

Anhydrous sodium thiosulfate for preventing hearing loss caused by cisplatin chemotherapy in people 1 month to 17 years with localised solid tumours

Technology appraisal guidance

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Your responsibility

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1 Recommendation

- 1.1 Anhydrous sodium thiosulfate is recommended, within its marketing authorisation, for preventing hearing loss caused by cisplatin chemotherapy in people 1 month to 17 years with localised, non-metastatic solid tumours. It is only recommended if the company provides it according to the commercial arrangement.

Why the committee made this recommendation

Babies, children and young people (1 month to 17 years) who have cisplatin chemotherapy for localised solid tumours can have hearing loss. There is no treatment to prevent this.

Clinical trial evidence shows that hearing loss is less likely in people having anhydrous sodium thiosulfate after cisplatin. If hearing loss develops, it is less severe in those who have had anhydrous sodium thiosulfate.

There are some uncertainties in the clinical evidence and in the economic model. But the cost-effectiveness estimates are within the range that NICE considers an acceptable use of NHS resources. So, anhydrous sodium thiosulfate is recommended.

2 Information about anhydrous sodium thiosulfate

Marketing authorisation indication

- 2.1 Anhydrous sodium thiosulfate (Pedmarqsi, Norgine) is indicated for 'the prevention of ototoxicity induced by cisplatin chemotherapy in patients 1 month to <18 years of age with localised, non-metastatic, solid tumours'.

Dosage in the marketing authorisation

- 2.2 The dosage schedule is available in the [summary of product characteristics for anhydrous sodium thiosulfate](#).

Price

- 2.3 The list price for anhydrous sodium thiosulfate is £8,277.71 per 8-g vial. The company has a commercial arrangement. This makes anhydrous sodium thiosulfate available to the NHS with a discount. The size of the discount is commercial in confidence.

3 Committee discussion

The [evaluation committee](#) considered evidence submitted by Norgine, a review of this submission by the external assessment group (EAG), and responses from stakeholders. See the [committee papers](#) for full details of the evidence.

The condition

Cisplatin-induced ototoxicity (hearing loss)

3.1 Cisplatin is routinely used to treat different cancers in babies, children and young people. After it enters the cochlea (inner ear) it can cause inflammation and damage, known as ototoxicity (referred to as hearing loss from here). Risk factors for more severe hearing loss in children with cancer include younger age and a high cisplatin dosage. The clinical experts noted that although cancer in children and young people is rare, cisplatin chemotherapy is commonly used to treat cancer in this population. About 60% of children having cisplatin-based treatment develop irreversible hearing loss, and 283 new cases of ototoxic hearing loss were diagnosed in people under 18 in England in 2022 to 2023. But diagnosis is often delayed because early signs of hearing loss may be missed.

Burden of the condition

3.2 The patient expert explained that, when children develop hearing loss, it goes beyond not being able to hear. It can affect their speech and language development, ability to communicate, performance at school and psychosocial functioning, especially in younger children. They explained that even mild hearing loss means it is difficult to hear quiet conversation when there is background noise, for example, in a classroom. So, even with mild hearing loss, there is a high risk of social and emotional difficulties. People with hearing loss above 40 dB will find it difficult to follow any conversation. The patient expert also noted the limitations with the technologies available to help people with hearing loss. Hearing aids and cochlear implants do not work well when there is a lot of

background noise, and implants need invasive surgery. Medical devices need ongoing maintenance, and technology in schools requires teachers who are familiar with and trained in using it. Waiting times to get support can be long, and when people do get support it may not be adequate. This can affect quality of life and increase health inequalities compared with people without hearing loss.

Hearing-loss grading scales

- 3.3 The clinical experts explained that the degree of hearing loss could be assessed using several grading scales. These scales measure how much hearing loss people have at different decibels (loudness), at different frequencies (how high or low a sound is), or both. The Brock and International Society of Paediatric Oncology (SIOP) Boston scales are more common in the UK, whereas the American Speech-Language-Hearing Association (ASHA) scale is more common in the US. A clinical expert confirmed that, in their experience, the Brock scale was most commonly used in the NHS.

