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Subject: Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) Modulators

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DESCRIPTION:

Vanzacaftor-Tezacaftor-Deutivacaftor (Alyftrek)

Vanzacaftor/tezacaftor/deutivacaftor (Alyftrek) combination fixed-dose tablets were approved by the U.S. Food and Drug Administration (FDA) in 2024 for use in patients aged 6 years and older with cystic fibrosis (CF) who have at least one F508del mutation or another responsive mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. An FDA-cleared test should be used to confirm the presence of an indicated mutation if the patient's genotype is unknown.

Vanzacaftor/tezacaftor/deutivacaftor is a CFTR modulator. It works by enhancing the function of the CFTR protein, a chloride channel present at the surface of epithelial cells in multiple organs, resulting in increases in chloride transplant. Vanzacaftor binds to a site on the CFTR protein (different from where tezacaftor binds) and has an additive effect in facilitating the cellular process and trafficking of select mutant forms of CFTR (including F508del-CFTR) to increase the amount of CFTR protein delivered to the cell surface compared to either molecule alone. Tezacaftor binds to a site on the CFTR protein and has an additive effect in facilitating the cellular process and trafficking of select mutant forms of CFTR (including F508del-CFTR) to increase the amount of CFTR protein delivered to the cell surface compared to either molecule alone. Deutivacaftor potentiates the channel open probability of the CFTR protein at the cell surface.

The efficacy and safety of vanzacaftor/tezacaftor/deutivacaftor (Van/Tez/Deut) were evaluated in two randomized, double-blind, active controlled Phase 3 clinical trials. Both trials enrolled patients with at least one F508del mutation or other mutation responsive to triple combination CFTR modulators. In trial 1 (SKYLINE 102, NCT05033080), patients that were heterozygous for F508del and a minimal function

mutation were initially treated with elexacaftor 200 mg/tezacaftor 100 mg/ivacaftor 150 mg (Elx/Tez/Iva; Trikafta) in the morning and ivacaftor 150 mg in the evening for 4 weeks before being randomized to continue the same treatment (n=202) or switch to vanzacaftor 20 mg/tezacaftor 100 mg/deutivacaftor 250 mg (n=196). The primary endpoint was mean absolute change in ppFEV1 from baseline through Week 24. A key secondary endpoint was mean absolute change in SwCl from baseline through Week 24. At Week 24, Van/Tez/Deut showed non-inferiority in terms of improving lung function (comparing mean absolute change in ppFEV1 from baseline).

In Trial 2 (SYLINE 103, NCT05076149), patients with F508del-F508del, F508del-residual function, F508del-gating, or Trikafta-responsive, non-F508del genotypes underwent a similar 4-week run-in period described in Trial 1 above. Patients were randomized to continue treatment with Elx/Tez/Iva (n=289) or switch to treatment with Van/Tez/Deut (n=284). The primary endpoint was mean absolute change in ppFEV1 from baseline through Week 24. A key secondary endpoint was mean absolute change in SwCl from baseline through Week 24. At Week 24, Van/Tez/Deut showed non-inferiority in terms of improving lung function (comparing mean absolute change in ppFEV1 from baseline).

Both studies showed a significant difference in sweat chloride reduction between treatments, although the study was not designed to assess this difference. A summary of efficacy outcomes in both trials is shown in Table 1:

Table 1. Efficacy at Week 24 in Patients 12 Years and Older with Cystic Fibrosis with a F508del or Other Responsive Mutation in the CFTR Gene

Primary Endpoint	*Trial 1 (N=398)*		*Trial 2 (N=573)*	
	Van/Tez/Deut	Elx/Tez/Iva	Van/Tez/Deut	Elx/Tez/Iva
Absolute change from baseline in ppFEV1 (percentage points)	0.5 (0.3)	0.3 (0.3)	0.2 (0.3)	0.0 (0.2)
LS Mean Difference (95% CI)*	*0.2 (-0.7 to 1.1)*		*0.2 (-0.5 to 0.9)*	
Key Secondary Endpoint				
Absolute change from baseline in SwCl (mmol/L)	-7.5 (0.8)	0.9 (0.8)	-5.1 (0.7)	-2.3 (0.7)
LS Mean Difference (95% CI)	*-8.4 (-10.5 to -6.3)*		*-2.8 (-4.7 to -0.9)*	

**The prespecified noninferiority margin was -3.0 percentage points.*

Key: CFTR, cystic fibrosis transmembrane conductance regulator; ppFEV1, percent predicted Forced Expiratory Volume in 1 second; Van/Tez/Deut, vanzacaftor/tezacaftor/deutivacaftor; Elx/Tez/Iva, elexacaftor/tezacaftor/ivacaftor

Most common adverse reactions to Van/Tex/Deut (≥5% of patients and at a frequency higher than Elx/Tez/Iva by ≥1%) were cough, nasopharyngitis, upper respiratory tract infection, headache, oropharyngeal pain, influenza, fatigue, increased ALT, rash, increased AST, and sinus congestion.

Elexacaftor-tezacaftor-ivacaftor (Trikafta)

Elexacaftor, tezacaftor, and ivacaftor combination therapy was approved by the U.S. Food and Drug Administration (FDA) in 2019 for the treatment of cystic fibrosis (CF) in patients aged 12 years and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR).

Elexacaftor, tezacaftor, and ivacaftor increase the quantity and function of the CFTR protein, a chloride channel present at the surface of epithelial cells in multiple organs, resulting in increases in chloride transplant. In patients with the *F508del* mutation, CFTR protein misfolding causes a defect in cellular processing and trafficking that targets the protein for degradation, resulting in a lower quantity of CFTR at the cell surface. The small amount of *F508del*-CFTR that does reach the cell surface is less stable and has low channel-open probability compared to the wild-type CFTR protein. Elexacaftor and tezacaftor facilitate the cellular processing and trafficking of normal and select mutant forms of CFTR (including *F508del*-CFTR) to increase the amount of mature CFTR protein delivered to the cell surface. Ivacaftor is a CFTR potentiator that increases chloride transport by potentiating the channel-opening probability of the CFTR protein. CFTR protein must be present at the cell surface for ivacaftor to function. Ivacaftor can potentiate the CFTR protein delivered to the cell surface by tezacaftor, leading to a further enhancement of chloride transport than either agent alone.

