetts under the trade name Boston Medical Center HealthNet Plan and in other states under the trade name Well Sense Health Plan.

	package labeling (see Appendix A). **AND** 3. If request is for oral granules **one** of the following: a. Member must be between 4 months and 10 years of **age OR** b. Member has documented difficulty swallowing tablets. **Symdeko™ (tezacaftor/ivacaftor)** 1. Diagnosis of Cystic Fibrosis; ***AND*** 2. Genetic testing documenting a confirmed presence of one of the mutations listed in the FDA package labeling (see Appendix A). **Orkambi® (lumacaftor/ivacaftor)** 1. Diagnosis of Cystic Fibrosis; ***AND*** 2. Genetic testing documenting a confirmed presence of homozygous *F508del* mutation in the *CFTR* gene. ***AND*** 3. If request is for oral granules **one** of the following: a. Member must be between 2 to 5 years of age **OR** b. Member has documented difficulty swallowing tablets. **Trikafta (Elexacaftor–Tezacaftor–Ivacaftor)** 1. Diagnosis of Cystic Fibrosis ***AND*** 2. Genetic testing documenting a confirmed presence of heterozygous F508del mutation in the CFTR gene OR a mutation in the CFTR gene that is responsive based on in vitro data from the package insert (see Appendix A).
Age Restriction	Kalydeco®(ivacaftor) – 4 months of age and older (oral granules); 6 years or older (tablets) Symdeko™ (tezacaftor/ivacaftor) – 6 years of age and older Orkambi® (lumacaftor/ivacaftor) **–** 2 years of age and older (oral granules); 6 years of age or older (tablets) Trikafta (Elexacaftor–Tezacaftor–Ivacaftor) -6 years of age and older
Prescriber Restriction	The prescriber is an appropriate specialist such as a pulmonologist or endocrinologist.
Coverage Duration	Initial: 6 months Reauthorization: 1 year
Other criteria	Reauthorization Documentation of the following: 1. Clinical response to therapy (the patient has shown improvement or stabilization in FEV1 compared to pre-therapy/baseline levels)

Clinical Background Information and References

1. Trikafta® [package insert]. Cambridge (MA): Vertex Pharmaceuticals, Inc; June 2021.
2. Katkin J. Cystic fibrosis: clinical manifestations and diagnosis. UpToDate. Last updated December 11,2015. Accessed February 2016. Available from http://www.uptodate.com.
3. Simon R. Cystic fibrosis: overview of the treatment of lung disease. UpToDate. Last updated January 6, 2016. Accessed February 2016. Available from http://www.uptodate.com.
4. Flume P, O'Sullivan B, Robinson K et al. Cystic fibrosis pulmonary guidelines: chronic medications for maintenance of lung health. Am J Respir Crit Care Med. 2007;176:957-69.
5. Kalydeco® [package insert]. Cambridge (MA): Vertex Pharmaceuticals, Inc; April 2019.
6. Orkambi (lumacaftor/ivacaftor) [prescribing information]. Boston, MA: Vertex Pharmaceuticals Incorporated; September 2016.
7. Mogayzel PJ Jr, et al. Cystic Fibrosis Pulmonary Guidelines: Chronic Medications for Maintenance of Lung health. *Am J Respir Crit Care Med*. 2013 Apr;187 (7): 680-9. https://www.cff.org/Care/Clinical-Care-Guidelines/Respiratory-Clinical-Care-Guidelines/Chronic-Medications-to-Maintain-Lung-Health-Clinical-Care-Guidelines/
8. Symdeko [package insert]. Boston, MA: Vertex Pharmaceuticals, Inc.; June 2019.

Appendix A – Mutations Responsive to Kalydeco, Symdeko™, Trikafta

The FDA approved package insert lists several mutations that are responsive to Kalydeco,Symdeko and Trikafta.