Clinical management

- 3.4 There is no treatment to prevent or reduce hearing loss caused by cisplatin chemotherapy in babies, children and young people with localised solid tumours. The clinical experts explained that cisplatin treatment is sometimes changed to carboplatin. This is because carboplatin is less likely to cause hearing loss, but it can be less effective than cisplatin. Once a child loses their hearing, they are usually offered hearing aids and other technologies to amplify sound at home and at school. Children with severe hearing loss may be offered a cochlear implant. The patient expert noted that they would welcome treatment strategies that recover hearing loss, as well as treatments that prevent hearing loss. The committee understood that there is an unmet need in preventing hearing loss caused by cisplatin in babies, children and young people with localised solid tumours.

Clinical effectiveness

Key clinical trials: SIOPEL 6 and COG ACCL0431

- 3.5 The clinical trial evidence for anhydrous sodium thiosulfate is from 2 phase 3, open-label, randomised controlled trials comparing cisplatin-based chemotherapy plus anhydrous sodium thiosulfate with cisplatin-based chemotherapy without anhydrous sodium thiosulfate.
- SIOPEL 6 included 109 children aged older than 1 month to 18 years (mean 18.5 months) with hepatoblastoma (localised disease) from 12 countries, including the UK, having single-agent cisplatin chemotherapy. The median follow up was 4.27 years and the primary outcome was incidence of hearing loss, measured on the Brock scale (graded 0 for no hearing loss to 4 for the most severe hearing loss). Secondary outcomes were overall survival and adverse events.
 - COG ACCL0431 included 125 children aged 1 year to 18 years (mean 9.2 years) with germ cell tumour, hepatoblastoma, medulloblastoma, neuroblastoma, osteosarcoma or other solid malignancy (localised and metastatic disease) from the US and Canada. They had any cisplatin-containing chemotherapy. The median follow up was 5.33 years and the primary outcome was incidence of hearing loss, measured using ASHA criteria. Secondary outcomes were overall survival and adverse events. The committee was aware that the ASHA scale can be used to measure grades of hearing loss, but in this trial it was used as a binary measure to detect whether or not hearing loss had happened.

Clinical trial results

Hearing loss

- 3.6 Both trials showed a statistically significant reduction in the incidence of hearing loss in children and young people who had anhydrous sodium thiosulfate after cisplatin chemotherapy. The analysis for SIOPEL 6 was for the whole-trial population and showed that hearing loss, measured using the Brock scale in

children and young people with localised hepatoblastoma only, occurred in:

- 63.0% (n=29) of children who had cisplatin only
- 32.7% (n=18) of children who had cisplatin then anhydrous sodium thiosulfate (relative risk 0.52, 95% confidence interval [CI] 0.34 to 0.79; p=0.002).

SIOPEL 6 also showed that, if children did develop hearing loss, it was less severe overall in children who had anhydrous sodium thiosulfate.

In COG ACCL0431, analysis based on the whole-trial population showed that hearing loss (measured using the ASHA scale in children with different tumour types and localised and metastatic disease) developed in:

- 56.4% (n=31) of children who had cisplatin only
- 28.6% (n=14) of children who had cisplatin then anhydrous sodium thiosulfate (odds ratio 0.27, 95% CI 0.11 to 0.66, p=0.0039; relative risk 0.52, 95% CI 0.32 to 0.84, p=0.004).

In the subgroup of people with localised disease in COG ACCL0431, the treatment effect of anhydrous sodium thiosulfate after cisplatin chemotherapy was largely in the same direction as in the whole-trial population. The results were not statistically significantly different (the company considers this data confidential, so it is not reported here).

