## Tyvaso® (treprostinil) – New indication

- On April 1, 2021, United Therapeutics announced the FDA approval of Tyvaso (treprostinil), for the treatment of pulmonary hypertension associated with interstitial lung disease (PH-ILD; WHO Group 3) to improve exercise ability.
    - The study establishing effectiveness predominately included patients with etiologies of idiopathic interstitial pneumonia (IIP) (45%) inclusive of idiopathic pulmonary fibrosis (IPF), combined pulmonary fibrosis and emphysema (CPFE) (25%), and WHO Group 3 connective tissue disease (22%).
- Tyvaso is also approved for the treatment of pulmonary arterial hypertension (PAH; WHO Group 1) to improve exercise ability.
- ILD is a group of lung diseases that are characterized by marked scarring or fibrosis of the bronchioles and alveolar sacs within the lungs. Increased fibrotic tissue in ILD can lead to a wide range of symptoms, including shortness of breath with activity, labored breathing, and fatigue. WHO Group 3 PH frequently complicates the course of patients with ILD and is associated with worse functional status and outcomes.
    - PH is estimated to affect at least 15% of patients with early-stage ILD (approximately 30,000 PH-ILD patients in the U.S.) and may affect up to 86% of patients with more severe ILD.
- The approval of Tyvaso for the new indication was based on the INCREASE trial, a 16-week, randomized, double-blind, placebo-controlled study in 326 patients with PH-ILD. Patients were randomized to either placebo or Tyvaso. The primary efficacy endpoint was the change in 6-Minute Walk Distance (6MWD) measured at peak exposure (between 10 and 60 minutes after dosing) from baseline to Week 16. Time to clinically worsening event was also evaluated, defined as the time of randomization until 1 of the following criteria were met: hospitalization due to a cardiopulmonary indication, decrease in 6MWD > 15% from baseline directly related to PH-ILD at 2 consecutive visits and at least 24 hours apart, death (all causes), or lung transplantation.
    - Patients receiving Tyvaso had a placebo-corrected median change from baseline in peak 6MWD of 21 meters at week 16 ($p = 0.004$).
    - In addition, Tyvaso demonstrated a statistically significant increase in the time to first clinical worsening event ($p = 0.041$) and a 39% overall reduction in the risk of a clinical worsening event (hazard ratio 0.61, 95% CI: 0.40, 0.92).
- The initial dosage of Tyvaso for both of its indications is 3 breaths (18 mcg of treprostinil) per treatment session 4 times daily. If 3 breaths are not tolerated, reduce to 1 or 2 breaths and subsequently increase to 3 breaths, as tolerated.
    - The dosage should be increased by an additional 3 breaths per treatment session, 4 times daily at approximately 1- to 2-week intervals. Studies establishing effectiveness in patients with PAH and PH-ILD have used target doses of 9 to 12 breaths per treatment session, 4 times daily. If adverse effects preclude titration to target dose, Tyvaso should be continued at the highest tolerated dose.

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— Tyvaso must be used only with the Tyvaso Inhalation System.