The efficacy and safety of elexacaftor in combination with tezacaftor plus ivacaftor was evaluated in participants with cystic fibrosis homozygous for the F508del mutation, aged 12 years or older with stable disease, and with a percentage predicted forced expiratory volume in 1 s (ppFEV1) of 40–90%, inclusive. After a 4-week tezacaftor plus ivacaftor run-in period, participants were randomly assigned (1:1) to 4 weeks of elexacaftor 200 mg-tezacaftor 100 mg once daily plus ivacaftor 150 mg twice daily (n=55) or tezacaftor 100 mg once daily plus ivacaftor 150 mg twice daily (n=52). The primary outcome was the absolute change from baseline (measured at the end of the tezacaftor plus ivacaftor run-in) in ppFEV1 at week 4. Key secondary outcomes were absolute change in sweat chloride and Cystic Fibrosis Questionnaire-Revised respiratory domain (CFQ-R RD) score.

The elexacaftor plus tezacaftor plus ivacaftor group had improvements in the primary outcome of ppFEV1 (least squares mean [LSM] treatment difference of 10.0 percentage points [95% CI 7.4 to 12.6], p<0.0001) and the key secondary outcomes of sweat chloride concentration (LSM treatment difference −45.1 mmol/L [95% CI −50.1 to −40.1], p<0.0001), and CFQ-R RD score (LSM treatment difference 17.4 points [95% CI 11.8 to 23.0], p<0.0001) compared with the tezacaftor plus ivacaftor group. The triple combination regimen was well tolerated, with no discontinuations. Most adverse events were mild or moderate; serious adverse events occurred in two (4%) participants receiving elexacaftor plus tezacaftor plus ivacaftor and in one (2%) receiving tezacaftor plus ivacaftor.

Tezacaftor-Ivacaftor (Symdeko)

Tezacaftor and ivacaftor combination therapy was approved by the U.S. Food and Drug Administration (FDA) in 2018 for use in patients aged 12 years and older with cystic fibrosis (CF) who are homozygous for the F508 del mutation in the CF transmembrane conductance regulator (CFTR) gene or have at least one mutation in the CFTR gene that is responsive to tezacaftor/ivacaftor. This approval was expanded to include children 6 to 12 years of age in July 2019.

Tezacaftor/ivacaftor increases the quantity and function of the CFTR protein, a chloride channel present at the surface of epithelial cells in multiple organs, resulting in increases in chloride transplant. In patients with the *F508del* mutation, CFTR protein misfolding causes a defect in cellular processing and trafficking that targets the protein for degradation, resulting in a lower quantity of CFTR at the cell surface. The small amount of *F508del*-CFTR that does reach the cell surface is less stable and has low channel-open probability compared to the wild-type CFTR protein. Tezacaftor facilitates the cellular processing and trafficking of normal and select mutant forms of CFTR (including *F508del*-CFTR) to increase the amount of mature CFTR protein delivered to the cell surface. Ivacaftor is a CFTR potentiator that increases chloride transport by potentiating the channel-opening probability of the CFTR protein. CFTR protein must be present at the cell surface for ivacaftor to function. Ivacaftor can potentiate the CFTR protein delivered to the cell surface by tezacaftor, leading to a further enhancement of chloride transport than either agent alone.

The efficacy and safety of tezacaftor/ivacaftor in patients with CF who are homozygous for the F508del mutation in the CFTR gene were evaluated in a randomized, double-blind, placebo-controlled, 24-week clinical trial in 504 patients. Treatment consisted of fixed-dose combination tezacaftor 100 mg/ivacaftor 150 mg orally in the morning and ivacaftor 150 mg orally in the evening or matching placebo. The placebo-adjusted absolute change from baseline in percentage of predicted FEV1 was a significant 4 percentage points in favor of tezacaftor/ivacaftor treatment (mean absolute change, +3.4 vs -0.6 percentage points, respectively). Also significantly improved with tezacaftor/ivacaftor versus placebo were the number of pulmonary exacerbations (estimated event rate, 0.64 vs 0.99 per year). Body mass index was not significantly different between groups at week 24. Discontinuation due to adverse events was 2.8% with active treatment and 3.1% with placebo. Overall, adverse event rates were similar between groups.

The efficacy and safety of tezacaftor/ivacaftor in patients with CF who are heterozygous for the F508del mutation but with a second allele with a CFTR mutation with residual function were evaluated in a randomized, double-blind, placebo-controlled, 8-week crossover trial in 248 patients.

Each patient received 2 of the following 3 treatment regimens in a crossover format that included 2 intervention periods of 8 weeks of active treatment followed by an 8-week washout period: (1) tezacaftor 100 mg orally once daily and ivacaftor 150 mg orally every 12 hours (combination therapy), (2) ivacaftor 150 mg orally every 12 hours (monotherapy), or (3) placebo. The mean difference versus placebo in absolute change in percentage of predicted FEV1 from baseline to the average of the week 4 and week 8 scores was significant for combination tezacaftor/ivacaftor (6.8 percentage points) and ivacaftor monotherapy (4.7 percentage points). The mean difference was also significant in favor of combination therapy versus monotherapy. The mean placebo-adjusted difference in absolute change from baseline to average of week 4 and week 8 in Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score was also significant for the combination therapy (11.1 points) and monotherapy (9.7 points), but there was no significant difference between the 2 active treatment groups. A clinically important difference of 4 points or greater in the CFQ-R respiratory domain score occurred in 65% of the combination therapy group, 58% of the monotherapy group, and in 33% of the placebo group. Rates of adverse events were similar across groups.