Because the ASHA scale was used in COG ACCL0431 as a binary outcome to detect incidence of hearing loss and did not capture the severity of hearing loss (see [section 3.5](#)), the company also presented evidence from Orgel et al. (2023). This was a post-hoc analysis of the audiology data from COG ACCL0431 using the SIOP scale based on the whole-trial population. It reported hearing loss using thresholds of SIOP grade 1 and above and SIOP grade 2 and above. This post-hoc analysis also showed a statistically significant reduction in risk of either SIOP grade 1 and above or SIOP grade 2 and above hearing loss in children who had anhydrous sodium thiosulfate in the whole-trial population of COG ACCL0431.

The EAG commented that both SIOPEL 6 (n=114) and COG ACCL0431 (n=125) included a small number of people, and that there are uncertainties

in the evidence. The company explained that the sample sizes were relatively large considering that tumours in children are rare. COG ACCL0431 was not powered to detect the difference in prevention of hearing loss with anhydrous sodium thiosulfate after cisplatin in the subgroup with localised disease only. But the company explained that evidence from both trials showed that anhydrous sodium thiosulfate after cisplatin was effective in reducing the occurrence of hearing loss across children and young people with different types and stages of cancers having cisplatin, despite differences in baseline characteristics.

The company, in response to clarification, also provided a pooled analysis of SIOPEL 6 and COG ACCL0431 trial data based on the whole-trial populations that included both people with localised tumours and people with metastatic tumours. It also provided another pooled analysis of the 2 trials for the localised, non-metastatic subgroup only (the population in the licensed indication). The analyses showed that cisplatin followed by anhydrous sodium thiosulfate was associated with a lower risk of hearing loss than cisplatin without anhydrous sodium thiosulfate, and the results were statistically significant (the company considers the data confidential so it is not reported here). But both the company and the EAG thought that pooling the 2 trials may not be appropriate because of the different populations and grading scales used. The committee noted the uncertainties in the evidence. Considering all the evidence, it concluded that anhydrous sodium thiosulfate was effective in preventing hearing loss in babies, children and young people with cancer who are having cisplatin.

Overall survival

3.7 Overall survival was a secondary outcome in SIOPEL 6 and COG ACCL0431.

- Analysis based on the whole-trial population of SIOPEL 6 showed that fewer people having cisplatin with anhydrous sodium thiosulfate died than those having cisplatin without anhydrous sodium thiosulfate. But the difference was not statistically significant (the company considers the results confidential so they are not reported here).

- In the COG ACCL0431 whole-trial population, at the median 5.33-year follow up, 18 children (29.5%) in the cisplatin with anhydrous sodium thiosulfate arm and 12 children (18.8%) in the cisplatin without anhydrous sodium thiosulfate arm had died, but the difference was not statistically significant (hazard ratio 1.79, 95% CI 0.86 to 3.72, $p=0.1132$). Results based on the subgroup with localised disease also showed no statistically significant difference in overall survival between the 2 arms (the company considers the results confidential so they are not reported here).
- In the 2 pooled analyses of SIOPEL 6 and COG ACCL0431, there was no statistically significant difference in overall survival in either those with localised and metastatic disease or those with localised disease only (the company considers the results confidential so they are not reported here).

A clinical expert noted that there were some concerns over the analysis on overall survival based on the whole-trial population of COG ACCL0431 compared with that done in the subgroup with localised disease alone. This led to metastatic disease being excluded from the licensed population. But they added that this was likely to be down to the underlying aggressive disease and metastatic stage. The company explained that the pharmacological effects of cisplatin in the body were cleared in 4 hours, after which there was no biologically plausible mechanism by which anhydrous sodium thiosulfate could affect its efficacy. It added that the randomisation in COG ACCL0431 was not stratified by stage of cancer, so some prognostic factors may not be balanced between the treatment arms. The company also explained that 67% of the children in the anhydrous sodium thiosulfate with cisplatin group had markers of more aggressive tumours, and it believed the overall survival outcomes were related to tumour type. The committee concluded that, while there are uncertainties, anhydrous sodium thiosulfate was unlikely to affect overall survival in the licensed population.

