National Institute for Health and Care Excellence

Health Technology Evaluation

Larotrectinib for treating NTRK fusion-positive advanced solid tumours (Managed access review of TA630) [ID6292]

Response to stakeholder organisation comments on the draft remit and draft scope

Please note: Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Bayer PLC	We agree that re-appraisal of larotrectinib at this time is appropriate and necessary, as the product is scheduled to exit the Cancer Drugs Fund (CDF) this year. This evaluation will enable NICE to review updated evidence to resolve prior uncertainties and determine the suitability of routine NHS commissioning, thereby ensuring continuity of patient access. We also consider the Single Technology Appraisal (STA) process to be the appropriate route for this evaluation, as larotrectinib is a single technology with a defined licensed indication. There are no other relevant comparators or interventions that would warrant an alternative appraisal route. The STA process allows for a timely and focused evaluation, which is particularly important given the current CDF-related time constraints and the clinical risks associated with CDF-specific treatment restrictions (please refer to the question regarding the urgency of this evaluation).	Comments noted. No action needed.

Section	Stakeholder	Comments [sic]	Action
	British Oncology Pharmacy Association	The use of single technology appraisal is appropriate.	Comment noted. No action needed.
	British Thoracic Oncology Group	It is appropriate	Comment noted. No action needed.
	Sarcoma UK	No comment.	Comment noted. No action needed.
Wording	Bayer PLC	No comment	Comment noted. No action needed.
	British Oncology Pharmacy Association	Yes it is	Comment noted. No action needed.
	British Thoracic Oncology Group	Yes	Comment noted. No action needed.
	Sarcoma UK	Yes	Comment noted. No action needed.
Timing issues	Bayer PLC	We would like to highlight that this re-appraisal of larotrectinib is time-sensitive due to the product's current status under the Cancer Drugs Fund (CDF), as recommended in TA630. In line with NHS England and NICE policy, therapies funded via the CDF must undergo re-evaluation within the agreed timeframes to determine their suitability for routine NHS commissioning. A delay in this evaluation could result in uncertainty regarding patient access, as continued funding through the CDF will not be available beyond the exit point. This represents a particular risk for this population of	Comments noted. NICE has scheduled this topic into its work programme. For further details, see the NICE website: https://www.nice.org.uk/guidance/indevelopmen

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		patients with NTRK gene fusion-positive solid tumours, who typically have limited or no alternative treatment options. In addition to the need to resolve this funding status, we have received feedback from clinicians that the current CDF criteria create challenges and potential clinical risks for patients. For example but not limited to the inability to re-initiate larotrectinib after a treatment interruption of more than six weeks, according to the current CDF criteria, may prevent clinicians from delivering optimal patient care. This restriction does not reflect real-world clinical practice where temporary treatment pauses or discontinuation may be clinically meaningful (e.g., to manage toxicity or when clinicians consider patient no longer needs treatment as a result of continued remission) and where re-treatment with larotrectinib might be life-critical if the disease resumes after this particular time window.	t/gid-ta11565. No action needed.
	British Oncology Pharmacy Association	Given that the treatment has been commissioned by the CDF since 2020 due to the uncertainty in clinical evidence and cost-effectiveness. This is longer than the usual maximum of 2 years for CDF. It is therefore in the best interest of the public, taxpayer and CDF to establish clinical evidence and cost-effectiveness after a prolonged period of data collection.	Comments noted. NICE has scheduled this topic into its work programme. For further details, see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta11565. No action needed.
	British Thoracic Oncology Group	Not urgent as already available via CDF	Comments noted. NICE has scheduled this topic into its work programme. For further

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			details, see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta11565. No action needed.
	Sarcoma UK	There are at present a lack of specialised treatments for sarcoma, which contributes to a five-year survival rate of just 55%. In addition to improving survival outcomes as a standalone treatment, larotrectinib can be used as neoadjuvant therapy, shrinking tumours to increase the effectiveness and reduce the disturbance of other treatments for sarcoma, including surgery. For these reasons, an urgent evaluation of the drug should be undertaken by the NHS.	Comments noted. NICE has scheduled this topic into its work programme. For further details, see the NICE website: https://www.nice.org.uk/guidance/indevelopment/gid-ta11565. No action needed.
Additional comments on the draft remit	Bayer PLC	No comment	Comment noted. No action needed.