Lumacaftor Ivacaftor (Orkambi)

Lumacaftor and ivacaftor combination therapy was approved by the U.S. Food and Drug Administration (FDA) in July 2015 for use in patients aged 12 years and older with cystic fibrosis (CF) who are homozygous for the F508 del mutation in the CF transmembrane conductance regulator (CFTR) gene. The approval was expanded to included children 6 years and older in September 2016 and to include those 2 years and older in August 2018. In the US, this mutation represents approximately 8,500 patients with CF (half of the total CF population). There is currently no treatment available that specifically targets this particular mutation; current treatment options only address complications associated with the disease. Prior to FDA approval, lumacaftor/ivacaftor was designated as an Orphan Drug for its FDA-approved indication.

Lumacaftor is a CFTR corrector and ivacaftor is a CFTR potentiator. The efficacy of lumacaftor/ivacaftor in patients with CF who are homozygous for the F508del mutation in the CFTR gene was evaluated in two randomized, double-blind, placebo-controlled, 24-week clinical trials (Trials 1 and 2) in 1108 clinically stable patients with CF of whom 369 patients received lumacaftor/ivacaftor twice daily.

Trial 1 evaluated 549 patients with CF who were aged 12 years and older (mean age 25.1 years) with ppFEV1 at screening between 40-90 [mean ppFEV1 60.7 at baseline (range: 31.1 to 94.0)]. Trial 2 evaluated 559 patients aged 12 years and older (mean age 25.0 years) with ppFEV1 at screening between 40-90 [mean ppFEV1 60.5 at baseline (range: 31.3 to 99.8)].

Patients in both trials were randomized 1:1:1 to receive either lumacaftor 400 mg q12h/ivacaftor 250 mg q12h; or lumacaftor 600 mg once daily/ivacaftor 250 mg q12h or placebo. Patients took the study drug with fat-containing food for 24 weeks in addition to their prescribed CF therapies (e.g., bronchodilators, inhaled antibiotics, dornase alfa, and hypertonic saline).

The primary efficacy endpoint in both trials was change in lung function as determined by absolute change from baseline in ppFEV1 at Week 24, assessed as the average of the treatment effects at Week 16 and at Week 24. In both trials, treatment with lumacaftor/ivacaftor resulted in a statistically significant improvement in ppFEV1. The treatment difference between lumacaftor/ivacaftor and placebo for the mean absolute change in ppFEV1 from baseline at Week 24 (assessed as the average of the treatment effects at Week 16 and at Week 24) was 2.6 percentage points [95% CI (1.2, 4.0)] in Trial 1 (P=0.0003) and 3.0 percentage points [95% CI (1.6, 4.4)] in Trial 2 (P<0.0001). These changes persisted throughout the 24-week treatment period (Figure 1). Improvements in ppFEV1 were observed regardless of age, disease severity, sex, and geographic region.

Ivacaftor (Kalydeco)

Ivacaftor (Kalydeco™) was approved by the US Food and Drug Administration (FDA) on January 31, 2012 for treatment of cystic fibrosis (CF) in persons who have any of the following mutations in the CF transmembrane conductance regulator (CFTR) gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R, or R117H. CF is a life-threatening, multisystem genetic disorder characterized by progressive lung disease. The disorder is the result of mutations in the CFTR gene located on chromosome 7. CF is inherited as an autosomal recessive trait. In an individual with a mutated CFTR gene, the risk of developing CF is dependent upon the mutation(s) present. The most common mutation is F508del. Another well-known mutation is G551D. Since the identification of CFTR in 1989 almost 2,000 mutations have been identified.

Ivacaftor exerts its effects by increasing chloride transport by potentiating the channel-open probability (or gating) of the G55ID-CFTR protein (an epithelial cell chloride channel). It is the first drug that directly targets the defective CFTR protein instead of the cystic fibrosis symptoms. In clinical studies of ivacaftor, it was ineffective in subjects who were homozygous for the F508del mutation in the CFTR gene; as such, it should not be used in this population. Ivacaftor is FDA-approved for use in children age 12 months of age and older.

POSITION STATEMENT:

Comparative Effectiveness

The FDA has deemed the drug(s) or biological product(s) in this coverage policy to be appropriate for self-administration or administration by a caregiver (i.e., not a healthcare professional). Therefore, coverage (i.e., administration) in a provider-administered setting such as an outpatient hospital, ambulatory surgical suite, physician office, or emergency facility is not considered medically necessary.

Elexacaftor-tezacaftor-ivacaftor (Trikafta)

Initiation of elexacaftor-tezacaftor-ivacaftor (Trikafta™) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with cystic fibrosis (CF)
2. Member meets **ONE** of the following:
    a. Member has at least one F508 del mutation in the CF transmembrane conductance regulator (CFTR) gene confirmed by an FDA-cleared cystic fibrosis mutation test – laboratory documentation must be provided
    b. Member has at least one mutation in the CFTR gene confirmed by an FDA-cleared cystic fibrosis mutation test that is responsive to treatment with elexacaftor-tezacaftor-ivacaftor per the FDA-approved label (Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f354423a-85c2-41c3-a9db-0f3aee135d8d – see CLINICAL PHARMACOLOGY (12.1)) – laboratory documentation must be provided
3. Elexacaftor-tezacaftor-ivacaftor is not administered in combination with single-agent ivacaftor (Kalydeco), lumacaftor-ivacaftor (Orkambi), or tezacaftor-ivacaftor co-packaged with ivacaftor (Symdeko™)
4. Dose does not exceed three tablets per day
5. One of the following:
    a. Member is 2 years of age or older
    b. Member's age is within FDA approved labeling

Approval duration: 6 months

Continuation of elexacaftor-tezacaftor-ivacaftor (Trikafta™) **meets the definition of medical necessity** for members meeting **ALL** of the following criteria:

