Symdeko™ (tezacaftor/ivacaftor and ivacaftor) – New drug approval

- On February 12, 2018, Vertex announced the FDA approval of Symdeko (tezacaftor/ivacaftor and ivacaftor) for the treatment of patients with cystic fibrosis (CF) aged 12 years and older 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.
    - 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.
- CF is a rare, life-shortening genetic disease caused by a defective or missing CFTR protein resulting from mutations in the CFTR gene.
    - The defective function or absence of CFTR protein results in poor flow of salt and water into and out of the cell in a number of organs. In the lungs, this leads to the buildup of abnormally thick, sticky mucus that can cause chronic lung infections and progressive damage in many patients that eventually leads to death.
- The efficacy of Symdeko was evaluated in two placebo-controlled trials, including one trial in CF patients with two copies of the F508del mutation (HoF508) and one trial in CF patients with one copy of the F508del mutation (HeF508). In both trials, the primary endpoint was the absolute change from baseline in percent predicted FEV_1 ($ppFEV_1$).
    - In HoF508 patients, treatment with Symdeko resulted in statistically significant improvement in $ppFEV_1$. The treatment difference between Symdeko vs. placebo for the mean absolute change in $ppFEV_1$ was 4.0 percentage points (95% CI: 3.1, 4.8; $p < 0.0001$).
    - In HeF508 patients, treatment with Symdeko compared to placebo resulted in statistically significant improvement in $ppFEV_1$ by 6.8 percentage points (95% CI: 5.7, 7.8; $p < 0.0001$). Treatment difference for $ppFEV_1$ was 4.7 percentage points (95% CI: 3.7, 5.8; $p < 0.0001$) between ivacaftor- and placebo-treated patients and was 2.1 percentage points (95% CI: 1.2, 2.9; $p < 0.0001$) between Symdeko- and ivacaftor-treated patients.
- Warnings and precautions of Symdeko include transaminase elevations, concomitant use with CYP3A inducers, and cataracts.
- The most common adverse events (≥ 3%) with Symdeko use were headache, nausea, sinus congestion, and dizziness.
- The recommended dose of Symdeko is 1 tablet (tezacaftor 100 mg/ivacaftor 150 mg) taken orally in the morning and 1 tablet (ivacaftor 150 mg) taken in the evening, approximately 12 hours apart.
    - Symdeko should be taken with fat-containing food. Examples of meals or snacks that contain fat are those prepared with butter or oils or those containing eggs, cheeses, nuts, whole milk, or meats.
- The wholesale acquisition cost for Symdeko will be $292,000 per year.

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- The Vertex Guidance & Patient Support program is available to help eligible patients who have been prescribed a Vertex medication to understand their insurance benefits and the resources available to help them. Vertex also offers a co-pay assistance program for patients with commercial insurance coverage and a free medicine program for select qualifying patients.

- Vertex will begin shipping Symdeko this week. Symdeko will be co-packaged as tezacaftor 100 mg/ivacaftor 150 mg fixed-dose combination tablets and ivacaftor 150 mg tablets.