Generalisability

Population

3.8 The EAG commented that the generalisability of the trial results to the NHS was

unclear. In SIOPEL 6 the people in the trial all had 1 type of localised tumour, standard-risk hepatoblastoma. In COG ACCL043 they had a mixture of localised and metastatic cancers of different tumour types, which is broader than the licensed indication (localised, non-metastatic cancer). The company explained that evidence from the 2 trials showed that the treatment effect of anhydrous sodium thiosulfate with cisplatin in preventing hearing loss was similar across the populations with different characteristics at baseline (age from 1.2 months to 18 years, weights from 2.6 kg to 127.9 kg, and different tumour types at different stages). The clinical experts explained that treatment with anhydrous sodium thiosulfate would not vary by tumour type. The EAG was also concerned that the 2 trials used different hearing-loss scales. These may not be generalisable to the NHS, which is most likely to use the Brock scale (see [section 3.3](#)). The committee was aware that the ASHA scale was used only to judge whether hearing loss had happened in COG ACCL0431 (see [section 3.5](#)). The trial's audiology data was reanalysed using the SIOP scale (Orgel et al. 2023; see [section 3.6](#)), but the results were graded into SIOP grade of 1 and above and 2 and above only without capturing other levels of hearing loss. The Brock scale used in SIOPEL 6 measures severity. But it only starts at 40 dB, so it is less sensitive to early hearing loss and does not detect mild hearing loss. The company pointed to a study (Clemens et al. 2019) that suggested good concordance between the Brock and SIOP scales. The committee concluded that, although there were uncertainties, overall the populations and results of the trials could be generalised to NHS clinical practice.

Timing and administration

- 3.9 According to its summary of product characteristics, anhydrous sodium thiosulfate should be given as a 15-minute infusion exactly 6 hours after the cisplatin infusion finishes. If it is given any earlier the cisplatin could be less effective, and if it is given any later it may not prevent hearing loss. The company explained that there were some instances of delayed administration in SIOPEL 6 (the company considers the exact figure confidential so it is not reported here). These were mainly because of delays in getting the anhydrous sodium thiosulfate from the pharmacy, ward staff changeovers, and blocked or unusable infusion lines. The committee asked if delays were likely in clinical practice in the NHS. A clinical expert said that if cisplatin was delayed, anhydrous sodium thiosulfate

would still be offered 6 hours later to maintain the treatment gap. The NHS England Cancer Drugs Fund lead explained that centres that use anhydrous sodium thiosulfate to prevent cisplatin-related hearing loss have revised protocols to minimise delays to administration. The preferred protocol is to use cisplatin during the day, to minimise potential delays in either administration of cisplatin or timing of anhydrous sodium thiosulfate. The clinical expert also noted that if there was a delay in administering anhydrous sodium thiosulfate, it would generally be given unless the delay was substantial. The company explained that the summary of product characteristics gives clear instructions about ensuring a 6-hour gap between cisplatin infusions and giving anhydrous sodium thiosulfate. It also stated that, if anhydrous sodium thiosulfate with cisplatin was recommended, it would continue to support the delivery of the protocol or adaptations in local areas. The committee noted that there were likely to be delays in clinical practice and therefore loss of efficacy, as the evidence suggests. It concluded that although there was uncertainty, the timing and administration of anhydrous sodium thiosulfate after cisplatin in the trials may be applicable to the NHS. It took this into account in its decision making.