1. Authorization/reauthorization has been previously approved by Florida Blue **OR** the member has previously met all indication-specific initiation criteria
2. Member meets **ONE** of the following:
    a. Member demonstrates a clinically meaningful response to treatment with elexacaftor-tezacaftor-ivacaftor as indicated by any of the following:
        i. Improvement in forced expiratory volume in one second (FEV1) – documentation must be provided
        ii. Improvement in body mass index (BMI) – documentation must be provided
        iii. Reduction in pulmonary exacerbations – documentation must be provided
        iv. Improvement in quality of life as demonstrated by Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score – documentation must be provided
    b. Member currently demonstrates a beneficial response to treatment with tezacaftor-ivacaftor **AND** has been receiving treatment with an ivacaftor-based regimen (Symdeko, Kalydeco, Orkambi) for a minimum of 18 months
3. Elexacaftor-tezacaftor-ivacaftor is not administered in combination with single-agent ivacaftor (Kalydeco), lumacaftor-ivacaftor (Orkambi), or tezacaftor-ivacaftor co-packaged with ivacaftor (Symdeko™)
4. Dose does not exceed
    a. Adults and children 6 years and older: three tablets per day
    b. Children 2 years to less than 6 years old: two packets per day
5. One of the following:
    a. Member is 2 years of age or older
    b. Member's age is within FDA approved labeling

Approval duration: 1 year

NOTE: If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of any mutation. Quest Diagnostics® can perform the CF mutation test. Additionally, documentation of member's mutation from the Cystic Fibrosis Foundation CF Patient Registry is acceptable in place of original laboratory documentation.

<u>Tezacaftor-Ivacaftor (Symdeko)</u>

Initiation of tezacaftor/ivacaftor co-packaged with ivacaftor (Symdeko™) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with cystic fibrosis (CF)
2. Member meets **ONE** of the following:
    a. Member has a homozygous F508 del mutation in the CF transmembrane conductance regulator (CFTR) gene confirmed by an FDA-cleared cystic fibrosis mutation test – laboratory documentation must be provided

b. Member has at least one mutation in the CFTR gene confirmed by an FDA-cleared cystic fibrosis mutation test that is responsive to treatment with tezacaftor/ivacaftor per the FDA-approved label (Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=302ae804-37db-44fd-ac2f-3dbdeda9aa4b – see CLINICAL PHARMACOLOGY (12.1)) – laboratory documentation must be provided

3. Tezacaftor-ivacaftor co-packaged with ivacaftor is not administered in combination with single-agent ivacaftor (Kalydeco), elexacaftor-tezacaftor-ivacaftor (Trikafta), or lumacaftor/ivacaftor (Orkambi)
4. Dose does not exceed two tablets per day
5. One of the following:
    a. Member is 6 years of age or older
    b. Member's age is within FDA approved labeling

Approval duration: 6 months

Continuation of tezacaftor/ivacaftor co-packaged with ivacaftor (Symdeko™) **meets the definition of medical necessity** for members meeting **ALL** of the following criteria:

1. Authorization/reauthorization has been previously approved by Florida Blue **OR** the member has previously met all indication-specific initiation criteria
2. Member meets **ONE** of the following:
    a. Member demonstrates a clinically meaningful response to treatment with tezacaftor/ivacaftor as indicated by any of the following:
        i. Improvement in forced expiratory volume in one second (FEV1) – documentation must be provided
        ii. Improvement in body mass index (BMI) – documentation must be provided
        iii. Reduction in pulmonary exacerbations – documentation must be provided
        iv. Improvement in quality of life as demonstrated by Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score – documentation must be provided
    b. Member currently demonstrates a beneficial response to treatment with tezacaftor/ivacaftor **AND** has been receiving treatment with an ivacaftor-based regimen (Symdeko, Kalydeco, Orkambi) for a minimum of 18 months
3. Tezacaftor-ivacaftor co-packaged with ivacaftor is not administered in combination with single-agent ivacaftor (Kalydeco), elexacaftor-tezacaftor-ivacaftor (Trikafta), or lumacaftor/ivacaftor (Orkambi)
4. Dose does not exceed two tablets per day
5. One of the following:
    a. Member is 6 years of age or older
    b. Member's age is within FDA approved labeling

Approval duration: 1 year

NOTE: If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of any mutation. Quest Diagnostics® can perform the CF mutation test. Additionally, documentation of member's mutation from the Cystic Fibrosis Foundation CF Patient Registry is acceptable in place of original laboratory documentation.

Lumacaftor Ivacaftor (Orkambi)

Initiation of lumacaftor/ivacaftor (Orkambi™) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with cystic fibrosis (CF)
2. Member has a homozygous F508 del mutation in the CF transmembrane conductance regulator (CFTR) gene confirmed by an FDA-cleared cystic fibrosis mutation test – laboratory documentation must be provided
3. Lumacaftor-ivacaftor is not administered in combination with single-agent ivacaftor (Kalydeco), elexacaftor-tezacaftor-ivacaftor (Trikafta), or co-packaged tezacaftor/ivacaftor (Symdeko)
4. Dose does not exceed:
    a. Adults and children 12 years of age and older: Two tablets (each containing lumacaftor 200 mg/ivacaftor 125 mg) twice daily
    b. Children 6 through 11 years of age: Two tablets (each containing lumacaftor 100 mg/ivacaftor 125 mg) twice daily
    c. Children 2 through 5 years of age:
        i. Body weight less than 14 kg: one packet (each containing lumacaftor 100 mg/ivacaftor 125 mg) twice daily
        ii. Body weight 14 kg or greater: one packet (each containing lumacaftor 150 mg/ivacaftor 188 mg) twice daily
    d. Children 1 through 2 years of age:
        i. Body weight 7 kg to less than 9 kg: one packet (each containing lumacaftor 75 mg/ivacaftor 94 mg) twice daily
        ii. Body weight 9 kg to less than 14 kg: one packet (each containing lumacaftor 100 mg/ivacaftor 125 mg) twice daily
        iii. Body weight 14 kg or greater: one packet (each containing lumacaftor 150 mg/ivacaftor 188 mg) twice daily
5. One of the following:
    a. Member is 1 year of age or older
    b. Member's age is within FDA approved labeling

Approval duration: 6 months

Continuation of lumacaftor/ivacaftor (Orkambi™) **meets the definition of medical necessity** for members meeting **ALL** of the following criteria:

