Nityr™ (nitisinone) – New drug approval

- On July 26, 2017, the FDA announced the approval of Cycle Pharmaceuticals' Nityr (nitisinone) tablets, for the treatment of hereditary tyrosinemia type 1 (HT-1) in combination with dietary restriction of tyrosine and phenylalanine.

- Worldwide, tyrosinemia type 1 affects about 1 in 100,000 individuals. Tyrosinemia is a genetic disorder in which the body is unable to breakdown tyrosine, a building block of most proteins. If untreated, tyrosine and its byproducts build-up in tissues and organs, leading to serious health problems.

    - There are 3 types of tyrosinemia. However, HT-1 is the most severe form of this disorder, with symptoms beginning in the first few months of life.
    - HT-1 can lead to liver and kidney failure, weakening of the bones, increased risk of liver cancer, neurological crises, abdominal pain, and respiratory failure. Left untreated, children with HT-1 often do not survive past the age of 10.

- Nityr contains nitisinone, a competitive inhibitor of an enzyme in the tyrosine catabolic pathway.

    - Nitisinone is also available for the same indication as Nityr as capsules and as an oral suspension under the brand name, Orfadin®.

- The safety and efficacy of Nityr have been established based on studies of another oral formulation of nitisinone in patients with HT-1.

    - In the study, for patients younger than 2 months of age who were treated with dietary restriction and nitisinone, the 2-year and 4-year survival probabilities were both 88% vs. 29% for historical controls treated with dietary restriction alone.
    - For patients 2 – 6 months of age, the 2-year and 4-year survival probabilities were both 94% vs. 74% and 60%, respectively, for historical controls in this age group.
    - The long-term effect of nitisinone on hepatic function was not assessed.

- Warnings and precautions of Nityr include elevated plasma tyrosine levels, ocular symptoms, developmental delay, and hyperkeratotic plaques; and leukopenia and severe thrombocytopenia.

- The most common adverse events (> 1%) with Nityr use were elevated tyrosine levels, thrombocytopenia, leukopenia, conjunctivitis, corneal opacity, keratitis, photophobia, eye pain, blepharitis, cataracts, granulocytopenia, epistaxis, pruritus, exfoliative dermatitis, dry skin, maculopapular rash, and alopecia.

- The recommended starting dose of Nityr is 0.5 mg/kg orally twice daily.

    - The dose should be round up to the nearest dosage that can be administered using the available tablet strengths.
    - Dose titration should be based on the patient's biochemical and/or clinical response.
    - For patients who have difficulties swallowing intact tablets, including pediatric patients, the tablets can be disintegrated in water and administered using an oral syringe. If patients can swallow semi-solid foods, the tablets can also be crushed and mixed with applesauce.
    - The maximum dose of Nityr is 1 mg/kg orally twice daily.

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- Cycle Pharmaceuticals' launch plans for Nityr are pending. Nityr will be available as 2 mg, 5 mg, and 10 mg tablets.