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Bayer PLC	No comment	Comment noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
	British Oncology Pharmacy Association	Agree	Comment noted. No action needed.
	British Thoracic Oncology Group	Its ok	Comment noted. No action needed.
	Sarcoma UK	The background information is accurate. Paragraph 3 would benefit from additional information about the prevalence of sarcoma, including its relative commonness in paediatric populations: Sarcoma accounts for 1.4% of all cancer diagnoses in the UK. It is the third most common cancer in children, making up 7-10% of all childhood cancers. (UK guidelines for the management of soft tissue sarcomas, British Journal of Cancer, 2025 Jan). The prevalence of NTRK fusion-positive tumours in adult sarcomas is 1.27%, compared to up to 3% in paediatric sarcoma patients (Genomic context of NTRK1/2/3 fusion-positive tumours from a large real-world population, npj Precision Oncology, 2021 July). In infantile fibrosarcoma, approximately 90% of cases are NTRK fusion-positive (NTRK Fusions in Sarcomas: Diagnostic Challenges and Clinical Aspects, Diagnostics (Basel). 2021 Mar).	Comments noted. The background information has been amended.
Population	Bayer PLC	Yes	Comment noted. No action needed.
	British Oncology Pharmacy Association	Yes it is	Comment noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
	British Thoracic Oncology Group	Yes	Comment noted. No action needed.
	Sarcoma UK	It should be stated clearly that the consultation covers both adult and paediatric populations (including infantile patients).	Comment noted. No action needed.
Subgroups	Bayer PLC	Larotrectinib is a tumour agnostic therapy specifically indicated for the use in patients with NTRK gene fusion-positive solid tumours, regardless of histological origin. The mechanism of action targets the oncogenic NTRK fusion driver rather than characteristics related to the tissue of origin. Consequently: • Larotrectinib received regulatory approval as a tumour agnostic therapy (EMA[1], FDA[2]) based on pooled data across tumour types, which aligns with its mechanism of action and intended use. Restricting the evaluation to individual tumour subgroups is inconsistent with this global regulatory precedent and clinical practice. • According to the ESMO Tumour-Agnostic Classifier and Screener (ETAC-S)[3] which asses the tumour-agnostic potential of therapies, larotrectinib satisfies the criteria to be defined as tumour agnostic i.e., it demonstrates an objective response (ORR) in at least 20% of patients in two-thirds of the investigated tumour types, with at least 5 patients in each tumour type. • Dividing patients by tumour type is inconsistent with the molecularly defined nature of the target population and contradicts the tumour-agnostic definition. It is clinically possible to analyse efficacy in subgroups, as has been shown in various congresses[4,5] but from a health economics perspective, exploring a tumour-specific approach in the model is not appropriate when trying to understand the overall effect of the treatment on the entire population.	Comments noted. The subgroups will be considered only if the evidence allows. If there is insufficient evidence to allow robust analyses, the company can make a case for deviating from the scope and/or present sensitivity analyses around its base case. No action needed.

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		• Given the rarity of NTRK fusions across any single tumour type, the resulting subgroups are too small and heterogeneous to generate reliable or meaningful estimates of cost-effectiveness outcomes. In the larotrectinib clinical development program, 30 distinct tumour sites are represented. Notably, 11 of these tumour types include only a single patient each, highlighting the heterogeneity and small numbers within individual tumour site categories. Any attempt to conduct site-specific subgroup analyses would therefore lack statistical power and could lead to unreliable or misleading conclusions. This further supports the appropriateness of evaluating the full population of NTRK gene fusion-positive patients as a single, molecularly defined group, consistent with the tumour agnostic indication. The larotrectinib clinical development program includes patients with varying prior treatment histories, and an exploratory analysis of treatment-naïve patients is available[6]. While this subgroup demonstrates particularly favourable outcomes, we propose that: • As with tumour site, the licensed indication for larotrectinib does not specify a number of prior therapies received, the required absence of 'satisfactory treatment options' is highly dependent on the tumour entity and the available treatment options that are specifically suitable for the patient. TRK fusion positivity alone should define treatment eligibility, and clinical decision-making in practice is based on this molecular marker rather than treatment history. • The treatment-naïve subgroup can provide valuable supporting information to illustrate larotrectinib's benefit when used earlier in the treatment pathway. This subgroup represents approximately 33% of the patients enrolled in larotrectinib's clinical trials as of 2023 (101/302 patients) and can be included as a supportive scenario analysis to	