1. Authorization/reauthorization has been previously approved by Florida Blue **OR** the member has previously met all indication-specific initiation criteria
2. Member meets **ONE** of the following:
    a. Member demonstrates a clinically meaningful response to treatment with lumacaftor/ivacaftor as indicated by any of the following:
        i. Improvement in forced expiratory volume in one second (FEV1) – documentation must be provided
        ii. Improvement in body mass index (BMI) – documentation must be provided
        iii. Reduction in pulmonary exacerbations – documentation must be provided
        iv. Improvement in quality of life as demonstrated by Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score – documentation must be provided
    b. Member currently demonstrates a beneficial response to treatment with lumacaftor/ivacaftor **AND** has been receiving treatment for a minimum of 18 months
3. Lumacaftor-ivacaftor is not administered in combination with single-agent ivacaftor (Kalydeco), elexacaftor-tezacaftor-ivacaftor (Trikafta), or co-packaged tezacaftor/ivacaftor (Symdeko)
4. Dose does not exceed:
    a. Adults and children 12 years of age and older: Two tablets (each containing lumacaftor 200 mg/ivacaftor 125 mg) twice daily
    b. Children 6 through 11 years of age: Two tablets (each containing lumacaftor 100 mg/ivacaftor 125 mg) twice daily
    c. Children 2 through 5 years of age:
        i. Body weight less than 14 kg: one packet (each containing lumacaftor 100 mg/ivacaftor 125 mg) twice daily
        ii. Body weight 14 kg or greater: one packet (each containing lumacaftor 150 mg/ivacaftor 188 mg) twice daily
    d. Children 1 through 2 years of age:
        i. Body weight 7 kg to less than 9 kg: one packet (each containing lumacaftor 75 mg/ivacaftor 94 mg) twice daily
        ii. Body weight 9 kg to less than 14 kg: one packet (each containing lumacaftor 100 mg/ivacaftor 125 mg) twice daily
        iii. Body weight 14 kg or greater: one packet (each containing lumacaftor 150 mg/ivacaftor 188 mg) twice daily
5. One of the following:
    a. Member is 1 year of age or older
    b. Member's age is within FDA approved labeling

Approval duration: 1 year

NOTE: If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of any mutation. Quest Diagnostics® can perform the CF mutation test. Additionally, documentation of member's mutation from the Cystic Fibrosis Foundation CF Patient Registry is acceptable in place of original laboratory documentation.

Ivacaftor (Kalydeco)

Initiation of ivacaftor (Kalydeco) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member has a diagnosis of cystic fibrosis (CF)
2. Member has a mutation on the CF transmembrane conductance regulator (CFTR) gene confirmed by an FDA-cleared cystic fibrosis mutation test that is responsive to treatment with ivacaftor per the FDA-approved label (Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=0ab0c9f8-3eee-4e0f-9f3f-c1e16aaffe25) – laboratory documentation must be provided
3. Member is not homozygous for the F508del mutation on the CFTR gene
4. Use is not in combination with elexacaftor-tezacaftor-ivacaftor (Trikafta), lumacaftor-ivacaftor (Orkambi), or co-packaged tezacaftor/ivacaftor (Symdeko)
5. One of the following:
    a. Member is 1 month of age or older
    b. Member's age is within FDA approved labeling
6. The dose does not exceed:
    a. Adults and children ages 6 years and older: 150 mg twice daily
    b. Children ages 6 months to less than 6 years:
        i. Body weight 5 kg to less than 7 kg: 25 mg twice daily
        ii. Body weight 7 kg to 14 kg: 50 mg twice daily
        iii. Body weight 14 kg or greater: 75 mg twice daily
    c. Children ages 4 months to less than 6 months:
        i. Body weight 5 kg or greater: 25 mg twice daily
    d. Children ages 2 months to less than 4 months:
        i. Body weight 3 kg or greater: 13.4 mg twice daily
    e. Children ages 1 month to less than 2 months:
        i. Body weight 3 kg or greater: 5.8 mg twice daily

Duration of approval: 6 months

Continuation of ivacaftor (Kalydeco) me**ets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Authorization/reauthorization has been previously approved by Florida Blue in the past two years **OR** the member has previously met all indication-specific initiation criteria
2. Member meets **ONE** of the following:
    a. Member demonstrates a clinically meaningful response to treatment with lumacaftor/ivacaftor as indicated by any of the following:
        i. Improvement in forced expiratory volume in one second (FEV1) – documentation must be provided
        ii. Improvement in body mass index (BMI) – documentation must be provided
        iii. Reduction in pulmonary exacerbations – documentation must be provided
        iv. Improvement in quality of life as demonstrated by Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score – documentation must be provided
    b. Member currently demonstrates a beneficial response to treatment with ivacaftor AND has been receiving treatment for a minimum of 18 months
3. Ivacaftor is not administered in combination with elexacaftor-tezacaftor-ivacaftor (Trikafta), lumacaftor/ivacaftor (Orkambi), or co-packaged tezacaftor/ivacaftor (Symdeko)
4. Dose does not exceed:
    a. Adults and children ages 6 years and older: 150 mg twice daily
    b. Children ages 6 months to less than 6 years:
        i. Body weight 5 kg to less than 7 kg: 25 mg twice daily
        ii. Body weight 7 kg to 14 kg: 50 mg twice daily
        iii. Body weight 14 kg or greater: 75 mg twice daily
    c. Children ages 4 months to less than 6 months:
        i. Body weight 5 kg or greater: 25 mg twice daily
    d. Children ages 2 months to less than 4 months:
        i. Body weight 3 kg or greater: 13.4 mg twice daily
    e. Children ages 1 month to less than 2 months:
        i. Body weight 3 kg or greater: 5.8 mg twice daily
5. One of the following:
    a. Member is 1 month of age or older
    b. Member's age is within FDA approved labeling

Duration of approval: 1 year

NOTE: If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of any mutation. Quest Diagnostics® can perform the CF mutation test. Additionally, documentation of member's mutation from the Cystic Fibrosis Foundation CF Patient Registry is acceptable in place of original laboratory documentation.

