



PRIOR AUTHORIZATION POLICY

POLICY: Cystic Fibrosis – Symdeko Prior Authorization Policy
• Symdeko® (tezacaftor/ivacaftor and ivacaftor tablets – Vertex)

REVIEW DATE: 02/07/2024

INSTRUCTIONS FOR USE

THE FOLLOWING COVERAGE POLICY APPLIES TO HEALTH BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. CERTAIN CIGNA COMPANIES AND/OR LINES OF BUSINESS ONLY PROVIDE UTILIZATION REVIEW SERVICES TO CLIENTS AND DO NOT MAKE COVERAGE DETERMINATIONS. REFERENCES TO STANDARD BENEFIT PLAN LANGUAGE AND COVERAGE DETERMINATIONS DO NOT APPLY TO THOSE CLIENTS. COVERAGE POLICIES ARE INTENDED TO PROVIDE GUIDANCE IN INTERPRETING CERTAIN STANDARD BENEFIT PLANS ADMINISTERED BY CIGNA COMPANIES. PLEASE NOTE, THE TERMS OF A CUSTOMER'S PARTICULAR BENEFIT PLAN DOCUMENT [GROUP SERVICE AGREEMENT, EVIDENCE OF COVERAGE, CERTIFICATE OF COVERAGE, SUMMARY PLAN DESCRIPTION (SPD) OR SIMILAR PLAN DOCUMENT] MAY DIFFER SIGNIFICANTLY FROM THE STANDARD BENEFIT PLANS UPON WHICH THESE COVERAGE POLICIES ARE BASED. FOR EXAMPLE, A CUSTOMER'S BENEFIT PLAN DOCUMENT MAY CONTAIN A SPECIFIC EXCLUSION RELATED TO A TOPIC ADDRESSED IN A COVERAGE POLICY. IN THE EVENT OF A CONFLICT, A CUSTOMER'S BENEFIT PLAN DOCUMENT ALWAYS SUPERSEDES THE INFORMATION IN THE COVERAGE POLICIES. IN THE ABSENCE OF A CONTROLLING FEDERAL OR STATE COVERAGE MANDATE, BENEFITS ARE ULTIMATELY DETERMINED BY THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT. COVERAGE DETERMINATIONS IN EACH SPECIFIC INSTANCE REQUIRE CONSIDERATION OF 1) THE TERMS OF THE APPLICABLE BENEFIT PLAN DOCUMENT IN EFFECT ON THE DATE OF SERVICE; 2) ANY APPLICABLE LAWS/REGULATIONS; 3) ANY RELEVANT COLLATERAL SOURCE MATERIALS INCLUDING COVERAGE POLICIES AND; 4) THE SPECIFIC FACTS OF THE PARTICULAR SITUATION. EACH COVERAGE REQUEST SHOULD BE REVIEWED ON ITS OWN MERITS. MEDICAL DIRECTORS ARE EXPECTED TO EXERCISE CLINICAL JUDGMENT AND HAVE DISCRETION IN MAKING INDIVIDUAL COVERAGE DETERMINATIONS. COVERAGE POLICIES RELATE EXCLUSIVELY TO THE ADMINISTRATION OF HEALTH BENEFIT PLANS. COVERAGE POLICIES ARE NOT RECOMMENDATIONS FOR TREATMENT AND SHOULD NEVER BE USED AS TREATMENT GUIDELINES. IN CERTAIN MARKETS, DELEGATED VENDOR GUIDELINES MAY BE USED TO SUPPORT MEDICAL NECESSITY AND OTHER COVERAGE DETERMINATIONS.

CIGNA NATIONAL FORMULARY COVERAGE:

OVERVIEW

Symdeko is indicated for the treatment of **cystic fibrosis** (CF) in patients ≥ 6 years of age who are homozygous for the F508del mutation or who have at least 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.¹

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. Table 1 lists the responsive CFTR mutations based on: 1) a clinical forced expiratory volume in 1 second (FEV₁) response and/or 2) *in vitro* data in Fischer rat thyroid cells, indicating that tezacaftor/ivacaftor increases chloride transport to $\geq 10\%$ of untreated normal over baseline. CFTR gene mutations that are not responsive to Kalydeco® (ivacaftor granule or tablet) alone are not expected to respond to Symdeko except for F508del homozygotes.

Table 1. List of CFTR Gene Mutations that Produce CFTR Protein and are Responsive to Symdeko.¹

| | | | |
|------|-------|-------|--------|
| E56K | E193K | S945L | F1074L |
| P67L | L206W | S977F | D1152H |

| | | | |
|-------------------|--------------|-------------|-------------------|
| R74W | R347H | F1052V | D1270N |
| D110E | R352Q | E831X | 2789+5G→A |
| D110H | A455E | K1060T | 3272-26A→G |
| R117C | D579G | A1067T | 3849 + 10kbC→T |
| F508del* | 711+3A→G | R1070W | G622D |
| A120T | E60K | F1016S | G970D |
| A234D | E92K | F1099L | G1069R |
| A349V | E116K | G126D | G1244E |
| A554E | E403D | G178E | G1249R |
| A1006E | E558V | G178R | G1349D |
| D192G | E822K | G194R | H939R |
| D443Y | F191V | G194V | H1054D |
| D443Y;G57A; R668C | F311del | G314E | H1375P |
| D614G | F311L | G551D | I148T |
| D836Y | F508C | G551S | I175V |
| D924N | F508C;S1251N | G576A | I336K |
| D979V | F575Y | G576A;R668C | I601F |
| I618T | L346P | M952T | R74Q |
| I807M | L967S | P5L | R74W;D1270N |
| I980K | L997F | P205S | R74W;V201M |
| I1027T | L1324P | Q98R | R74W;V201M;D1270N |
| I1139V | L1335P | Q237E | R75Q |
| I1269N | L1480P | Q237H | R117G |
| I1366N | M152V | Q359R | R117H |
| L15P | M265R | Q1291R | R117L |
| L320V | M952I | R31L | R117P |
| R170H | R1066H | S1251N | W1282R |