Population appropriate for decision making

- 3.10 The company and EAG had different views on the population appropriate for decision making, as well as the population that informs the model (see [section 3.12](#)). The EAG noted that the efficacy data from COG ACCL0431 was from children with localised and metastatic cancer, although the marketing authorisation was for localised disease only. Noting the differences in population characteristics at baseline in SIOPEL 6 and COG ACCL0431 (see [section 3.5](#)), the EAG thought that the localised disease subgroup from COG ACCL0431 was more appropriate for decision making and informing the model. It also noted that the reduction in hearing loss was not statistically significant for the localised disease subgroup in COG ACCL0431. The company explained that the study was not powered to detect efficacy in this subgroup. The committee was aware that both the company and EAG did not consider the pooled analysis of children with localised disease only from COG ACCL0431 and SIOPEL 6 to be appropriate (see [section 3.6](#)). The committee asked if the efficacy data for the overall population could be extrapolated to localised cancer. The clinical experts explained there were differences in the chemotherapy that children with different types of cancer

had. They added that children with hepatoblastoma, as in SIOPEL 6, usually have cisplatin monotherapy. If they have other types of cancer, or metastatic cancer, as in COG ACCL0431, they may have radiotherapy and other types of chemotherapy, as well as cisplatin. These treatments may also cause hearing loss. But the clinical experts noted no reason to exclude the results from children with metastatic cancer. This is because hearing loss outcomes were similar overall for localised and metastatic cancer. The company said there was no biologically plausible reason why hearing loss would be different between people with localised and metastatic disease. The committee noted that the evidence across the trials and different analyses showed a consistent efficacy benefit from anhydrous sodium thiosulfate in preventing hearing loss in children having cisplatin, and this was likely to be similar in different tumour types and in localised and metastatic cancer. It also noted the different study designs, population characteristics and grading scales used in SIOPEL 6 and COG ACCL0431. So, it concluded that the COG ACCL0431 whole-trial population was appropriate for decision making, but there was uncertainty. It took this into account in its decision making.

Economic model

Company's modelling approach

3.11 The company's model had a decision-tree structure in the first year with 5 health states: minimal or no hearing loss, mild hearing loss, moderate hearing loss, marked hearing loss, and severe hearing loss. After this first year, people enter a Markov model in one of those states. At that point they cannot move between states, that is, no further hearing loss or improvement is possible. Anhydrous sodium thiosulfate was assumed to increase costs through the cost of the drug itself and reduce the costs of managing hearing loss and depression linked to hearing loss. It was modelled to increase health-related quality of life by reducing the number of people with cisplatin chemotherapy-related hearing loss, and reducing its severity in people who did develop it. The model has a lifetime time horizon and a cycle length of 1 year with a half-cycle correction. Baseline characteristics are from the localised disease subgroup of COG ACCL0431.

Sources of efficacy data

3.12 The company's model uses 3 different sources of efficacy data. Incidence of hearing loss in the model came from the overall efficacy population in COG ACCL0431, measured using the ASHA scale. Severity of hearing loss came from published papers: data from Orgel et al. (2023) was used to estimate the proportions of people with grade 1 and above and grade 2 and above hearing loss. Because the Orgel et al. analysis did not discriminate between all hearing loss levels, grade 2 and above was then split into grades 2, 3 or 4 based on the percentage distributions in a paper by Knight et al. (2005), which used the Brock scale. Grades 1, 2, 3 and 4 hearing loss are assumed equal to the mild, moderate, marked and severe hearing-loss health states in the model. The EAG had concerns with this approach. Firstly, it thought that the efficacy data should come from people with localised cancer only, because this is the population included in the marketing authorisation (see [section 3.8](#)). It also noted that the company had used the baseline characteristics from the localised disease population, so it thought that it made sense for the efficacy data to come from the same population. Secondly, the efficacy data uses 3 different grading scales and 3 different sources, with no adjustment for the differences across the scales. The company explained that there was not enough data available to adjust for differences in grading scales between the studies. It said it had explored various scenarios using different sources for hearing loss incidence and severity. The committee also asked why the company had not used the SIOPEL 6 data in its base case, given that it included only non-metastatic disease. The company explained that it did not use the SIOPEL 6 data because the children in the trial all had hepatoblastoma and were on average younger than children who would be eligible for anhydrous sodium thiosulfate in the NHS. It considered the population in COG ACCL0431 better matched the NHS population. It used the localised disease baseline characteristics to match the licensed population. The committee recalled that the clinical experts saw no reason to exclude the results on hearing loss from children with metastatic cancer because they were similar for localised and metastatic cancer (see [section 3.6](#)). It also recalled the patient expert's comment about concerns around overall survival in people with metastatic cancer in COG ACCL0431, but which may have been caused by the underlying cancer (see [section 3.7](#)). It concluded that it was reasonable to use the efficacy data from the overall trial population in the model. But, it noted the uncertainties associated with the small trial population, the fact that it included children with