Vanzacaftor-Tezacaftor-Deutivacaftor (Alyftrek)

Initiation of vanzacaftor-tezacaftor-deutivacaftor (Alyftrek) **meets the definition of medical necessity** when **ALL** of the following criteria are met:

1. Member is diagnosed with cystic fibrosis (CF)
2. Member meets **ONE** of the following:
    a. Member has at least one F508 del mutation in the CF transmembrane conductance regulator (CFTR) gene confirmed by an FDA-cleared cystic fibrosis mutation test – laboratory documentation must be provided
    b. Member has at least one mutation in the CFTR gene confirmed by an FDA-cleared cystic fibrosis mutation test that is responsive to treatment with vanzacaftor-tezacaftor-deutivacaftor per the FDA-approved label (Available at: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7e635909-c6fd-4f0d-ae77-cdff03653a20 – see CLINICAL PHARMACOLOGY (12.1)) – laboratory documentation must be provided
3. Vanzacaftor-tezacaftor-deutivacaftor is not administered in combination with single-agent ivacaftor (Kalydeco), elexacaftor-tezacaftor-ivacaftor (Trikafta), lumacaftor/ivacaftor (Orkambi), or tezacaftor-ivacaftor co-packaged with ivacaftor (Symdeko)
4. Dose does not exceed two tablets of vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg daily with the following exception:
    a. Member is 6 to less than 12 years old AND weighs less than 40 kg: Three tablets of vanzacaftor 4 mg/tezacaftor 20 mg/deutivacaftor 50 mg daily
5. One of the following:
    a. Member is 6 years of age or older
    b. Member's age is within FDA approved labeling

Approval duration: 6 months

Continuation of vanzacaftor-tezacaftor-deutivacaftor (Alfytrek) **meets the definition of medical necessity** for members meeting **ALL** of the following criteria:

1. Authorization/reauthorization has been previously approved by Florida Blue **OR** the member has previously met all indication-specific initiation criteria
2. Member meets **ONE** of the following:
    a. Member demonstrates a clinically meaningful response to treatment with vanzacaftor-tezacaftor-deutivacaftor as indicated by any of the following:
        i. Improvement in forced expiratory volume in one second (FEV1) – documentation must be provided
        ii. Improvement in body mass index (BMI) – documentation must be provided
        iii. Reduction in pulmonary exacerbations – documentation must be provided

iv. Improvement in quality of life as demonstrated by Cystic Fibrosis Questionnaire-Revised (CFQ-R) respiratory domain score – documentation must be provided

b. Member currently demonstrates a beneficial response to treatment with vanzacaftor-tezacaftor-deutivacaftor **AND** has been receiving treatment with an ivacaftor-based regimen (Symdeko, Kalydeco, Orkambi, Trikafta) for a minimum of 18 months

3. Vanzacaftor-tezacaftor-deutivacaftor is not administered in combination with single-agent ivacaftor (Kalydeco), elexacaftor-tezacaftor-ivacaftor (Trikafta), lumacaftor/ivacaftor (Orkambi), or tezacaftor-ivacaftor co-packaged with ivacaftor (Symdeko)
4. Dose does not exceed two tablets of vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg daily with the following exception:
    a. Member is 6 to less than 12 years old AND weighs less than 40 kg: Three tablets of vanzacaftor 4 mg/tezacaftor 20 mg/deutivacaftor 50 mg daily
5. One of the following:
    a. Member is 6 years of age or older
    b. Member's age is within FDA approved labeling

Approval duration: 1 year

NOTE: If the member's genotype is unknown, an FDA-cleared CF mutation test should be used to detect the presence of any mutation. Quest Diagnostics® can perform the CF mutation test. Additionally, documentation of member's mutation from the Cystic Fibrosis Foundation CF Patient Registry is acceptable in place of original laboratory documentation.

DOSAGE/ADMINISTRATION:

FDA-approved

<u>Elexacaftor-tezacaftor-ivacaftor (Trikafta)</u>

- Adults and pediatric patients aged 12 years and older:
    - Morning dose: two elexacaftor 100 mg, tezacaftor 50 mg and ivacaftor 75 mg tablets
    - Evening dose: one ivacaftor 150 mg tablet
- 6 to less than12 years weighing 30 kgs or more
    - Morning dose: two elexacaftor 100 mg, tezacaftor 50 mg and ivacaftor 75 mg tablets
    - Evening dose: one ivacaftor 150 mg tablet
- 6 to less than 12 years weighing less than 30 kgs
    - Morning dose: two elexacaftor 50 mg, tezacaftor 25 mg and ivacaftor 37.5 mg tablets
    - Evening dose: one ivacaftor 75 mg tablet
- 2 to less than 6 years weighing 14 kg or more:

    - Morning dose: One packet (containing elexacaftor 100 mg/tezacaftor 50 mg/ivacaftor 75 mg) oral granules
    - Evening dose: One packet (containing ivacaftor 75 mg) oral granules
- 2 to less than 6 years weight less than 14 kg:
    - Morning dose: One packet (containing elexacaftor 80 mg/tezacaftor 40 mg/ivacaftor 60 mg) oral granules
    - Evening dose: One packet (containing ivacaftor 59.5 mg) oral granules
- Morning and evening dose should be taken approximately 12 hours apart with fat-containing food

<u>Tezacaftor-Ivacaftor (Symdeko)</u>

- Pediatric patients age 6 to less than 12 years weighing less than 30 kg: one tablet (containing tezacaftor 50 mg/ivacaftor 75 mg) in the morning and one tablet (containing ivacaftor 75 mg) in the evening, approximately 12 hours apart
- Adults and pediatric patients ages 12 years and older: one tablet (containing tezacaftor 100 mg/ivacaftor 150 mg) in the morning and one tablet (containing ivacaftor 150 mg) in the evening, approximately 12 hours apart
- Take with fat-containing food

<u>Lumacaftor Ivacaftor (Orkambi)</u>

- Age 12 years and older: Two tablets (each containing lumacaftor 200 mg/ivacaftor 125 mg) taken orally every 12 hours
- Age 6 through 11 years: Two tablets (each containing lumacaftor 100 mg/ivacaftor 125 mg) taken orally every 12 hours
- Children 2 through 5 years of age:
    - Body weight less than 14 kg: one packet (each containing lumacaftor 100 mg/ivacaftor 125 mg) twice daily
    - Body weight 14 kg or greater: one packet (each containing lumacaftor 150 mg/ivacaftor 188 mg) twice daily