Table 1 (continued). List of CFTR Gene Mutations that Produce CFTR Protein and are Responsive to Symdeko.¹

| | | | |
|--------|-----------|--------|--------|
| R258G | R1070Q | S1255P | Y109N |
| R334L | R1162L | T338I | Y161S |
| R334Q | R1283M | T1036N | Y1014C |
| R347L | R1283S | T1053I | Y1032C |
| R347P | S549N | V201M | R792G |
| R352W | S549R | V232D | R933G |
| R553Q | S589N | V562I | S1159F |
| R668C | S737F | V754M | S1159P |
| R751L | S912L | V1153E | V1240G |
| V1293G | 546insCTA | | |

CFTR – Cystic fibrosis transmembrane regulator; * A patient must have two copies of the F508del mutation or at least one copy of a responsive mutation presented in Table 1 to be indicated.

Guidelines

Guidelines from the CF Foundation (2018) provide guidance on the use of CFTR therapy in patients with CF; Symdeko is not addressed.²

POLICY STATEMENT

Prior Authorization is recommended for prescription benefit coverage of Symdeko. All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with Symdeko as well as the monitoring required for adverse events and efficacy, approval requires

Symdeko to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Symdeko® (tezacaftor/ivacaftor and ivacaftor tablets [Vertex]) is(are) covered as medically necessary when the following criteria is(are) met for FDA-approved indication(s) or other uses with supportive evidence (if applicable):

FDA-Approved Indication

1. Cystic Fibrosis. Approve for 1 year if the patient meets the following (A, B, and C):

A) Patient is ≥ 6 years of age; AND

B) Patient meets ONE of the following (i or ii):

i. Patient has at least one of the following mutations in the cystic fibrosis transmembrane conductance regulator gene: E56K, P67L, R74W, D110E, D110H, R117C, E193K, L206W, R347H, R352Q, A455E, D579G, 711+3A \rightarrow G, S945L, S977F, F1052V, E831X, K1060T, A1067T, R1070W, F1074L, D1152H, D1270N, 2789+5G \rightarrow A, 3272-26A \rightarrow G, 3849 + 10kbC \rightarrow T, 546insCTA, A120T, A234D, A349V, A554E, A1006E, D192G, D443Y, D443Y;G57A;R668C, D614G, D836Y, D924N, D979V, I618T, I807M, I980K, I1027T, I1139V, I1269N, I1366N, L15P, L320V, R170H, R258G, R334L, R334Q, R347L, R347P, R352W, R553Q, R668C, R751L, V1293G, E60K, E92K, E116K, E403D, E558V, E822K, F191V, F311del, F311L, F508C, F508C;S1251N, F575Y, L346P, L967S, L997F, L1324P, L1335P, L1480P, M152V, M265R, M952I, R1066H, R1070Q, R1162L, R1283M, R1283S, S549N, S549R, S589N, S737F, S912L, F1016S, F1099L, G126D, G178E, G178R, G194R, G194V, G314E, G551D, G551S, G576A, G576A;R668C, M952T, P5L, P205S, Q98R, Q237E, Q237H, Q359R, Q1291R, R31L, S1251N, S1255P, T338I, T1036N, T1053I, V201M, V232D, V562I, V754M, V1153E, G622D, G970D, G1069R, G1244E, G1249R, G1349D, H939R, H1054D, H1375P, I148T, I175V, I336K, I601F, R74Q, R74W;D1270N, R74W;V201M, R74W;V201M;D1270N, R75Q, R117G, R117H, R117L, R117P, W1282R, Y109N, Y161S, Y1014C, Y1032C, R792G, R933G, S1159F, S1159P, or V1240G; OR

ii. Patient has two copies of the F508del mutation; AND

C) The medication is prescribed by or in consultation with a pulmonologist or a physician who specializes in the treatment of cystic fibrosis.

CONDITIONS NOT COVERED

Symdeko® (tezacaftor/ivacaftor and ivacaftor tablets [Vertex]) is(are) considered experimental, investigational, or unproven for ANY other use(s) including the following (this list may not be all inclusive; criteria will be updated as new published data are available):

- 1. Cystic Fibrosis (CF), Patients with Unknown Cystic Fibrosis Transmembrane Regulator (CFTR) Gene Mutation.** An FDA-cleared CF mutation test should be used to detect the presence of the CFTR mutation prior to use of Symdeko.¹
- 2. Combination Therapy with Orkambi, Kalydeco, or Trikafta.** Symdeko contains ivacaftor, the active agent in Kalydeco and part of Orkambi and Trikafta. Symdeko also contains tezacaftor, part of Trikafta. Symdeko is not indicated in combination with Kalydeco, Orkambi, or Trikafta.

REFERENCES

1. Symdeko® tablets [prescribing information]. Cambridge, MA: Vertex; August 2023.
2. Ren CL, Morgan RL, Oermann C, et al. Cystic Fibrosis Foundation Pulmonary Guidelines: Use of cystic fibrosis transmembrane conductance regulator modulator therapy in patients with cystic fibrosis. *Ann Am Thorac Soc.* 2018;15(3):271-280.

HISTORY

| Type of Revision | Summary of Changes | Review Date |
|------------------|----------------------|-------------|
| Annual Revision | No criteria changes. | 02/08/2023 |
| Annual Revision | No criteria changes. | 02/07/2024 |

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