NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Proposed Single Technology Appraisal

Sodium thiosulfate for preventing hearing loss in people with cancer who are under 18 and having cisplatin chemotherapy

Draft scope (pre-referral)

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of sodium thiosulfate within its marketing authorisation for preventing hearing loss in people with cancer who are under 18 and having cisplatin chemotherapy.

Background

The ear has three main parts: the outer, middle and inner ear. The inner ear houses the cochlea: a spiral-shaped fluid-filled tube containing around 20,000 sensory hair cells. As sound waves pass through, the fluid begins to move, setting the hair cells in motion. In turn, these hairs transform the vibrations into electrical impulses that travel along the auditory nerve to the brain.

Cisplatin is a chemotherapy that is widely used to treat a variety of cancers in children and young people.[1] However, after it enters the cochlea it can be retained for years, leading to the inflammation and destruction of sensory hair cells, which can result in permanent hearing loss (ototoxicity).[2] The onset of hearing loss can occur immediately or may occur progressively years after cisplatin treatment. Hearing loss usually occurs in both ears (bilateral) and is often accompanied by hearing sounds in the absence of external noises (tinnitus) and spinning dizziness (vertigo).[3] A persons age and cisplatin dosage can affect whether hearing loss occurs.[4] Hearing loss can delay speech and language development in children and can have a significant impact on school performance and psychosocial functioning.[2,5]

Cancer in people aged under 15 is rare compared with the adult population, accounting for less than 1% of all cancers.[6] In 2017 there were 1577 new cases of cancer in people aged under 15 in the UK.[6] All people who are under 18 and receiving cisplatin are at risk of hearing loss.[7] The reported incidence of cisplatin induced hearing loss is highly variable, with estimates between 22-90%.[2,8]

There are currently no treatment options available to prevent loss of hearing in people under 18 receiving cisplatin chemotherapy.

The technology

Sodium thiosulfate (PEDMARK, Fennec Pharmaceuticals) inactivates platinum complexes by binding electrophilic platinum with thiol, therefore forming a covalent complex that is not cytotoxic and can be excreted rapidly. It is administered intravenously.

Sodium thiosulfate does not currently have a marketing authorisation in the UK for preventing hearing loss. It has been studied in clinical trials in combination with cisplatin compared with cisplatin alone, in people who are under 18 with newly diagnosed cancer.

Intervention(s)	Sodium thiosulfate
Population(s)	People under 18 with newly diagnosed cancer and receiving cisplatin chemotherapy
Comparators	Established clinical management without sodium thiosulfate
Outcomes	The outcome measures to be considered include: • audiological outcomes (e.g. sound perception, speech recognition and sound localisation) • language and communication outcomes (e.g. intelligibility, sentence comprehension) • psychosocial development/adjustment • adverse effects of treatment including impact on response to cisplatin and survival • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective.
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Guidelines: 'Improving outcomes in children and young people with cancer' (2005, updated 2014) NICE cancer service guideline 7. Review date TBC. Related Quality Standards: 'Cancer services for children and young people' (2014) NICE quality standard 55
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2013) 2013/14 Standard Contract for Paediatric Oncology NHS England (2013) 2013/14 NHS Standard Contract for Cancer: Teenagers and Young Adults NHS England B02: Chemotherapy. Clinical Reference Group.

	[Accessed November 2019] NHS England B05. Children and Young Adult Cancer Services. Clinical Reference Group. [Accessed November 2019] NHS England (2018/2019) NHS manual for prescribed specialist services (2018/2019) Chapter 106: Specialist cancer services for children and young people Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 2 - 5. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

For children who become deaf and are used to functioning in a hearing environment, deafness can have a significant impact on their quality of life. This may also have significant consequences for educational and social development. Should the remit be broadened to allow adoption of a wider perspective than the NHS and Personal and Social Services? If so, what should be included in the wider perspective?

Have all relevant comparators for sodium thiosulfate been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for cisplatin induced hearing loss in people under 18 with cancer?

Are the outcomes listed appropriate?

How is hearing loss measured in clinical practice?

Are there any subgroups of people in whom sodium thiosulfate is expected to be more clinically effective and cost effective or other groups that should be examined separately?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which sodium thiosulfate will be licensed;
- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;
- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider sodium thiosulfate to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of sodium thiosulfate can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Langer T, am Zehnhoff-Dinnesen A, Radtke S, Meitert J, Zolk O (2013) Understanding platinum-induced ototoxicity. Trends In Pharmacological Sciences 34(8): 458-69.

2. van As J et al (2019) Medical interventions for the prevention of platinum-induced hearing loss in children with cancer (Review) Cochrane Database of Systematic. Accessed: November 2019

3. Choeyprasert W, Sawangpanich R, Lertsukprasert K, et al. (2013) Cisplatin-induced Ototoxicity in Pediatric Solid Tumors: The Role of Glutathione S-Transferases and Megalin Genetic Polymorphisms. Journal of Pediatric Hematology/Oncology 35(4): 138-43.

4. Skinner R. (2006) Preventing platinum-induced ototoxicity in children – is there a potential role for sodium thiosulfate? Pediatric Blood & Cancer. 47: 120-22.

5. Choeyprasert W, Sawangpanich R, Lertsukprasert K et al. (2013) Cisplatin-induced ototoxicity in pediatric solid tumors: the role of glutathione S-transferases and megalin genetic polymorphisms. Journal of Pediatric Hematology/Oncology 35(4): 138-43.

6. Cancer Research UK. Childhood cancer key statistics. Accessed November 2019

7. Brock PR, Knight KR, Freyer DR, et al. (2012) Platinum-induced ototoxicity in children: a consensus review on mechanisms, predisposition, and protection including a new International Society of Pediatric Oncology Boston Ototoxicity Scale. Journal of Clinical Oncology. 30(19): 2408-17.

8. Yancey A, Harris M, Egbelakin A, et al. (2012) Risk factors for cisplatin-associated ototoxicity in pediatric oncology patients, Paediatric Blood Cancer. 59(1): 144-48