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		inform committee considerations. The main evaluation and model should be based on the full licensed population and rely on clinicians' decision-making as presented in available real-world data (please refer to the question on larotrectinib's positioning within the existing care pathway).	
	British Oncology Pharmacy Association	Agree	Comment noted. No action needed.
	British Thoracic Oncology Group	No	Comment noted. No action needed.
	Sarcoma UK	In addition to the existing subgroups, adult and paediatric populations should be considered separately. Suitability and line of use of larotrectinib for sarcoma differs between adult and paediatric populations. As stated above, the prevalence of NTRK fusion-positive tumours in adult sarcomas is 1.27%, compared to up to 3% in paediatric sarcoma patients (Genomic context of NTRK1/2/3 fusion-positive tumours from a large real-world population, npj Precision Oncology, 2021 July). In infantile fibrosarcoma, 90% of cases are NTRK fusion-positive (NTRK Fusions in Sarcomas: Diagnostic Challenges and Clinical Aspects, Diagnostics (Basel). 2021 Mar). Therefore, use of larotrectinib is appropriate for larger proportions of paediatric than patients. It should also be noted that tumour site does not effectively account for differences between sarcoma and other cancers. While other cancers (e.g. breast) will typically originate in one site of the body, sarcoma can affect any part of the body. Tumour site, therefore, is not an effective means of comparison if intended to differentiate clinical or cost effectiveness of larotrectinib between types of cancer.	Comments noted. Varying prevalence of tumours across age groups can be captured in the economic modelling. Subgroups will be considered only if the evidence allows. If there is insufficient evidence to allow robust analyses, the company can make a case for deviating from the scope and/or present sensitivity analyses around its base case. No action needed.

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Comparators	Bayer PLC	There are no treatment options routinely available in the NHS that specifically target TRK fusion-driven cancers. In the absence of TRK-fusion specific treatments, it is assumed that patients with TRK fusion-driven cancer are currently treated according to guideline recommendations based on the tumour location, with standard of care available for advanced or metastatic solid tumour cancers such as chemotherapy, immunotherapy, molecularly targeted treatment or best supportive care.	Comments noted. No action needed.
	British Oncology Pharmacy Association	Agree	Comment noted. No action needed.
	British Thoracic Oncology Group	Tricky as there are no real standards of care outside of resection for early disease. However the lung cases would get treated with chemoimmunotherapy as first line therapy	Comments noted. No action needed.
	Sarcoma UK	Given the breadth of treatments for NTRK fusion-positive solid tumours, this is an appropriate prompt for gathering the evidence required.	Comment noted. No action needed.
Outcomes	Bayer PLC	Yes	Comment noted. No action needed.
	British Oncology Pharmacy Association	The outcomes are appropriate.	Comment noted. No action needed.
	British Thoracic Oncology Group	Yes, appropriate	Comment noted. No action needed.

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	Sarcoma UK	Outcomes should include a measure to capture how larotrectinib can be used as a neoadjuvant therapy for other treatments for NTRK fusion-positive tumours, e.g. shrinking the tumour to maximise effectiveness and minimise morbidity of surgery.	Comments noted. The outcomes in the scope are broad and overarching, more specific outcomes relevant to these broader outcome headings can be considered as part of the evaluation process. No action needed.
Equality	Bayer PLC	Access restriction to TRK inhibitors would raise important equality considerations within the UK healthcare system. While NTRK testing is essential to ensure appropriate use of larotrectinib, current implementations in the UK vary significantly, which could limit access to this targeted therapy. Especially variation in genomic services as depicted in the Sarcoma UK report published in 2024. Patients with sarcomas (including bone sarcoma and soft tissue sarcoma) account for almost 1/4 of patients enrolled in larotrectinib's clinical trials and the CDF (cut-off July 2024). The Sarcoma UK report mentions three main health inequalities identified by hospitals and healthcare specialists in the UK which we could generalise for NTRK fusion-positive patients across the country: • Regional disparities, particularly inequalities between patients treated in smaller hospitals and those treated in urban hospitals.	Comments noted. These equality issues will be considered by the committee during the evaluation. No action needed.

