The first and only FDA-approved therapy to reduce the risk of ototoxicity[1]

pedmark®
(sodium thiosulfate injection)

Plan for PEDMARK
Dosage and Administration Guide

- Dosage is calculated based on the patient's body weight
- Ready to administer—no mixing required

>

Indications and Usage

PEDMARK (sodium thiosulfate injection) is indicated to reduce the risk of ototoxicity associated with cisplatin in pediatric patients 1 month of age and older with localized, non-metastatic solid tumors.

Limitations of Use

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.

Important Safety Information

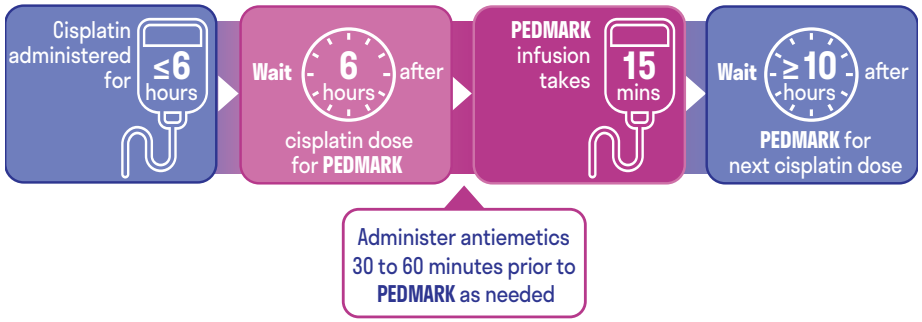
- PEDMARK is contraindicated in patients with history of a severe hypersensitivity to sodium thiosulfate or any of its components.

FDA=Food & Drug Administration.

Before Administering PEDMARK® (sodium thiosulfate injection)

Planning for PEDMARK[1]

- PEDMARK is indicated to reduce the risk of ototoxicity associated with cisplatin in pediatric patients 1 month of age and older with localized, non-metastatic solid tumors
- PEDMARK is **not** indicated and **not** recommended for use in patients <1 month of age due to the increased risk of hypernatremia; patients <1 month have less well-developed sodium homeostasis compared with other pediatric patients
- There are timing considerations when administering PEDMARK to minimize potential interference with cisplatin antitumor activity



Important Safety Information

- Hypersensitivity reactions occurred in 8% to 13% of patients in clinical trials. Monitor patients for hypersensitivity reactions. Immediately discontinue PEDMARK and institute appropriate care if a hypersensitivity reaction occurs. Administer antihistamines or glucocorticoids (if appropriate) before each subsequent administration of PEDMARK. PEDMARK may contain sodium sulfite; patients with sulfite sensitivity may have hypersensitivity reactions, including anaphylactic symptoms and life-threatening or severe asthma episodes. Sulfite sensitivity is seen more frequently in people with asthma.

Please see additional Important Safety Information throughout and on page 7, and full Prescribing Information, including Patient Product Information, or go to PEDMARK.com.

Recommended premedications[1]

Administer antiemetics before each PEDMARK infusion. Multiagent antiemetics (per institutional/clinician preferences) should be given 30 to 60 minutes prior to PEDMARK administration.[2]

PEDMARK-associated nausea and vomiting is transient and manageable[2]

- In clinical studies, only 2 patients discontinued PEDMARK due to nausea and vomiting (n=112)[1]
- All grades of nausea (40%) and vomiting (85%) were seen in patients on PEDMARK and cisplatin[1]
  - Grade 3 or 4 nausea was reported in 3.8% to 8% of clinical study participants
  - Grade 3 or 4 vomiting was reported in 7% to 8% of clinical study participants
- Other guideline-recommended antiemetic combinations for emesis prevention include NK-1 receptor agonist, D2 agonist, and dexamethasone[3]
- Treatment should be individualized based on patient characteristics and clinician experience[3]

Other considerations[1]

- For patients who experience a hypersensitivity reaction, administer antihistamines and glucocorticoids (if appropriate) before each subsequent PEDMARK infusion
- PEDMARK is contraindicated in patients with a history of severe hypersensitivity to sodium thiosulfate or to its components

Important Safety Information

- PEDMARK is not indicated for use in pediatric patients less than 1 month of age due to the increased risk of hypernatremia or in pediatric patients with metastatic cancers.

D2=dopamine D2 receptor blocker; NK-1=neurokinin-1.

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Administering PEDMARK® (sodium thiosulfate injection)

Preparation[1]

- Calculate the dose (grams) and determine the number of vial(s) needed
- Visually inspect the contents of each single-dose vial for particulate matter and discoloration. Discard any vial with visible particulates or discoloration
- Withdraw the calculated dose from the vial(s) into a syringe or transfer the calculated dose into an **empty infusion bag**
  - **Use immediately** after withdrawing into a syringe or transferring to an empty infusion bag
  - If not used immediately, PEDMARK can be **stored in an infusion bag for no more than 18 hours** at 20°C to 22°C (68°F to 72°F). Discard unused portion
  - **No incompatibilities have been observed** between PEDMARK and infusion bags made of polyvinyl chloride, ethylene vinyl acetate, or polyolephin

Administration[1]

- Administer an intravenous infusion over **15 minutes**, following cisplatin infusions that are 1 to 6 hours in duration
- Administer PEDMARK **6 hours after** completion of a cisplatin infusion
- For multiday cisplatin regimens, administer PEDMARK 6 hours after completion of each cisplatin infusion and **at least 10 hours before** the next cisplatin infusion
- **Do not administer PEDMARK if the next cisplatin infusion is scheduled to begin in less than 10 hours**

Important Safety Information

- Hypernatremia occurred in 12% to 26% of patients in clinical trials, including a single Grade 3 case. Hypokalemia occurred in 15% to 27% of patients in clinical trials, with Grade 3 or 4 occurring in 9% to 27% of patients. Monitor serum sodium and potassium at baseline and as clinically indicated. Withhold PEDMARK in patients with baseline serum sodium greater than 145 mmol/L.

