Skyclarys™ (omaveloxolone) – New orphan drug approval

- On February 28, 2023, Reata Pharmaceuticals announced the FDA approval of Skyclarys (omaveloxolone), for the treatment of Friedreich's ataxia in adults and adolescents aged 16 years and older.

- Friedreich's ataxia is a rare, genetic, neurodegenerative condition. Patients with Friedreich's ataxia typically experience symptoms in childhood, including progressive loss of coordination, muscle weakness, and fatigue. Patients typically require a wheelchair in their 20s.

    — Approximately 5,000 patients are currently diagnosed with Friedreich's ataxia in the U.S.

- Skyclarys is the first FDA approved treatment for Friedreich's ataxia.

    — The precise mechanism by which Skyclarys exerts its therapeutic effect in patients with Friedreich's ataxia is unknown. Skyclarys has been shown to activate the Nrf2 pathway. This pathway is involved in the cellular response to oxidative stress.

- The efficacy of Skyclarys was established in a randomized, double-blind, placebo-controlled study in patients 16 to 40 years of age with Friedreich's ataxia. Patients were randomized to receive Skyclarys or placebo. The prespecified primary analysis was the change from baseline in the modified Friedreich's Ataxia Rating Scale (mFARS) score compared to placebo at week 48 in the Full Analysis Population of patients without pes cavus (n = 82). The mFARS is a clinical assessment tool assessing patient function, which consists of 4 domains to evaluate bulbar function, upper limb coordination, lower limb coordination, and upright stability. The mFARS has a maximum score of 99, with a lower score signifying lesser physical impairment.

    — In the Full Analysis Population, the mFARS least squares change from baseline at week 48 was -1.56 with Skyclarys vs. 0.85 with placebo (treatment difference of -2.41, 95% CI: -4.32, -0.51; p = 0.0138).
    — The All Randomized Population (N = 103), which included all patients regardless of pes cavus status, demonstrated similar results to the Full Analysis Population of lower mFARS scores in patients treated with Skyclarys vs. placebo, with a nominally significant least squares mean difference between treatment groups of -1.94 (95% CI: -3.71, -0.16, p = 0.0331).
    — In a post hoc, propensity-matched analysis, lower mFARS scores were observed in patients treated with Skyclarys after 3 years relative to a matched set of untreated patients from a natural history study. These exploratory analyses should be interpreted cautiously given the limitations of data collected outside of a controlled study, which may be subject to confounding.

- Warnings and precautions for Skyclarys include elevation of aminotransferases, elevation of B-type natriuretic peptide, and lipid abnormalities.

- The most common adverse reactions (≥ 20% and greater than placebo) with Skyclarys use were elevated liver enzymes, headache, nausea, abdominal pain, fatigue, diarrhea, and musculoskeletal pain.

- The recommended dose of Skyclarys is 150 mg (3 capsules) taken orally once daily.

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- Reata Pharmaceuticals plans to launch Skyclarys in the second quarter of 2023. Skyclarys will be available as a 50 mg capsule.