Highly Specialised Technologies (HST) criteria checklist

**Sodium thiosulfate for preventing ototoxicity caused by cisplatin chemotherapy in people aged 1 month to 17 years with localised solid tumours**

**Introduction:** The NICE HST criteria checklist is to highlight where a technology meets/partially meets or does not meet the criteria for routing to the HST programme. Its purpose is to show the details of why a technology may not be appropriate for HST evaluation, but also where it has been identified as suitable.

### Key – does the technology meet the criteria? Please use the colour key to advise if the technology meets the criteria

|  |  |
| --- | --- |
| Met  | There is clear and strong evidence that this criterion is met |
| Not met | There is no evidence or limited evidence that the criterion is met.  |

### MA wording: ‘Pedmarqsi 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*’

| **Number** | **Criterion** | **Description of how the technology meets the criteria**  | **Does the technology meet the criteria?** |
| --- | --- | --- | --- |
|  | The condition is very rare defined by 1:50,000 in England  | **Not met****The underlying condition:** if considering HST criteria, the underlying condition is paediatric solid tumours in this topic, because: * ***“Localized, non-metastatic***” is about staging of cancer, and [Stage is one of the standard factors for treatment stratification](https://www.mdpi.com/2072-6694/13/13/3142) in oncology, a way of classifying severity.
* A condition is not defined by treatment receivedsuch as cisplatin Clinical advice to the technical team noted that, among the 8 pediatric solid tumors (*included in the company’s pivotal trial*) the company listed for consideration, 3 of them (neuroblastoma, malignant extracranial germ cell tumours, and retinoblastomas) are treated by carboplatin instead of cisplatin in the NHS. And for malignant gonadal germ cell tumours, either carboplatin or cisplatin could be considered depending on the age of the child.
* In addition to the 8 considered by the company, there are other types of solid tumours in children and young people ([Kline et al. 2003](https://www.pediatricnursing.org/article/S0882-5963%2802%2943913-9/fulltext)), common or less common. The technical team considered that they should also be considered when taking “solid tumours” as the underlying condition here.

**Incidence and prevalence**: reporting of theincidence or prevalence of paediatric solid tumours is limited in the literature, but: * Each year, about 1,200 children aged 0 to 14 years, and about 500 teenagers aged between 15 and 18 years are diagnosed with cancer (p 281-285, [NHSE, 2023](https://www.england.nhs.uk/wp-content/uploads/2017/10/PRN00115-prescribed-specialised-services-manual-v6.pdf)) in England; Between 2016-8 there were 1838 new cases of cancer per year (average) in people aged under 15 in the UK ([Cancer Research UK stats in children](http://www.cancerresearchuk.org/cancer-info/cancerstats/keyfacts/Childhoodcancers/uk-childhood-cancer-statistics); [definition of children 0-14](https://www.cancerresearchuk.org/about-cancer/childrens-cancer/about)).
* For brain tumors alone (one common type of pediatric solid tumors), each year about [400 children](https://www.childrenwithcancer.org.uk/childhood-cancer-info/cancer-types/brain-spinal-tumours/#:~:text=There%20are%20more%20than%20100,include%20headaches%2C%20nausea%20and%20seizures.) are diagnosed with brain, CNS, or intracranial tumors in the UK.
* Studies and information suggested that in children and young people diagnosed with cancers, a range between [30%](https://www.pediatricnursing.org/article/S0882-5963%2802%2943913-9/fulltext) and [53%](https://www.cclg.org.uk/Types-of-childhood-cancer) have solid tumours.

***Incidence*: (about 697 in England each year):**

|  |  |  |
| --- | --- | --- |
| Number (n) of children diagnosed with cancer each year  | Proportion (%) of children with solid tumours (**mid-point**) | Number (n) of children diagnosed with solid tumours each year  |
| Children diagnosed with cancer each year, n = [1,700](https://www.england.nhs.uk/wp-content/uploads/2017/10/PRN00115-prescribed-specialised-services-manual-v6.pdf), England | About **41%** ( a range between [30%](https://www.pediatricnursing.org/article/S0882-5963%2802%2943913-9/fulltext), [40%,](https://publications.aap.org/pediatricsinreview/article-abstract/39/2/57/35136/Pediatric-Solid-Tumors-of-Infancy-An-Overview?redirectedFrom=fulltext?autologincheck=redirected) and [53%](https://www.cclg.org.uk/Types-of-childhood-cancer)) | **N = 697** |