Calculating the dosage[1]

- Dosage is calculated based on the patient's actual body weight and body surface area; this will determine the number of 12.5 g/100 mL single-dose vials to use

Actual Body Weight	PEDMARK Dose
Less than 5 kg	10 g/m^2
5 to 10 kg	15 g/m^2
Greater than 10 kg	20 g/m^2

- PEDMARK is provided ready to use, with no dilution required
- **PEDMARK is not substitutable with other sodium thiosulfate products**
- Ensure serum sodium level is within normal range prior to initiating PEDMARK

Dose Modifications for Adverse Reactions[1]

Adverse Reaction	Severity	Dosage Modification
Hypersensitivity	Grade 3 or 4	Permanently discontinue PEDMARK.
Hypernatremia	>145 mmol/L	Withhold PEDMARK until sodium is within normal limits. Resume at the same dose.
Hypokalemia	Grade 3 or 4	Withhold PEDMARK until potassium is within normal limits. Resume at the same dose.
Other Adverse Reactions	Grade 3	Withhold until ≤Grade 1. Resume at the same dose.
	Grade 4	Permanently discontinue PEDMARK.

Important Safety Information

- Monitor for signs and symptoms of hypernatremia and hypokalemia more closely if the glomerular filtration rate (GFR) falls below 60 mL/min/1.73m^2.
- Administer antiemetics prior to each PEDMARK administration. Provide additional antiemetics and supportive care as appropriate.

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Important Safety Information

- PEDMARK is contraindicated in patients with history of a severe hypersensitivity to sodium thiosulfate or any of its components.
- Hypersensitivity reactions occurred in 8% to 13% of patients in clinical trials. Monitor patients for hypersensitivity reactions. Immediately discontinue PEDMARK and institute appropriate care if a hypersensitivity reaction occurs. Administer antihistamines or glucocorticoids (if appropriate) before each subsequent administration of PEDMARK. PEDMARK may contain sodium sulfite; patients with sulfite sensitivity may have hypersensitivity reactions, including anaphylactic symptoms and life-threatening or severe asthma episodes. Sulfite sensitivity is seen more frequently in people with asthma.
- PEDMARK is not indicated for use in pediatric patients less than 1 month of age due to the increased risk of hypernatremia or in pediatric patients with metastatic cancers.
- Hypernatremia occurred in 12% to 26% of patients in clinical trials, including a single Grade 3 case. Hypokalemia occurred in 15% to 27% of patients in clinical trials, with Grade 3 or 4 occurring in 9% to 27% of patients. Monitor serum sodium and potassium at baseline and as clinically indicated. Withhold PEDMARK in patients with baseline serum sodium greater than 145 mmol/L.
- Monitor for signs and symptoms of hypernatremia and hypokalemia more closely if the glomerular filtration rate (GFR) falls below 60 mL/min/1.73m^2.
- Administer antiemetics prior to each PEDMARK administration. Provide additional antiemetics and supportive care as appropriate.
- The most common adverse reactions (≥25% with difference between arms of >5% compared to cisplatin alone) in SIOPEL6 were vomiting, nausea, decreased hemoglobin, and hypernatremia. The most common adverse reaction (≥25% with difference between arms of >5% compared to cisplatin alone) in COG ACCL0431 was hypokalemia.

Please read the accompanying full Prescribing Information, including Patient Product Information or go to PEDMARK.com.

COG=Children's Oncology Group; SIOPEL=International Childhood Liver Tumor Strategy Group.

References: 1. PEDMARK [package insert]. Hoboken, NJ: Fennec Pharmaceuticals, Inc.; September 2022. **2.** Data on file, Fennec Pharmaceuticals, Inc. **3.** NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Adolescent and Young Adult Oncology V.2.2024. © National Comprehensive Cancer Network, Inc. 2023. All rights reserved. Accessed October 11, 2023. To view the most recent and complete version of the guideline, go online to NCCN.org.

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Overview

Efficacy

- The efficacy of PEDMARK in reducing the risk of cisplatin-associated ototoxicity was evaluated in 2 multicenter studies: SIOPEL 6 and COG ACCL0431; in each study, the incidence of hearing loss was lower in the PEDMARK + cisplatin arm compared with the cisplatin alone arm
- For details about the designs and findings of PEDMARK clinical trials, please see Section 14 of the Full Prescribing Information

Dosing & Administration

- Dosage is calculated based on the patient's actual body weight
- Ready to administer—no mixing required
- Administer an intravenous infusion over **15 minutes**, following cisplatin infusions that are 1 to 6 hours in duration
- Administer PEDMARK **6 hours after** completion of a cisplatin infusion
- Do not administer PEDMARK if the next cisplatin infusion is scheduled to begin in **less than 10 hours**

How Supplied & Storage

- PEDMARK is a clear, colorless, sterile solution in a flint glass single-dose vial with a rubber stopper containing 12.5 g/100 mL (125 mg/mL)
- Store at 20°C to 25°C (68°F to 77°F); excursions are permitted between 15°C and 30°C (59°F to 86°F)

Important Safety Information

- The most common adverse reactions (≥25% with difference between arms of >5% compared to cisplatin alone) in SIOPEL6 were vomiting, nausea, decreased hemoglobin, and hypernatremia. The most common adverse reaction (≥25% with difference between arms of >5% compared to cisplatin alone) in COG ACCL0431 was hypokalemia.

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