metastatic disease (see [section 3.10](#)), and the different sources of efficacy data in the model and different grading scales used, which had not been adjusted for.

Mortality estimates

3.13 The company's base case assumed that treatment with anhydrous sodium thiosulfate does not affect survival. The model used overall survival estimates from COG ACCL0431 for both treatment groups for the first 5 years. For years 6 to 10, risk of death was increased by a standardised mortality ratio (SMR) of 9.1 compared with the general population because of the risk from the underlying cancer. This figure came from a study by Fidler et al. (2016), which looked at causes of death in people who had survived childhood cancer. After 10 years, people were assumed in the model to have the same risk of death as the general population. Clinical advice to the EAG indicated that people who had childhood cancer had an increased risk of death even 40 years later. The EAG preferred to apply SMRs that varied by the length of follow up in Fidler et al. (2016). The clinical expert agreed that mortality was increased after 10 years because of, for example, secondary cancers and heart and kidney problems related to chemotherapy. The company explained that it had since talked to clinical experts, and it agreed that there was likely to be an increased risk of death after 10 years. It also agreed with the EAG's SMR assumptions. The committee concluded that the risk of death was likely to be higher after 10 years for people who had survived childhood cancer, and preferred the EAG's approach for modelling mortality.

Utility values

3.14 The company used health utilities from the literature based on the health utility index 3 (HUI3) values. The utility value for children who did not have hearing loss (minimal or no hearing loss state) was from Pogany et al. (2006), which reports quality of life using the HUI3 for a Canadian national retrospective cohort study with long-term survivors of childhood cancer compared with controls. The company used a utility estimate of 0.92, which corresponds to the mean utility value for the study controls aged 5 to 12 years. There was no data for the mild hearing-loss health state, so the company assumed a utility value at the midpoint

between the minimal or no hearing loss and moderate hearing-loss states. For the moderate, marked and severe hearing-loss states, utility values were from Barton et al. (2006). The committee noted an alternative source of utility values was available (Gumbie et al. 2022) although the EAG and company base cases were based on Barton, which it accepted. The model also includes a quality-adjusted life year (QALY) gain associated with using cochlear implants applied to a proportion of people in the marked and severe hearing-loss health states. The company said it had used HUI3 because it considered it the most sensitive at capturing the effects of hearing treatment on overall health status. It also noted that HUI3 was used in [NICE's technology appraisal guidance on cochlear implants for children and adults with severe to profound deafness](#). [NICE's manual on health technology evaluations](#) recommends using the EQ-5D-3L for adults, but for evaluations in children and young people alternative measures of health-related quality of life can be considered. The committee concluded that the company's approach to calculating utility values was acceptable for decision making.

Costs associated with depression and anxiety

- 3.15 The company's model included costs for depression and anxiety associated with hearing loss, based on a study by Gurney et al. (2007). The study looked at quality of life in people who had survived childhood neuroblastoma, some of whom had hearing loss. It reported the proportion of people with and without hearing loss who had depression and anxiety. The EAG preferred to remove these costs because the study noted that the differences in depression and anxiety between the people with and without hearing loss were not substantive. The company maintained that the costs associated with depression should be retained, and that this assumption was supported by patient impact statements that said that hearing loss was associated with depression and anxiety. The committee recalled the patient expert's explanation of how hearing loss in childhood increased the risk of emotional difficulties. It concluded that it was reasonable to consider the costs for depression and anxiety associated with hearing loss in the model.