List of CFTR Gene Mutations that Produce CFTR Protein and are Responsive to *Kalydeco*				
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***	

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**Clinical data exists for these mutations*

†Complex/compound mutations. Most people with CF have 2 CF mutations, 1 on each copy of the CF gene. However, in rare instances, 1 copy of the CF gene can have more than 1 mutation. This is called a compound, or complex, mutation.

List of CFTR Gene Mutations that Produce CFTR Protein and are Responsive to *Symdeko*					
E56K	*R117C*	*A455E*	*S945L*	*R1070W*	*3272-26A→G*
P67L	*E193K*	*F508del**	*S977F*	*F1074L*	*3849+10kbC→T*
R74W	*L206W*	*D579G*	*F1052V*	*D1152H*	
D110E	*R347H*	*711+3A→G*	*K1060T*	*D1270N*	
D110H	*R352Q*	*E831X*	*A1067T*	*2789+5G→A*	
** A patient must have two copies of the F508del mutation or at least one copy of a responsive mutation presented in this table to be indicated*					

List of *CFTR* Gene Mutations that are 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;R6	*G126D*	*I502T*	*P574H*	*R792G*	*V562I*

68C †					
D579G	*G178E*	*I601F*	*Q98R*	*R933G*	*V754M*
D614G	*G178R*	*I618T*	*Q237E*	*R1066 H*	*V1153E*
D836Y	*G194R*	*I807M*	*Q237H*	*R1070 Q*	*V1240G*
D924N	*G194V*	*I980K*	*Q359R*	*R1070 W*	*V1293G*
D979V	*G314E*	*I1027T*	*Q1291R*	*R1162L*	*W361R*
D1152H	*G463V*	*I1139V*	*R31L*	*R1283 M*	*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;R668 C †*	*L165S*	*R74W;V201M;D12 70N †*	*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.

Original Approval Date	Original Effective Date	Policy Owner	Approved by
12/1/2020	1/1/2021	Pharmacy Services	Pharmacy & Therapeutics (P&T) Committee

Policy Revisions History			
Review Date	**Summary of Revisions**	**Revision Effective Date**	**Approved by**
12/1/2020	P&T Committee; discontinued policy 9.036 and created a new policy for QHP	1/1/2021	P&T Committee

Policy Revisions History			
7/1/2021	Updated age restriction for Trikafta to 6 years of age	7/16/2021	P&T Committee
8/12/2021	Annual P&T Review: Added in vitro data to criteria and appendix for Trikafta. Changed approval duration to 6 months intitial, 12 months reauth. Updated approved age for Kalydeco from 6 to 4 months.	1/1/2022	P&T Committee

Next Review Date

8/2022

Other Applicable Policies

Reference to Applicable Laws and Regulations, If Any

Disclaimer Information

Medical Policies are the Plan's guidelines for determining the medical necessity of certain services or supplies for purposes of determining coverage. These Policies may also describe when a service or supply is considered experimental or investigational, or cosmetic. In making coverage decisions, the Plan uses these guidelines and other Plan Policies, as well as the Member's benefit document, and when appropriate, coordinates with the Member's health care Providers to consider the individual Member's health care needs.

Plan Policies are developed in accordance with applicable state and federal laws and regulations, and accrediting organization standards (including NCQA). Medical Policies are also developed, as appropriate, with consideration of the medical necessity definitions in various Plan products, review of current literature, consultation with practicing Providers in the Plan's service area who are medical experts in the particular field, and adherence to FDA and other government agency policies. Applicable state or federal mandates, as well as the Member's benefit document, take precedence over these guidelines. Policies are reviewed and updated on an annual basis, or more frequently as needed. Treating providers are solely responsible for the medical advice and treatment of Members.

The use of this Policy is neither a guarantee of payment nor a final prediction of how a specific claim(s) will be adjudicated. Reimbursement is based on many factors, including member eligibility and benefits on the date of service; medical necessity; utilization management guidelines (when applicable); coordination of benefits; adherence with applicable Plan policies and procedures; clinical coding criteria; claim editing logic; and the applicable Plan – Provider agreement.