Highly Specialised Technologies (HST) criteria checklist

**Omburtamab I-131 for treating neuroblastoma with central nervous system or leptomeningeal metastasis ID1664**

### 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. For more information, please see [section 7 of NICE health technology evaluation topic selection: the manual](https://www.nice.org.uk/process/pmg37/chapter/highly-specialised-technologies)

### 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 |
| Unclear | There is some evidence, or the evidence available is unclear. |
| Not met | There is no evidence or limited evidence that the criterion is met. |

### MA wording: \*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*\*

| **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 | **The condition meets the definition of ‘very rare’ (approximately 1,100 patients) regardless of whether considering neuroblastoma as a whole or neuroblastoma with CNS/leptomeningeal metastasis (decided at March 2022 TSOP meeting).**  **Prevalence (England)**   * Difficult to calculate due to limited data * Estimated prevalence of neuroblastoma: **584 to 779**   + Based on [9,747](https://www.cancerdata.nhs.uk/prevalence) children aged 0-14 living with a cancer diagnosis in England in 2018   + Neuroblastoma accounts for between [6%](http://www.ncin.org.uk/cancer_type_and_topic_specific_work/cancer_type_specific_work/cancer_in_children_teenagers_and_young_adults/) to [8%](https://www.cclg.org.uk/Neuroblastoma) of cancers in children * Estimated prevalence of neuroblastoma with CNS/leptomeningeal metastasis: **16 to 78**   + Based on 584 to 779 total with neuroblastoma and different % estimates of the proportion of these people who have with CNS metastasis  |  |  |  | | --- | --- | --- | | Prevalence of neuroblastoma = 584 | | **Estimated prevalence of neuroblastoma with CNS/leptomeningeal metastasis** | | **Estimated % with CNS metastasis** | **2.7%a** | 16 | | [**5%**](https://reader.elsevier.com/reader/sd/pii/S0959804920312946?token=3F4F5366AE1D7848110C66EFEF76AEE240D29CE2A5886F27860ACA1BE12DA30C8D60D390B437236134373BCF7FF3E6BF&originRegion=eu-west-1&originCreation=20220211103713) | 29 | | [**8%**](https://www.redjournal.org/article/S0360-3016(03)00502-9/fulltext) | 47 | | [**10%**](https://cancercommun.biomedcentral.com/articles/10.1186/s40880-015-0038-2#Tab1) | 58 | | aClinical expert advice | | |  |  |  |  | | --- | --- | --- | | Prevalence of neuroblastoma = 779 | | **Estimated prevalence of neuroblastoma with CNS/leptomeningeal metastasis** | | **Estimated % with CNS metastasis** | **2.7%a** | 21 | | [**5%**](https://reader.elsevier.com/reader/sd/pii/S0959804920312946?token=3F4F5366AE1D7848110C66EFEF76AEE240D29CE2A5886F27860ACA1BE12DA30C8D60D390B437236134373BCF7FF3E6BF&originRegion=eu-west-1&originCreation=20220211103713) | 39 | | [**8%**](https://www.redjournal.org/article/S0360-3016(03)00502-9/fulltext) | 62 | | [**10%**](https://cancercommun.biomedcentral.com/articles/10.1186/s40880-015-0038-2#Tab1) | 78 | | aClinical expert advice | | |   **Incidence (England)**   * Estimated incidence of neuroblastoma: 90   + Based on [1,645 children aged 0 to 14 years diagnosed with any cancer per year in UK, 91.15% of these being in England, and 6% having neuroblastoma](http://www.ncin.org.uk/cancer_type_and_topic_specific_work/cancer_type_specific_work/cancer_in_children_teenagers_and_young_adults/) * Estimated incidence of neuroblastoma with CNS/leptomeningeal metastasis: 2 to 9   + Based on 90 total with neuroblastoma and different % estimates of the proportion of these people who have stage 4 neuroblastoma with CNS metastasis  |  |  |  | | --- | --- | --- | | Incidence of neuroblastoma = 90 | | **Estimated incidence of neuroblastoma with CNS/leptomeningeal metastasis** | | **Estimated % with CNS metastasis** | **2.7%a** | 2 | | [**5%**](https://reader.elsevier.com/reader/sd/pii/S0959804920312946?token=3F4F5366AE1D7848110C66EFEF76AEE240D29CE2A5886F27860ACA1BE12DA30C8D60D390B437236134373BCF7FF3E6BF&originRegion=eu-west-1&originCreation=20220211103713) | 5 | | [**8%**](https://www.redjournal.org/article/S0360-3016(03)00502-9/fulltext) | 7 | | [**10%**](https://cancercommun.biomedcentral.com/articles/10.1186/s40880-015-0038-2#Tab1) | 9 | | aClinical expert advice | | | | 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 | **As stated above, there is going to be significantly less than 300 people in England eligible for the technology in its licensed indication (see prevalence of neuroblastoma with CNS/leptomeningeal metastasis).