***Prevalence*:** exact prevalence unknown. But it reported that: * About 35,000 people in the UK have survived more than 5 years and are alive after having been diagnosed with a childhood cancer ([Children’s Cancer and Leukemia Group](https://www.cclg.org.uk/csoir/prognosis-and-survival-in-the-uk#:~:text=It%20is%20estimated%20that%20there,40%20years%20in%20the%20UK.)).
* 78% of children and young people diagnosed in 1997 to 2001 survived for at least 5 years, and this went up to 86% for those diagnosed in 2012 to 2016 ([UK Health Security Agency](https://ukhsa.blog.gov.uk/2021/03/15/cancer-in-children-and-young-people-what-do-the-statistics-tell-us/)). And for spinal and brain tumor, 5-year survival rate is 74% in England ([Children with cancer UK](https://www.childrenwithcancer.org.uk/childhood-cancer-info/cancer-types/brain-spinal-tumours/#:~:text=There%20are%20more%20than%20100,include%20headaches%2C%20nausea%20and%20seizures.)).
* **Crude prevalence of pediatric solid tumors**: 35,000 x 0.41= 14,350 UK, **and 12,197** inEngland (84% of UK population, [ONS, 2021](https://www.statista.com/statistics/281296/uk-population/#:~:text=The%20vast%20majority%20of%20people,percent%20of%20the%20UK%20population.)).
 | Not met  |
|  | Normally no more than 300 people in England are eligible for the technology in its licensed indication and no more than 500 across all its indications  |  **Met: about 239 each year** considering both paediatric tumours and cyanide poisoning (another indication of sodium thiosulfate)* **Incidence/new cases each year**: 697 each year in England (see above).
* **% proportion with localised disease**: reporting limited and about **61.5%,** which is the mid-point between 28% and 93% as referenced by the company for the 8 types solid tumours considered;
* **Clinical experts to NICE technical team**: about 60% localised although it varies by disease type;
* **Proportion of solid tumors treated by cisplatin:** about **32.5%;** reporting of it scarce in the literature, the company assumed 70%, clinical advice to NICE technical team indicated that 10% to 15% may be too low, but 50% may be too high, so the mid-point of 32.5% between 15% and 50% was taken.

So, for **number of population eligible for treatment for:** * Incidence each year x % localised x % treated by cisplatin = 697 x 61.5% x 32.5% = **139**.

Further, sodium thiosulfate is also licensed for sequential use with hydroxocobalamin or sodium nitrite for the treatment of acute cyanide poisoning that is judged to be life-threatening; the license for this use is for a stronger formulation: [250 mg/ml (12.5g per 50ml vial)](https://mhraproducts4853.blob.core.windows.net/docs/482b148651a9f3073625031d00c1ef8b31949bde) compared with [80mg/ml for prevention of ototoxicity (8g per 100ml vial)](https://mhraproducts4853.blob.core.windows.net/docs/60e64648b4b279e72464f2ad3b995affba23f83c). Cyanide poisoning occurred in around 1300 cases between 2008 and 2019 (12-year period) ([Haden et al](https://pubmed.ncbi.nlm.nih.gov/35635241/)), around **100** cases each year. About **239** in total each year.  | Met  |
|  | The very rare condition significantly shortens life or severely impairs its quality  | **Not met*** Ototoxicity/hearing loss is a side effect/complication caused by chemotherapy used to treat cancer (solid cancer for this topic).
* Manifestation and impact of ototoxicity on individuals may vary. A review on cisplatin-associated ototoxicity by [Paken et al. 2019](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6486385/) reported that ototoxicity associated with cisplatin usually presents as irreversible, progressive, bilateral, high frequency sensorineural hearing loss with tinnitus. And tinnitus may occur with or without a hearing loss, may be permanent or transient. Sporadic and partial recovery of hearing loss has also been reported. Further, the extent of hearing loss often varies and is related to the dose.
* Ototoxicity may not be associated with shortened life, but hearing loss caused by ototoxicity could impact on quality of life for some. It can delay speech and language development in children and can have a significant impact on school performance and psychosocial functioning. However, with the right treatment / support, people with hearing loss can go on to lead fulfilling lives.
* The underlying cancer could be life shortening, however, depending on the type of cancer, stages, and treatment available, the severity of the cancer varies.
* As reported above, 78% of children and young people diagnosed in 1997 to 2001 survived for at least 5 years, went up to 86% for those diagnosed in 2012 to 2016 ([UK Health Security Agency](https://ukhsa.blog.gov.uk/2021/03/15/cancer-in-children-and-young-people-what-do-the-statistics-tell-us/)).
 | Not met |
|  | There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options. | **Met*** If considering paediatric solid tumours and the treatment options available, sodium thiosulfate is unlikely to offer significant additional benefit over existing treatment options such as radiology, surgery, and chemotherapies.
* Clinical experts’ advice to the technical team was for hearing loss induced by cisplatin, sometimes cisplatin is substituted for other drugs including carboplatin.
* However, acknowledges that currently there is no treatment for reversing hearing loss if it occurs. A treatment option to prevent hearing loss would offer significant additional benefit to current practice for children with solid tumours. While there are other options to address hearing loss including aids, etc, there are no current treatment options to prevent ototoxicity caused by having cisplatin in children and young people with cancer.
 | Met |

