

Pedmark (sodium thiosulfate)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Pedmark (sodium thiosulfate)	1
Summary	1
Definitions	2
Medical Necessity Criteria for Initial Clinical Review	3
Initial Indication-Specific Criteria	3
Cisplatin-Induced Ototoxicity Prevention	3
Experimental or Investigational / Not Medically Necessary	3
Applicable Billing Codes	4
References	4
Clinical Guideline Revision / History Information	5

Summary

Cisplatin is a potent chemotherapy drug that is commonly used to treat pediatric cancers such as neuroblastoma, osteosarcoma, and medulloblastoma. While cisplatin is highly effective in treating cancer, it can also cause ototoxicity, which is damage to the inner ear and the hearing system.

Ototoxicity is a common side effect of cisplatin treatment in pediatric patients, with a reported incidence ranging from 20% to 80%. The risk of ototoxicity is dependent on various factors, including the dose and duration of cisplatin treatment, patient age, and pre-existing hearing deficits.

Cisplatin-induced ototoxicity can present in different ways, including tinnitus (ringing in the ears), hearing loss, and balance disorders (such as vertigo). The severity of hearing loss can vary from mild to profound and can affect one or both ears. The hearing loss may be temporary or permanent, and the degree of recovery depends on the individual patient and the severity of the damage.

The mechanism of cisplatin-induced ototoxicity is not fully understood, but it is thought to involve damage to the hair cells in the inner ear, which are responsible for detecting sound and transmitting it to the brain. Cisplatin can also cause damage to the auditory nerve and other structures in the ear.

To minimize the risk of cisplatin-induced ototoxicity, various strategies have been investigated, including administering early detection monitoring techniques, reducing the dose and duration of cisplatin treatment, administering cisplatin as a continuous infusion, and using otoprotective agents such as Pedmark (sodium thiosulfate) or amifostine. Pedmark (sodium thiosulfate) is thought to reduce the risk of ototoxicity by interacting directly with cisplatin to produce an inactive platinum species.

Pedmark (sodium thiosulfate) is an intravenous product indicated to reduce the risk of ototoxicity associated with cisplatin in those 1 month of age and older with localized, non-metastatic solid tumors.

- The safety and efficacy of Pedmark (sodium thiosulfate) have not been established when administered following cisplatin infusions longer than 6 hours.
- Pedmark (sodium thiosulfate) may not reduce the risk of ototoxicity when administered following longer cisplatin infusions, because irreversible ototoxicity may have already occurred.
- The dosage of Pedmark (sodium thiosulfate) is based on surface area according to actual body weight.

Definitions

“Cisplatin” is a chemotherapy drug that is commonly used to treat various types of cancer, including ovarian, bladder, and lung cancer. However, cisplatin is also known to cause ototoxicity, and can result in hearing loss, tinnitus, and balance problems. Otoprotective agents are often used alongside cisplatin to reduce the risk of ototoxicity.

“Chemotherapy” is a type of cancer treatment that uses drugs to kill cancer cells. Chemotherapy drugs work by targeting rapidly dividing cells, which includes cancer cells. However, they can also affect normal, healthy cells in the body, leading to side effects such as hair loss, nausea, and fatigue.

“Metastatic” tumors (or metastasis) refer to the spread of cancer cells from the site of the primary cancer to another part of the body.

“Otoprotective agents” are drugs or compounds that are used to protect the ear from damage caused by ototoxic drugs or chemicals. Otoprotective agents may work by reducing the amount of ototoxic drug

that reaches the ear, by reducing oxidative stress and inflammation in the ear, or by promoting the repair of damaged cells in the ear.

"Ototoxicity" refers to the harmful effects of drugs or chemicals on the auditory system, including the cochlea, auditory nerve, and other parts of the ear. Ototoxicity can result in hearing loss, tinnitus, and balance problems.

"[s]" indicates state mandates may apply.

Medical Necessity Criteria for Initial Clinical Review

Initial Indication-Specific Criteria

Cisplatin-Induced Ototoxicity Prevention

The Plan considers Pedmark (sodium thiosulfate) medically necessary when ALL of the following criteria are met:

1. The member is between 1 month and 18 years of age; *AND*
2. The member is being treated for a localized, non-metastatic solid tumor; *AND*
3. The member is receiving a chemotherapy regimen that includes cisplatin; *AND*
4. Individual cisplatin doses will be infused over 6 hours or less.

If the above prior authorization criteria are met, the requested medication will be approved for up to 12 months.^[s]

Experimental or Investigational / Not Medically Necessary^[s]

Pedmark (sodium thiosulfate) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- for the treatment of acute cyanide toxicity
- When administered following cisplatin infusions longer than 6 hours. Pedmark (sodium thiosulfate) may not reduce the risk of ototoxicity when administered following longer cisplatin infusions, because irreversible ototoxicity may have already occurred.