Other differences between the company and EAG

models

3.16 The company and the EAG differed on other assumptions in the model:

- The company based the frequency of hearing assessments on Dionne et al. (2012) and assumptions informed by audiologists. The EAG thought it more appropriate to use all frequencies from Dionne et al. if available.
- The company assumed no speech and language therapy for people with mild and moderate hearing loss, and a weekly session until age 18 for people with marked and severe hearing loss. The EAG thought this could overestimate the frequency of therapy sessions in the marked and severe hearing-loss state, and preferred alternative frequencies of language therapy informed by the company's audiologist report.
- The company assumed frequency modulation (FM) system costs applied for everyone in the model while they were under 18. The EAG thought that this could overestimate the costs of these systems, noting that Dionne et al. included these costs only for people with grade 2 and above hearing loss. It preferred to apply FM system costs only if people have hearing aids or cochlear implants.
- The company included the impact of treatment-related adverse events reported in 2% or more of people in either arm of the COG ACCL0431 full-safety population (observed frequency was less than 2%, so the model does not include any impact of adverse events). The EAG thought that this could underestimate the negative impact of treatment-related adverse events on quality of life and costs. It preferred to include grade 3 and above adverse events in 10% or more of people to better capture their impact on quality of life and costs.

The committee concluded that the EAG's approach was more clinically appropriate for decision making.

Uncertainties and preferred assumptions

3.17 The committee noted the uncertainty in the evidence and modelling, specifically

around:

- the evidence relating to the treatment effect of anhydrous sodium thiosulfate after cisplatin on overall survival in its licensed indication (see [section 3.7](#))
- the applicability of timing and administration of anhydrous sodium thiosulfate after cisplatin in the trials (see [section 3.9](#))
- using the whole-trial population of COG ACCOL 0431 to inform decision making and the model; efficacy data used in the model was not in line with the licensed population and came from different sources that used different grading scales and had not been adjusted for (see [section 3.8](#) and [section 3.10](#)).

Noting the uncertainties, the committee's preferred model assumptions were:

- efficacy data for hearing-loss incidence from the COG ACCL0431 overall population (see [section 3.12](#))
- long-term risk of mortality after 5 years in the model calculated using multiple SMR estimates by follow-up period, as reported by Fidler et al. (2016; see [section 3.13](#))
- health utility values from Pogany et al. (2006) and Barton et al. (2006) based on HUI3 values (see [section 3.14](#))
- including costs for treating depression and anxiety associated with hearing loss (see [section 3.15](#)).

The committee also agreed with the following assumptions in the EAG's preferred base case (see [section 3.16](#)):

- frequencies of hearing assessments reported by Dionne et al. (2012) for all age groups and hearing-loss health states
- costs of FM systems only for children and young people with hearing aids or cochlear implants
- incidence of adverse events based on safety data for grade 3 and above adverse events occurring in 10% or more of babies, children and young people in COG ACCL0431.

Cost-effectiveness estimates

3.18 [NICE's manual on health technology evaluations](#) notes that, above a most plausible incremental cost-effectiveness ratio (ICER) of £20,000 per QALY gained, judgements about the acceptability of a technology as an effective use of NHS resources will take into account the degree of certainty around the ICER. The committee will be more cautious about recommending a technology if it is less certain about the ICERs presented. But it will also take into account other aspects, including uncaptured health benefits. The committee recalled the statements from the clinical and patient experts about the need for a treatment to prevent cisplatin-related hearing loss and the associated effects on speech and language development and psychosocial functioning. It noted that:

- there is no other medicine available to prevent cisplatin-related hearing loss
- hearing loss, once it happens, is a permanent condition
- anhydrous sodium thiosulfate prevents a drug-induced toxicity.

