Pedmark® (sodium thiosulfate) – New orphan drug approval

- On September 20, 2022, the FDA announced the approval of Fennec Pharmaceuticals' Pedmark (sodium thiosulfate), to reduce the risk of ototoxicity associated with cisplatin in pediatric patients 1 month of age and older with localized, non-metastatic solid tumors.

    — The safety and efficacy of Pedmark have not been established when administered following cisplatin infusions longer than 6 hours. Pedmark may not reduce the risk of ototoxicity when administered following longer cisplatin infusions, because irreversible ototoxicity may have already occurred.

- Platinum-based therapies can cause ototoxicity, or hearing loss, which is irreversible. The incidence of ototoxicity depends upon the dose and duration of chemotherapy. Many children who are impacted require lifelong hearing aids or cochlear implants, which can be helpful for some, but do not reverse the hearing loss and can be costly over time.

- The efficacy of Pedmark was established in SIOPEL 6 and COG ACCL0431. SIOPEL 6 was a randomized, controlled, open-label study in 114 patients between 1 month and 18 years of age receiving cisplatin-based chemotherapy for standard-risk hepatoblastoma. Patients were randomized to receive 6 cycles of perioperative cisplatin-based chemotherapy without (cisplatin alone arm) or with Pedmark (Pedmark + cisplatin arm). The major outcome measure was hearing loss defined as a Brock Grade ≥ 1; hearing was assessed using pure tone audiometry after study treatment or at an age of at least 3.5 years, whichever was later.

    — Hearing loss was experienced in 39% of patients receiving Pedmark + cisplatin vs. 68% with cisplatin alone (unadjusted relative risk 0.58, 95% CI: 0.40, 0.83).

- COG ACCL0431 was a randomized, controlled, open-label study in 125 patients between 1 and 18 years of age who were receiving a chemotherapy regimen that included a cumulative cisplatin dose of 200 mg/m^2 or higher, with individual cisplatin doses to be infused over 6 hours or less. Patients were randomized to receive cisplatin-based chemotherapy without (cisplatin alone arm) or with Pedmark (Pedmark + cisplatin arm). The major outcome measure was hearing loss assessed by American Speech-Language-Hearing Association (ASHA) criteria; hearing was assessed at baseline and 4 weeks after the final course of cisplatin.

    — Hearing loss was experienced in 44% of patients receiving Pedmark + cisplatin vs. 58% with cisplatin alone (unadjusted relative risk 0.75, 95% CI: 0.48, 1.18).

- Warnings and precautions for Pedmark include hypersensitivity, hypernatremia and hypokalemia, and nausea and vomiting.

- The most common adverse reactions (≥ 25% with difference between arms of > 5% compared to cisplatin alone) with Pedmark use in SIOPEL 6 were vomiting, nausea, decreased hemoglobin, and hypernatremia.

- The most common adverse reaction (≥ 25% with difference between arms of > 5% compared to cisplatin alone) with Pedmark use in COG ACCL0431 was hypokalemia.

- The recommended intravenous dose of Pedmark is based on surface area according to actual body weight. For patients less than 5 kg, the dose is 10 g/m^2; for patients 5 to 10 kg, the dose is 15 g/m^2; and for patients greater than 10 kg, the dose is 20 g/m^2.

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  - Pedmark should be administered following cisplatin infusions that are 1 to 6 hours in duration.
  - Refer to the Pedmark drug label for complete dosing and administration recommendations.

- Fennec's launch plans for Pedmark are pending. Pedmark will be available as a 12.5 grams/100 mL single-dose vial.