<u>Ivacaftor (Kalydeco)</u>

- Adults and children ages 6 years and older: 150 mg twice daily
- Children ages 6 months to less than 6 years:
    - Body weight 5 kg to less than 7 kg: 25 mg twice daily
    - Body weight 7 kg to 14 kg: 50 mg twice daily
    - Body weight 14 kg or greater: 75 mg twice daily
- Children ages 4 months to less than 6 months:
    - Body weight 5 kg or greater: 25 mg twice daily

- Children ages 2 months to less than 4 months:
    - Body weight 3 kg or greater: 13.4 mg twice daily
- Children ages 1 month to less than 2 months:
    - Body weight 3 kg or greater: 5.8 mg twice daily

Vanzacaftor-Tezacaftor-Deutivacaftor (Alyftrek)

- 6 to less than 12 years old:
    - Less than 40 kg: Three tablets of vanzacaftor 4 mg/tezacaftor 20 mg/deutivacaftor 50 mg (total dose of vanzacaftor 12 mg/tezacaftor 60 mg/ deutivacaftor 150 mg) daily
    - Greater than or equal to 40 kg: Two tablets of vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg (total dose of vanzacaftor 20 mg/tezacaftor 100 mg/ deutivacaftor 250 mg) daily
- 12 years and older: Two tablets of vanzacaftor 10 mg/tezacaftor 50 mg/deutivacaftor 125 mg (total dose of vanzacaftor 20 mg/tezacaftor 100 mg/ deutivacaftor 250 mg) daily

Dose Adjustments

Elexacaftor-tezacaftor-ivacaftor (Trikafta)

- Reduce dose when co-administered with drugs that are moderate or strong CYP3A inhibitors

Tezacaftor-Ivacaftor (Symdeko)

- Reduce dose in patients with moderate and severe hepatic impairment
- Reduce dose when co-administered with drugs that are moderate or strong CYP3A inhibitors

Lumacaftor Ivacaftor (Orkambi)

- Reduce dose in patients with moderate or severe hepatic impairment
- Reduce dose for the first week of treatment in patients taking strongCYP3A inhibitors

Ivacaftor (Kalydeco)

- Hepatic Impairment: The dose of ivacaftor should be reduced to 150 mg once daily for persons with moderate hepatic impairment. Ivacaftor should be used with caution in persons with severe hepatic impairment at a dose of 150 mg once daily or less frequently.
- CYP3A inhibitors: When ivacaftor is being co-administered with strong CYP3A inhibitors (e.g., ketoconazole) the dose should be reduced to 150 mg twice-a-week.
- The dose of ivacaftor should be reduced to 150 mg once daily when co-administered with moderate CYP3A inhibitors (e.g., fluconazole). Food containing grapefruit or Seville oranges should be avoided.

Vanzacaftor-Tezacaftor-Deutivacaftor (Alyftrek)

- Reduce dose when co-administered with drugs that are moderate or strong CYP3A inhibitors

Drug Availability

Elexacaftor-tezacaftor-ivacaftor (Trikafta)

- Tablets:
    - Fixed-dose combination containing elexacaftor 50 mg, tezacaftor 25 mg and ivacaftor 37.5 mg co-packaged with ivacaftor 75 mg
    - Fixed-dose combination containing elexacaftor 100 mg, tezacaftor 50 mg, and ivacaftor 75 mg co-packaged with ivacaftor 150 mg
- Oral granules:
    - Unit-dose packets of elexacaftor 100 mg, tezacaftor 50 mg and ivacaftor 75 mg co-packaged with unit-dose packets of ivacaftor 75 mg
    - Unit-dose packets of elexacaftor 80 mg, tezacaftor 40 mg and ivacaftor 60 mg co-packaged with unit-dose packets of ivacaftor 59.5 mg

Tezacaftor-Ivacaftor (Symdeko)

- Co-packaged as tezacaftor 100 mg/ivacaftor 150 mg fixed dose combination tablets and ivacaftor 150 mg tablets
- Co-packaged as tezacaftor 50 mg/ivacaftor 75 mg fixed-dose combination tablets and ivacaftor 75 mg tablets

Lumacaftor Ivacaftor (Orkambi)

- Tablets: lumacaftor 100 mg and ivacaftor 125 mg; lumacaftor 200 mg and ivacaftor 125 mg
- Oral granules: Unit-dose packets of lumacaftor 100 mg and ivacaftor 125 mg; lumacaftor 150 mg and ivacaftor 188 mg

Ivacaftor (Kalydeco)

- Tablets: 150 mg
- Oral granules: Unit-dose packets of 5.8 mg, 13.4 mg, 25 mg, 50 mg, and 75 mg

Vanzacaftor-Tezacaftor-Deutivacaftor (Alyftrek)

- Tablets:
    - Fixed-dose combination containing vanzacaftor 4 mg, tezacaftor 20 mg, and deutivacaftor 50 mg
    - Fixed-dose combination containing vanzacaftor 10 mg, tezacaftor 50 mg, and deutivacaftor 125 mg

PRECAUTIONS:

Boxed Warning

Elexacaftor-tezacaftor-ivacaftor (Trikafta)

- None

Tezacaftor-Ivacaftor (Symdeko)

- None

Lumacaftor Ivacaftor (Orkambi)

- None

Ivacaftor (Kalydeco)

- None

Vanzacaftor-Tezacaftor-Deutivacaftor (Alyftrek)

- None

Contraindications

Elexacaftor-tezacaftor-ivacaftor (Trikafta)

- None

Tezacaftor-Ivacaftor (Symdeko)

- None

Lumacaftor Ivacaftor (Orkambi)

- None

Ivacaftor (Kalydeco)

- None

Vanzacaftor-Tezacaftor-Deutivacaftor (Alyftrek)

- None

Precautions/Warnings

Elexacaftor-tezacaftor-ivacaftor (Trikafta)

- Elevated liver function tests (ALT, AST or bilirubin): Liver function tests (ALT, AST, and bilirubin) should be assessed prior to initiating TRIKAFTA, every 3 months during the first year of treatment, and annually thereafter. In patients with a history of hepatobiliary disease or liver function test elevations, more frequent monitoring should be considered. Dosing should be interrupted in patients with ALT or AST >5 × upper limit of normal (ULN) or ALT or AST >3 × ULN with bilirubin >2 × ULN. Following resolution of transaminase elevations, consider the benefits and risks of resuming treatment.