Applicable Billing Codes

Table 1	
CPT/HCPCS code for reduction of the risk of ototoxicity in those receiving cisplatin considered medically necessary if criteria are met:	
Code	Description
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to 1 hour
96374	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug
J0208	Injection, sodium thiosulfate (pedmark), 100 mg

Table 2	
ICD-10 diagnosis codes considered medically necessary for reduction of the risk of ototoxicity in those receiving cisplatin with Table 1 (CPT/HCPCS) codes if criteria are met:	
Code	Description
T45.1X5A	Adverse effect of antineoplastic and immunosuppressive drugs, initial encounter
T45.1X5D	Adverse effect of antineoplastic and immunosuppressive drugs, subsequent encounter
H91.01	Ototoxic hearing loss, right ear
H91.02	Ototoxic hearing loss, left ear
H91.03	Ototoxic hearing loss, bilateral
H91.09	Ototoxic hearing loss, unspecified ear

References

1. Brock PR, Maibach R, Childs M, et al. Sodium thiosulfate for protection from cisplatin-induced hearing loss. *N Engl J Med.* 2018;378(25):2376-2385. doi:10.1056/NEJMoa1801109
2. Chen CH, Huang CY, Lin HH, Wang MC, Chang CY, Cheng YF. Association of Sodium Thiosulfate With Risk of Ototoxic Effects From Platinum-Based Chemotherapy: A Systematic Review and Meta-analysis. *JAMA Netw Open.* 2021 Aug 2;4(8):e2118895. doi: 10.1001/jamanetworkopen.2021.18895.
3. Dickey DT, Wu YJ, Muldoon LL, Neuwelt EA. Protection against cisplatin-induced toxicities by N-acetylcysteine and sodium thiosulfate as assessed at the molecular, cellular, and in vivo levels. *J Pharmacol Exp Ther.* 2005 Sep;314(3):1052-8. doi: 10.1124/jpet.105.087601. Epub 2005 Jun 10.
4. Doolittle ND, Muldoon LL, Brummett RE, et al. Delayed sodium thiosulfate as an otoprotectant against carboplatin-induced hearing loss in patients with malignant brain tumors. *Clin Cancer Res.* 2001 Mar;7(3):493-500.

5. Freyer DR, Brock PR, Chang KW, et al. Prevention of cisplatin-induced ototoxicity in children and adolescents with cancer: a clinical practice guideline. *Lancet Child Adolesc Health.* 2020;4(2):141-150. doi:10.1016/S2352-4642(19)30336-0
6. Freye DR, Brock P, Knight K, et al. Interventions for cisplatin-induced hearing loss in children and adolescents with cancer. *Lancet Child Adolesc Health.* 2019 Aug;3(8):578-584. doi:10.1016/S2352-4642(19)30115-4. Epub 2019 May 31.
7. Freyer DR, Chen L, Kralo MD, et al. Effects of sodium thiosulfate versus observation on development of cisplatin-induced hearing loss in children with cancer (ACCL0431): a multicentre, randomised, controlled, open-label, phase 3 trial. *Lancet Oncol.* 2017;18(1):63-74. doi:10.1016/S1470-2045(16)30625-8.
8. Jordan B, Margulies A, Cardoso F, et al. Systemic anticancer therapy-induced peripheral and central neurotoxicity: ESMO-EONS-EANO clinical practice guidelines for diagnosis, prevention, treatment and follow-up. *Ann Oncol.* 2020 Oct;31(10):1306-1319. doi:10.1016/j.annonc.2020.07.003. Epub 2020 Jul 30.
9. National Cancer Institute - Metastasis. Available at <https://www.cancer.gov/publications/dictionaries/cancer-terms/def/metastasis>. Accessed 20 February 2025.
10. National Cancer Institute. Sodium thiosulfate prevents cisplatin-induced hearing loss in some children. July 13, 2018. Accessed January 28, 2022. <https://www.cancer.gov/news-events/cancer-currents-blog/2018/cisplatin-hearing-loss-sodium-thiosulfate>
11. Orgel E, Knight KR, Villaluna D, et al. Reevaluation of sodium thiosulfate otoprotection using the consensus international society of paediatric oncology ototoxicity scale: a report from the children's oncology group study ACCL0431. *Pediatr Blood Cancer.* 2023 Jul 7:e30550. doi:10.1002/pbc.30550. Online ahead of press.
12. Orgel E, Villaluna D, Kralo MD, Esbenshade A, Sung L, Freyer DR. Sodium thiosulfate for prevention of cisplatin-induced hearing loss: updated survival from ACCL0431. *Lancet Oncol.* 2022 May;23(5):570-572. doi: 10.1016/S1470-2045(22)00155-3.
13. Pedmark (sodium thiosulfate) [prescribing information]. Hoboken, NJ: Fennec Pharmaceuticals Inc; September 2022.
14. Romano A, Capozza MA, Mastrangelo S, Maurizi P, Triarico S, Rolesi R, Attinà G, Fetoni AR, Ruggiero A. Assessment and Management of Platinum-Related Ototoxicity in Children Treated for Cancer. *Cancers (Basel).* 2020 May 17;12(5):1266. doi: 10.3390/cancers12051266.
15. Sodium thiosulfate [prescribing information]. Scottsdale, AZ: Hope Pharmaceuticals; June 2020.

Clinical Guideline Revision / History Information

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