NICE's manual on health technology evaluations states that when evidence generation is particularly difficult because, for example, technologies are for use in a population that is predominantly children and young people (under 18 years old), the committee may be able to accept a higher degree of uncertainty when making recommendations. The committee acknowledged this, taking into account the uncertainties in the company's clinical evidence and model assumptions. It decided that an acceptable ICER would be towards the upper end of the range NICE considers a cost-effective use of NHS resources (£20,000 to £30,000 per QALY gained).

After the committee meeting, the company accepted the committee's preferred assumptions and amended its base case in line with them. The list price was also reduced, and the company increased its confidential patient access scheme discount for anhydrous sodium thiosulfate. When these were applied, the company's revised base-case ICER was within the range that NICE considers a cost-effective use of NHS resources.

Other factors

Equality

- 3.19 The patient organisation submissions noted that deaf children from ethnic minority backgrounds have poorer educational outcomes than children with no hearing loss. Also, Black and Asian deaf children have lower attainment scores than other ethnic groups and White deaf children, respectively. The patient expert explained how, although technologies to help with hearing loss were available to everyone on the NHS, there is evidence of inequalities in access based on socioeconomic status. People may also have differences in their ability to access support, for example, with ongoing technology maintenance. The committee noted that anhydrous sodium thiosulfate to prevent cisplatin-related hearing loss, if recommended, may reduce health inequalities.

Conclusion

Anhydrous sodium thiosulfate is recommended

- 3.20 Using the company's revised base-case model, and the updated list price and confidential patient access scheme discount, the ICER was within the range that NICE considers a cost-effective use of NHS resources. So, the committee recommended anhydrous sodium thiosulfate for use in the NHS.

4 Implementation

- 4.1 Section 7 of the [National Institute for Health and Care Excellence \(Constitution and Functions\)](#) and the [Health and Social Care Information Centre \(Functions\) Regulations 2013](#) requires integrated care boards, NHS England and, with respect to their public health functions, local authorities to comply with the recommendations in this evaluation within 3 months of its date of publication.
- 4.2 Section 4f of [The Innovative Medicines Fund Principles](#) states that a discretionary source of early funding (from the overall Innovative Medicines Fund budget) is available for certain medicines recommended by NICE. In this instance, interim funding has been agreed for anhydrous sodium thiosulfate. Interim funding is available from 26 February 2025 and will end 90 days after positive final guidance is published (or 30 days in the case of drugs with an Early Access to Medicines Scheme designation or cost comparison evaluation), at which point funding will switch to routine commissioning budgets.
- 4.3 The Welsh ministers have issued directions to the NHS in Wales on implementing NICE technology appraisal guidance. When a NICE technology appraisal guidance recommends the use of a drug or treatment, or other technology, the NHS in Wales must usually provide funding and resources for it within 2 months of the first publication of the final draft guidance.
- 4.4 When NICE recommends a treatment 'as an option', the NHS must make sure it is available within the period set out in the paragraphs above. This means that, if a patient is being treated with cisplatin chemotherapy and the healthcare professional responsible for their care thinks that anhydrous sodium thiosulfate is the right treatment, it should be available for use, in line with NICE's recommendations.

5 Evaluation committee members and NICE project team

Evaluation committee members

The 4 technology appraisal committees are standing advisory committees of NICE. This topic was considered by [committee B](#).

Committee members are asked to declare any interests in the technology being evaluated. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The [minutes of each evaluation committee meeting](#), which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

Chair

Charles Crawley

Chair, technology appraisal committee B

NICE project team

Each evaluation is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the evaluation), a technical adviser, a project manager and an associate director.

Emma McCarthy and Emilene Coventry

Technical leads

Yelan Guo

Technical adviser

Vonda Murray

Project manager

Richard Diaz

Associate director

Update information

March 2025: we updated section 4 to refer to availability of early funding.

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