- Use with CYP3A inducers: Concomitant use with strong CYP3A inducers (e.g., rifampin, St. John's wort) significantly decrease ivacaftor exposure and are expected to decrease elexacaftor and tezacaftor exposure, which may reduce TRIKAFTA efficacy. Therefore, co-administration is not recommended.
- Cataracts: Non-congenital lens opacities/cataracts have been reported in pediatric patients treated with ivacaftor-containing regimens. Baseline and follow-up examinations are recommended in pediatric patients initiating TRIKAFTA treatment.

Tezacaftor-Ivacaftor (Symdeko)

- Elevated transaminases (ALT or AST)
- Use with CYP3A4 inducers
- Cataracts

Lumacaftor Ivacaftor (Orkambi)

- Liver-related events: Elevated transaminases (ALT/AST) have been observed in some cases associated with elevated bilirubin
- Respiratory events: Chest discomfort, dyspnea, and respiration abnormal were observed more commonly during initiation
- Drug interactions: Use with sensitive CYP3A substrates or CYP3A substrates with a narrow therapeutic index may decrease systemic exposure of the medicinal products and co-administration is not recommended

Ivacaftor (Kalydeco)

- **Transaminase (ALT or AST) Elevations:** Elevated transaminases have been reported in persons with CF receiving ivacaftor. Transaminases (ALT and AST) should be assessed prior to initiating ivacaftor, every 3 months during the first year of treatment, and annually thereafter. If a member develops increased transaminase levels, levels should be closely monitored until the abnormalities resolve. Dosing should be interrupted in persons with ALT or AST of greater than 5 times the upper limit of normal (ULN). Following resolution of transaminase elevations, consider the benefits and risks of resuming ivacaftor dosing.
- **Concomitant Use with CYP3A Inducers:** Use of ivacaftor with strong CYP3A inducers, such as rifampin, substantially decreases the exposure of ivacaftor, which may reduce the therapeutic effectiveness of ivacaftor. Therefore, co-administration of ivacaftor with strong CYP3A inducers (e.g., rifampin, St. John’s Wort) is not recommended.

Vanzacaftor-Tezacaftor-Deutivacaftor (Alyftrek)

- Drug-Induced Liver Injury and Liver Failure: Elevated transaminases have been observed in patients treated with ALYFTREK. Cases of serious and potentially fatal drug-induced liver injury and liver failure have been reported with a drug that contains the same or similar active ingredients as ALYFTREK. Assess liver function tests (ALT, AST, alkaline phosphatase, and bilirubin) in all patients prior to initiating and throughout treatment with ALYFTREK. Interrupt ALYFTREK in the event of significant elevations in liver function tests or signs or symptoms of liver injury. ALYFTREK should not be used in patients with severe hepatic impairment (Child-

Pugh Class C). ALYFTREK is not recommended in patients with moderate hepatic impairment (Child-Pugh Class B).

- Hypersensitivity Reactions: Hypersensitivity reactions, including anaphylaxis, have been reported in the postmarketing setting for drugs containing elexacaftor, tezacaftor, and/or ivacaftor. If signs or symptoms of serious hypersensitivity reactions develop during ALYFTREK treatment, discontinue ALYFTREK and initiate appropriate therapy.
- Patients Who Discontinued or Interrupted Elexacaftor-, Tezacaftor-, or Ivacaftor-Containing Drugs Due to Adverse Reactions: Consider benefits and risks before using ALYFTREK in patients who discontinued or interrupted elexacaftor-, tezacaftor-, or ivacaftor-containing drugs due to adverse reactions. If ALYFTREK is used, closely monitor for adverse reactions as clinically appropriate.
- Reduced Effectiveness in Patients with Concomitant Use with CYP3A Inducers: Concomitant use with strong and moderate CYP3A inducers decreased vanzacaftor, tezacaftor, and deutivacaftor exposure, which may reduce ALYFTREK efficacy. Therefore, concomitant use is not recommended.
- Adverse Reactions with Concomitant Use with CYP3A Inhibitors: Concomitant use with strong or moderate CYP3A inhibitors increased vanzacaftor, tezacaftor, and deutivacaftor exposure, which may increase the risk of ALYFTREK associated adverse reactions. Reduce the ALYFTREK dosage with concomitant use.
- Cataracts: Non-congenital lens opacities/cataracts have been reported in patients with CF aged 18 years or less treated with drugs containing ivacaftor. Baseline and follow up ophthalmological examinations are recommended in pediatric patients.

BILLING/CODING INFORMATION:

HCPCS Coding

J3590	Unclassified biologic

ICD-10 Diagnosis Codes That Support Medical Necessity

E84.0	Cystic fibrosis with pulmonary manifestations
E84.11	Meconium ileus in cystic fibrosis
E84.19	Cystic fibrosis with other intestinal manifestations
E84.8	Cystic fibrosis with other manifestations
E84.9	Cystic fibrosis, unspecified

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Part D: Florida Blue has delegated to Prime Therapeutics authority to make coverage determinations for the Medicare Part D services referenced in this guideline.

Medicare Advantage: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

None

RELATED GUIDELINES:

Genetic Testing, 05-82000-28

OTHER:

None

REFERENCES:

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10. Vertex Pharmaceuticals. Symdeko (tezacaftor and ivacaftor) tablet. 2025 [cited 2/1/25]. In: DailyMed [Internet]. Bethesda (MD): National Library of Medicine. Available from: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=7e635909-c6fd-4f0d-ae77-cdff03653a20 /.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Pharmacy Policy Committee on 02/11/26.

GUIDELINE UPDATE INFORMATION:

03/15/26	New Medical Coverage Guideline: Merging MCGs 09-J2000-76, Deflazacort (Emflaza) and 09-J4000-76, Vamorolone (Agamree).