**  The technology does not currently have a UK marketing authorisation for any other indication. However, there are other indications in the pipeline for this technology (e.g. desmoplastic small round cell tumour, medulloblastoma). See: <https://ymabs.com/research-development/pipeline/>   * Intrathecal Immunotherapy for CNS/Leptomeningeal Metastases: estimates that there are between 7,000 and 15,000 patients diagnosed with cerebral metastases in England each year * Diffuse Intrinsic Pontine Glioma (paediatric) : Less than 40 children a year develop pontine glioma in the UK [(Pontine glioma | TRM Trust and Private Care (royalmarsden.nhs.uk)](https://www.royalmarsden.nhs.uk/your-care/cancer-types/paediatric-cancers/pontine-glioma)) * Desmoplastic Small Round Cell Tumor (paediatric): no incidence data found, but thought to be [very rare](https://www.cancer.gov/pediatric-adult-rare-tumor/rare-tumors/rare-soft-tissue-tumors/desmoplastic-small-round-cell-tumors) * Medulloblastoma (paediatric): Less than 90 children a year [(Medulloblastoma/PNET | TRM Trust and Private Care (royalmarsden.nhs.uk)](https://www.royalmarsden.nhs.uk/your-care/cancer-types/paediatric-cancers/medulloblastomapnet#:~:text=Less%20than%2090%20children%20a%20year%20develop%20medulloblastoma,are%20slightly%20more%20common%20in%20boys%20than%20girls.)) * B7-H3 Positive CNS/LM tumors: no incidence data found | Met |
|  | The very rare condition significantly shortens life or severely impairs its quality | **Overall, data are uncertain and it is difficult to estimate survival for neuroblastoma with central nervous system/leptomeningeal metastases with standard of care. However, even with the most conservative estimate, the condition was deemed to significantly shorten life.**   * The 5 year survival rate for Neuroblastoma in children in England is [67%](https://www.childrenwithcancer.org.uk/childhood-cancer-info/cancer-types/neuroblastoma/). 5-year survival is thought to range from [over 95% in low risk cases to 40% in high risk cases](https://www.solvingkidscancer.org.uk/blog/exploring-the-statistics-behind-neuroblastoma-in-the-uk). * Outcomes are worse for children who have neuroblastoma with central nervous system/leptomeningeal metastases. It is difficult to estimate survival for this group with standard of care (surgery, chemotherapy, radiotherapy) – no recent trial data from the UK. Some estimates from observational studies, some of which are old. * No English data are available on survival for this subgroup with central nervous system/leptomeningeal metastases, however [registry data from Germany](https://ascopubs.org/doi/10.1200/JCO.2017.35.15_suppl.10555) suggests that <10% of patients with CNS metastasis survive 36 months. The company provided data suggesting 3-year survival is estimated to be 13% to 15% (company’s own analysis). * Estimates of median survival for neuroblastoma with CNS/leptomeningeal metastasis with standard of care (chemotherapy, radiotherapy or surgery) vary from 1 month to 14 months:  |  |  | | --- | --- | | **Source (year)** | **Median survival (months)** | | CGCCR (2017) a | 9.9 | | SIOPEN (2021) a | 9.0 | | [Zhu et al](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4593360/) (2015) | 4 | | [Astigarraga et.al (1987 – 1990) b](https://acsjournals.onlinelibrary.wiley.com/doi/10.1002/%28SICI%291096-911X%28199612%2927%3A6%3C529%3A%3AAID-MPO4%3E3.0.CO%3B2-N) | 1 | | [Blatt et.al (1978 – 1993) b](https://www.tandfonline.com/doi/abs/10.3109/08880019709009493) | 4.5 | | [Kellie et.al. (1978 – 1989) b](https://acsjournals.onlinelibrary.wiley.com/doi/epdf/10.1002/1097-0142%2819911101%2968%3A9%3C1999%3A%3AAID-CNCR2820680926%3E3.0.CO%3B2-0) | 14.1 | | [Shaw (1982 – 1989) b](https://onlinelibrary.wiley.com/doi/10.1002/mpo.2950200211) | 5 | | [Kramer et al. (1980 – 1999)](https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/1097-0142%2820010415%2991%3A8%3C1510%3A%3AAID-CNCR1159%3E3.0.CO%3B2-I) | 6.7 | | a Company’s own analysis of registry data; bIdentified via [literature review from Kramer et al. (2001)](https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/1097-0142%2820010415%2991%3A8%3C1510%3A%3AAID-CNCR1159%3E3.0.CO%3B2-I) | |  * Median survival with standard of care could be \*\*\*\*\*\*\*\*\*\*\*\*\* for people who previously had all 3 treatment modalities (radiotherapy, chemotherapy and surgery; data from CGCCR registry provided by company). | Met |
