Rivfloza™ (nedosiran) – New orphan drug approval

- On September 29, 2023, Novo Nordisk announced the FDA approval of Rivfloza (nedosiran), to lower urinary oxalate levels in children 9 years of age and older and adults with primary hyperoxaluria type 1 (PH1) and relatively preserved kidney function, e.g., estimated glomerular filtration rate (eGFR) ≥ 30 mL/min/1.73 m^2.

- PH is a rare genetic disease that causes overproduction of oxalate by the liver. PH1 is the most clinically prevalent (roughly ~80% of PH patients) and severe of the three subtypes of PH. PH1 is a progressive metabolic disorder that primarily affects the kidneys and can lead to progressive kidney damage.

    — In the U.S., it is estimated that over 2,000 people are living with PH1.

- Rivfloza is a double-stranded small interfering RNA (siRNA). Rivfloza reduces levels of hepatic lactate dehydrogenase (LDH) via the degradation of LDHA messenger ribonucleic acid (mRNA) in hepatocytes through RNA interference. The reduction of hepatic LDH by Rivfloza reduces the production of oxalate by the liver, thereby reducing subsequent oxalate burden.

- The efficacy of Rivfloza was established in PHYOX2, a randomized, double-blind study in 35 patients aged 6 years or older with PH1 or PH2 and an eGFR ≥ 30 mL/min/1.73 m^2. Too few PH2 patients were enrolled to evaluate efficacy in the PH2 population. Therefore, Rivfloza is only indicated for patients with PH1. The data are presented for the complete study population (PH1 and PH2). The primary endpoint was the area under the curve, from days 90 to 180, of the percent change from baseline in 24-hour urinary oxalate excretion ($AUC_{24\text{-hour Uox}}$).

    — The least-squares (LS) mean $AUC_{24\text{-hour Uox}}$ was -3486 (95% CI: -5025, -1947) in the Rivfloza group compared to 1490 (95% CI: 781, 3761) in the placebo group, for a between group difference of 4976 (95% CI: 2803, 7149; $p < 0.0001$).

- The most common adverse reaction (≥ 20%) with Rivfloza use was injection site reactions.

- Rivfloza is administered subcutaneously once monthly at the recommended doses shown in the table below.

Age	Body weight	Dosing regimen
Adults and adolescents 12 years and older	Greater than or equal to 50 kg	160 mg once monthly (Pre-filled Syringe, 1 mL)
	Less than 50 kg	128 mg once monthly (Pre-filled Syringe, 0.8 mL)
Children 9 to 11 years	Greater than or equal to 50 kg	160 mg once monthly (Pre-filled Syringe, 1 mL)
	Less than 50 kg	3.3 mg/kg once monthly, not to exceed 128 mg (Vial, dose volume rounded to nearest 0.1 mL)

Continued . . .

  - A healthcare professional, caregiver, or patient 12 years of age and older may inject Rivfloza using the pre-filled syringe. In pediatric patients 9 to 11 years of age who weigh ≥ 50 kg, a healthcare professional or caregiver may inject Rivfloza using the pre-filled syringe.
  - Rivfloza vials are intended for use under the guidance and supervision of a healthcare professional. A caregiver may administer Rivfloza to pediatric patients after proper training in preparing Rivfloza vials for administration, if a healthcare professional determines that it is appropriate, and with medical follow-up as necessary.

- Novo Nordisk plans to launch Rivfloza in early 2024. Rivfloza will be available as a 160 mg/mL solution as follows:

  - 80 mg (0.5 mL) single-dose vial
  - 128 mg (0.8 mL) single-dose pre-filled syringe
  - 160 mg (1 mL) single-dose pre-filled syringe.