Miplyffa™ (arimoclomol) – New orphan drug approval

- On September 20, 2024, the FDA announced the approval of Zevra Therapeutics' Miplyffa (arimoclomol), for use in combination with miglustat for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adult and pediatric patients 2 years of age and older.

- NPC is a rare genetic disease that results in progressive neurological symptoms and organ dysfunction. On average, individuals affected by this devastating disease only live for about 13 years.

    - In the U.S., it is estimated that 900 people are living with NPC, of which approximately one-third have been diagnosed.

- Miplyffa is the first approved therapy for NPC. The mechanism(s) by which Miplyffa exerts its clinical effects in patients with NPC is unknown.

- The efficacy of Miplyffa was established in a randomized, double-blind, placebo-controlled study in 50 patients 2 to 19 years of age who had a diagnosis of NPC. Patients were randomized to Miplyffa or placebo. The randomization was stratified by miglustat use status at baseline; 76% and 81% of patients in the Miplyffa and placebo groups, respectively, received miglustat 6 months or longer prior to the time of enrollment. Efficacy was assessed using the rescored 4-domain NPC Clinical Severity Scale (R4DNPCCSS) score. R4DNPCCSS is a measure of NPC disease progression that looks at four items that patients with NPC, their caregivers and physicians have identified as most relevant including ambulation, speech, swallow and fine motor skills. Higher scores signify a greater severity of disease.

    - Compared to placebo, Miplyffa resulted in a slower disease progression as measured by the R4DNPCCSS score.
    - In patients receiving Miplyffa with miglustat, the least-square mean R4DNPCCSS score decreased by 0.2 vs. increased by 2 in patients receiving placebo with miglustat (placebo-subtracted difference of -2.2, 95% CI: -3.8, -0.6).
    - There were insufficient data to determine the effectiveness of the use of Miplyffa without miglustat for the treatment of neurological manifestations in patients with NPC.

- Warnings and precautions for Miplyffa include hypersensitivity reactions, embryofetal toxicity, and increased creatinine without affecting glomerular function.

- The most common adverse reactions (≥ 15%) with Miplyffa use were upper respiratory tract infection, diarrhea, and decreased weight.

- The recommended oral dosage of Miplyffa, in combination with miglustat, for patients with an actual body weight of:

    - 8 kg to 15 kg, is 47 mg three times a day
    - > 15 kg to 30 kg, is 62 mg three times a day
    - > 30 kg to 55 kg, is 93 mg three times a day
    - > 55 kg, is 124 mg three times a day

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- Zevra plans to launch Miplyffa in 8 to 12 weeks. Miplyffa will be available as a 47 mg, 62 mg, 93 mg and 124 mg capsule.