Dojolvi™ (triheptanoin) – New orphan drug approval

- On June 30, 2020, Ultragenyx announced the FDA approval of Dojolvi (triheptanoin), as a source of calories and fatty acids for the treatment of pediatric and adult patients with molecularly confirmed long-chain fatty acid oxidation disorders (LC-FAOD).

- LC-FAODs are a group of genetic disorders characterized by metabolic deficiencies in which the body is unable to convert long-chain fatty acids into energy. The inability to produce energy from fat can lead to severe depletion of glucose in the body and serious complications, which can lead to hospitalizations or early death. LC-FAODs affect an estimated 2,000 to 3,500 children and adults in the U.S.

- Dojolvi is a highly purified, pharmaceutical-grade, odd-carbon medium-chain triglyceride consisting of three 7-carbon fatty acids on a glycerol backbone. It is designed to provide medium-chain, odd-carbon fatty acids as an energy source and metabolite replacement for people with LC-FAOD.

- The efficacy of Dojolvi was established in a 4month, double-blind, randomized controlled study comparing triheptanoin (7-carbon chain fatty acid) with trioctanoin (8-carbon chain fatty acid). The study enrolled 32 adult and pediatric patients with LC-FAOD.

    - After 4 months, patients in both groups had similar mean changes from baseline in left ventricular ejection fraction and wall mass on resting echocardiogram and similar maximal heart rates on treadmill ergometry.
    - Five patients experienced 7 events of rhabdomyolysis in the triheptanoin group and 4 patients experienced 7 events of rhabdomyolysis in the trioctanoin group.
    - No differences were observed between triheptanoin and trioctanoin groups in blood markers of metabolism including glucose, insulin, lactate, total serum, ketones, acylcarnitines, and serum-free fatty acid concentrations.

- Warnings and precautions for Dojolvi include feeding tube dysfunction and intestinal malabsorption in patients with pancreatic insufficiency.

- The most common adverse reactions (≥ 10%) with Dojolvi use were abdominal pain, diarrhea, vomiting, and nausea.

- The recommended target daily dosage of Dojolvi is up to 35% of the patient's total prescribed daily caloric intake (DCI) divided into at least four doses and administered at mealtimes or with snacks. Dojolvi should be administered mixed with semi-solid food or liquids orally or enterally via a silicone or polyurethane feeding tube.

    - Metabolic requirements should be assessed by determining DCI prior to calculating the dosage of Dojolvi.
    - For patients receiving another medium-chain triglyceride product, discontinue prior to the first dose of Dojolvi.
    - Refer to the Dojolvi drug label for additional dosing and administration recommendations.

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- Ultragenyx plans to launch Dojolvi in the next 30 days. Dojolvi will be available as an oral liquid supplied in 500 mL bottles containing 100% w/w of triheptanoin.