|  | There are no other satisfactory treatment options, or the technology is likely to offer significant additional benefit over existing treatment options. | **There is insufficient evidence that this criterion is met:**   1. **There may be satisfactory treatment options depending on disease status and position in the neuroblastoma pathway** 2. **The magnitude and duration of benefit of omburtamab over existing treatment options is highly uncertain, and therefore unlikely to meet this criterion**   **Current treatment options**   * Treatment options for neuroblastoma include chemotherapy, surgery, radiotherapy on primary tumour, stem cell transplant and dinutuximab ([TA538](https://www.nice.org.uk/guidance/ta538)). Dinutuximab is the only targeted immunotherapy for neuroblastoma recommended by NICE. It is used for initial treatment of high-risk neuroblastoma without relapsed/refractory disease – this is estimated to be ~60 to 70% of patients presenting with neuroblastoma (based on clinical expert opinion). * Treatment options for CNS or leptomeningeal metastasis of neuroblastoma are limited. They include neurosurgical resection (surgery), craniospinal radiotherapy and chemotherapy. Feedback from the scoping workshop was that there is a significant and urgent need for new treatments for this condition as there are no known effective and curative treatments for neuroblastoma with CNS/leptomeningeal metastasis currently available in the UK. * Omburtamab would be the first treatment licensed specifically for CNS or leptomeningeal metastasis. It is administered as an ‘add on’ therapy after surgery, chemotherapy or radiotherapy (i.e. it is not given alone). * Comparators for omburtamab are chemotherapy, neurosurgical resection and cranio-spinal irradiation (without omburtamab add on therapy). Dinutuximab is not a comparator, but a large proportion of people eligible for omburtamab will have previously received dinutuximab at an earlier line (i.e. people treated for initial high-risk disease who later develop CNS metastasis). * Omburtamab is a later line treatment for most people. People will likely already have benefitted cumulatively from dinutuximab, stem cell transplant, and/or chemotherapy, surgery and radiotherapy before developing CNS/leptomeningeal metastasis and becoming eligible for omburtamab.   **Benefit with omburtamab**   * As noted above, estimates of median survival for neuroblastoma with CNS/leptomeningeal metastasis with standard of care (chemotherapy, radiotherapy or surgery) vary from 1 month to 14 months, but could be up to \*\*\*\*\*\*\*\* for people who previously had all 3 treatment modalities. 3-year survival is estimated to be 13% to 15%. * Comparatively, median survival with omburtamab in Trial 03-133 was 50 months, and 3-year survival was 56%. However, results are uncertain because this trial was single arm, open label and included a small number of patients (n=109). * Survival gains with omburtamab uncertain and difficult to estimate – could range from 20 to 49 months (1.7 to 4.1 years) based on naïve comparison of median survival from omburtamab trial and external control data. For comparative purposes, life-year gains in dinutuximab appraisal (vs isotretinoin), which was routed as a TA, ranged from 3.6 to 5.2 years. * Feedback from the scoping workshop was that it is unknown whether omburtamab is curative. The company highlighted that in Trial 03-133, the overall survival rate plateaus at around 40% with very few patients dying between 5 and 10 years, and several patients surviving 10 years and longer. Company suggests omburtamab is likely to be curative for some, but not all, patients. * Omburtamab is likely to offer a benefit over existing treatment options, but the extent of benefit is highly uncertain. Therefore, this criterion is not met. | **Not met** |