JOHNS HOPKINS MEDICINE JOHNS HOPKINS HEALTHCARE	Johns Hopkins HealthCare LLC **Pharmacy Public** **Pharmacy Management Drug Policies**	*Policy Number*	MEDS122
		Effective Date	01/15/2020
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	Subject **CFTR Modulators: Kalydeco, Orkambi, Symdeko, Trikafta**	*Revision Date*	07/19/2023
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This document applies to the following Participating Organizations:

Priority Partners

Keywords: Kalydeco, Orkambi, Symdeko, Trikafta

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I. POLICY

Kalydeco (ivacaftor), Orkambi (lumacaftor/ivacaftor), Symdeko (tezacaftor/ivacaftor), and Trikafta (elexacaftor/ivacaftor/ tezacaftor) will require prior authorization to ensure appropriate use. The process for initiating a prior authorization request can be found in policy PHARM 20.

A. PPMCO members are subject to the Priority Partners formulary, available at www.ppmco.org.
B. USFHP members are subject to prior authorization criteria, step-edits and days-supply limits outlined in the Tricare Policy Manual. Tricare Policy supersedes JHHC Medical/Pharmacy Policies. Tricare limits may be accessed at: http://pec.ha.osd.mil/formulary_search.php?submenuheader=1

II. POLICY CRITERIA

A. **Kalydeco** may be approved for patients meeting the following:
   1. Patient is one month of age or older
   2. Documentation has been provided confirming a diagnosis of Cystic Fibrosis
   3. Patient has been determined by an FDA-approved CF mutation test to have at least one of the following cystic fibrosis transmembrane conductance regulator (CFTR) gene mutations that is responsive to ivacaftor: 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 D,110H, 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
   4. Documentation has been provided showing baseline liver function tests
   5. Documentation has been provided showing percent predicted FEV_1 within the previous 30 days

6. Additionally, if the patient is less than 18 years of age, the following is required:
    a. Baseline ophthalmic examination to monitor for lens opacities/cataracts

B. **Orkambi** may be approved for patients meeting the following:
1. Patient is one year of age or older
2. Documentation has been provided confirming a diagnosis of Cystic Fibrosis
3. Patient has been determined to be homozygous for the F508del mutation in the CFTR gene as confirmed by an FDA-approved CF mutation test
4. Documentation has been provided showing baseline liver function tests
5. Documentation has been provided showing percent predicted FEV_1 within the previous 30 days
6. Additionally, if the patient is less than 18 years of age, the following is required:
    a. Baseline ophthalmic examination to monitor for lens opacities/cataracts

C. **Symdeko** may be approved for patient meeting the following:
1. Patient is six years of age or older
2. Documentation has been provided confirming a diagnosis of Cystic Fibrosis
3. Patient has been determined to have one of the following mutations confirmed by an FDA-approved CF mutation test:
    a. Homzygous F508del mutation
    b. At least one mutation in the CFTR gene that is responsive to tezacaftor-ivacaftor: 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
4. Documentation has been provided showing baseline liver function tests
5. Documentation has been provided showing percent predicted FEV_1 within the previous 30 days
6. Additionally, if the patient is less than 18 years of age, the following is required:
    a. Baseline ophthalmic examination to monitor for lens opacities/cataracts

D. **Trikafta** may be approved for patients meeting the following:
1. Patient is two years of age or older
2. Documentation has been provided confirming a diagnosis of Cystic Fibrosis
3. Patient has been determined to have one of the following mutations confirmed by an FDA-approved CF mutation test:
    a. At least one F508del mutation in the CFTR gene
    b. At least one mutation in the CFTR gene that is responsive to elexacaftor-tezacaftor-ivacaftor: 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, 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

4. Documentation has been provided showing baseline liver function tests
5. Documentation has been provided showing percent predicted FEV_1 within the previous 30 days
6. Additionally, if the patient is less than 18 years of age, the following is required:
    a. Baseline ophthalmic examination to monitor for lens opacities/cataracts

III. AUTHORIZATION PERIOD/LIMITATIONS

A. Initial approval will be restricted to 6 months of therapy
B. Approval for continuation of therapy may be extended in 12-month intervals with documentation showing:
    1. Patient is having a beneficial patient response, evidenced by two or more of the following:
        a. Improvement or stabilization of lung function as demonstrated by percent predicted expiratory volume in 1 second ($ppFEV_1$)
        b. Reduction in pulmonary exacerbations from baseline
        c. Improvement in Quality of life as demonstrated by Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score
        d. Weight gain
        e. Documented improvement of patient symptoms
    2. Patient has follow-up liver function tests showing one of the following:
        a. Serum ALT or AST less than 5 times the upper limit of normal (ULN)
        b. Serum ALT or AST less than 3 times the ULN with bilirubin less than 2 times the ULN
    3. Patient has not received a lung transplant
    4. If patient is younger than 18 years of age, a follow-up ophthalmic evaluation has submitted
C. If the patient's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of a CFTR mutation followed by verification with bi-directional sequencing when recommended by the mutation test instructions for use.

IV. EXCLUSIONS

A. Kalydeco will not be approved for the following:
    1. Any indications or uses that are not FDA-approved, or guideline-supported
    2. Patient who are homozygous for the F508del mutation
    3. Concurrent use with another cystic fibrosis transmembrane conductance regulator (CFTR) agent

B. Orkambi will not be approved for the following:
   1. Any indications or uses that are not FDA-approved, or guideline-supported
   2. Patients with CF other than those homozygous for the F508del mutation
   3. Concurrent use with another cystic fibrosis transmembrane conductance regulator (CFTR) agent

C. Symdeko will not be approved for the following:
   1. Any indications or uses that are not FDA-approved, or guideline-supported
   2. Concurrent use with another cystic fibrosis transmembrane conductance regulator (CFTR) agent

D. Trikafta will not be approved for the following:
   1. Any indications that are not FDA-approved, or guideline-supported
   2. Patients with severe hepatic impairment
   3. Concurrent use with another cystic fibrosis transmembrane conductance regulator (CFTR) agent

E. The use of physician samples, or manufacturer product discounts, does not guarantee coverage under the provisions of the medical and/or pharmacy benefit. All pertinent criteria must be met in order to be eligible for benefit coverage.

V. REFERENCES

1. Kalydeco [Prescribing Information]. Vertex Pharmaceuticals Incorporated: Boston, MA; May 2023
2. Orkambi [Prescribing Information]. Vertex Pharmaceuticals Incorporated: Boston, MA; September 2022
3. Symdeko [Prescribing Information]. Vertex Pharmaceuticals Incorporated: Boston, MA; December 2020
4. Trikafta [Prescribing Information]. Vertex Pharmaceuticals Incorporated: Boston, MA; April 2023

VI. APPROVALS

Signature on file at JHHC

DATE OF REVISION	SUMMARY OF CHANGE
01/15/2020	Policy Creation
12/08/2021	Updated Exclusions section regarding physician samples
07/19/2023	Criteria updates

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