Highly specialised technologies vision and routing criteria

The Highly Specialised Technologies Programme is designed to be used in exceptional circumstances. Its purpose is to evaluate technologies for very rare diseases that have:

* small numbers of patients
* limited or no treatment options
* challenges for research and difficulties with collecting evidence, because of the uniqueness of the disease.

The Highly Specialised Technologies Programme aims to:

* encourage research on, and innovation for, very rare conditions when there are challenges in generating an evidence base that is robust enough to bring the product to market
* secure fairer and more equitable treatment access for very small populations with very rare diseases
* recognise that an approach that maximises health gain for the NHS may not always be acceptable: it could deliver results that are not equitable.

The Highly Specialised Technologies Programme acknowledges that:

* It is important for NICE to apply appropriate limits on the very rare populations that can potentially be routed to the programme. This is because the Highly Specialised Technologies Programme is a deliberate departure from the standard technology appraisal process (valuing the benefits from these technologies more highly by having a much higher [incremental cost-effectiveness ratio [ICER]](https://www.nice.org.uk/Glossary/incremental-cost-effectiveness-ratio) threshold) for the reasons outlined above.
* Each time NICE routes a topic to the Highly Specialised Technologies Programme it is deciding that, if the technology is recommended, the NHS must commit to allocate resources that would have otherwise been used on activities that would be expected to generate greater health benefits.
* NICE has sought to strike a balance between the desirability of supporting access to treatments for very rare diseases against the inevitable reduction in overall health gain across the NHS that this will cause. Both considerations are valid and important, and neither can be given absolute priority over the other. Therefore, the Highly Specialised Technologies Programme criteria and their anticipated application intentionally do not seek to capture every case when there are challenges in generating an evidence base or when there is a small population with a rare disease.
* This approach ensures that technologies routed to the Highly Specialised Technologies Programme fulfil the vision of the programme and manages the displacement in the wider NHS.

However, it can be difficult to identify the exceptional circumstances when the highly specialised technologies methods and processes should be used because of the difficulty in getting the information needed. Proxy information is often relied on and used to make subjective judgements. The routing criteria identify which technologies should be routed for highly specialised technologies guidance. These criteria help make subjective judgements as informed, justifiable, consistent and predictable as possible. NICE’s capacity to develop highly specialised technologies guidance can react to need and there is no limit on the number of technologies that can be routed.

The final routing criteria for the Highly Specialised Technologies Programme are:

* The disease is very rare – defined as 1:50,000 population in England.
* Normally no more than 300 people in England are eligible for the technology in its licensed indication and no more than 500 across all its indications.
* The very rare disease for which the technology is indicated significantly shortens life or severely impairs quality of life.
* There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options.