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		• Conscious/unconscious biases made by some healthcare professionals, especially for patients from black and ethnic minority backgrounds who may be excluded from being tested. • Lack of inclusivity of certain ethnic groups being excluded due to language barriers, for example. Furthermore, in the absence of continued funding for larotrectinib, access to TRK inhibitors would likely depend on the ability to self-fund or access private healthcare if not funded by the NHS, which may not be possible for all patients. This situation would introduce socio-economic inequalities into the system. TRK-fusion patients treated in the UK would be denied the same opportunity for targeted treatment as patients across Europe where access to treatment, as per label, is widespread (e.g., German approval, Danish approval). Finally, there is a risk that patients with rare conditions are systematically disadvantaged in HTA processes because the rarity of these biomarkers often limits the availability of robust clinical and economic evidence (especially the absence of randomised trials). This could lead to structural inequalities in access to innovation for ultra-rare patient populations.	
	British Oncology Pharmacy Association	No specific comments	Comment noted. No action needed.

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	British Thoracic Oncology Group	No issues	Comment noted. No action needed.
	Sarcoma UK	As referenced above, age should be included as a subgroup in order to account for potential inequalities in usage and accessibility between age groups.	Comments noted. Varying prevalence of tumours across age groups can be captured in the economic modelling. Subgroups will be considered only if the evidence allows. If there is insufficient evidence to allow robust analyses, the company can make a case for deviating from the scope and/or present sensitivity analyses around its base case. No action needed.
Other considerations	Bayer PLC	No comment	Comment noted. No action needed.
	British Thoracic Oncology Group	None	Comment noted. No action needed.
	Sarcoma UK	No comment	Comment noted. No action needed.

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Questions for consultation	Bayer PLC	**1. Where do you consider larotrectinib will fit into the existing care pathway for NTRK fusion-positive advanced solid tumours?** Following its exit from the Cancer Drugs Fund (CDF), larotrectinib is expected to become an integral option in the treatment pathway for patients with NTRK fusion-positive locally advanced or metastatic solid tumours, with flexibility for physician-led decision-making on its placement in the treatment sequence. International guidelines, such as those from the NCCN 2025[7] or ESMO 2023[8], recommend that oncogenic driver-targeted therapies should be considered as early as possible when a validated biomarker and an effective targeted agent are available. This is particularly relevant for larotrectinib, a highly selective TRK inhibitor demonstrating durable response across a range of tumour types. In addition, emerging real-world evidence (RWE) on the use of larotrectinib may further inform its positioning in clinical practice. As an example, ON-TRK is an international, prospective, open-label, multicentre, multicohort, non-interventional study that describes the safety of larotrectinib in real-world practice conditions. A total of 120 patients are enrolled in this study at the interim cut-off, with tumours in various sites (e.g., Central Nervous System (CNS), Soft Tissue Sarcoma (STS), head and neck, lung, Gastrointestinal Stromal Tumour (GIST), etc.). This study reports the number of prior cancer therapy received before larotrectinib according to the tumour site and can be used as an indication for clinicians' preferences. Recognising the heterogeneity of tumour types, prior therapies, and individual patient circumstances, the decision to initiate larotrectinib in the first-line or	Comments noted. No action needed.

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		subsequent lines should remain at the discretion of the treating clinician, informed by tumour biology, available standard of care options, patient fitness and preferences. An advisory board is scheduled with oncologists specialising in various tumour types to collect real-world insights and recommendations. Finally, larotrectinib's optimal place in therapy should allow for physician flexibility, enabling its use in either first-line or subsequent lines depending on the clinical context, in line with the principle of precision oncology and individualised patient care. Introducing a targeted therapy for reimbursement also aligns with UK GIRFT[9] objectives by supporting equitable access, reducing unwarranted variation, and ensuring efficient, evidence-based adoption of innovative treatments across the NHS. **2. What treatments are established clinical management for NTRK fusion-positive advanced solid tumours? Is diagnostic testing for NTRK fusion routinely used in the NHS for people with advanced solid tumours? If so, is it routinely done in the NHS for all solid tumours?** There are currently no tumour-agnostic standard treatments specifically established for NTRK fusion-positive solid tumours within routine NHS clinical practice, beyond targeted therapies that are currently recommended under a managed access agreement through the Cancer Drugs Fund (TA630 and TA644). In the absence of such targeted therapies, NTRK fusion-positive patients are typically managed according to standard treatments for their tumour histology and stage (e.g., chemotherapy, radiotherapy, immunotherapy, or histology-specific targeted agents).	Comments noted. No action needed.

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		In order to be eligible for precision medicine using targeted therapies, patients need to be tested to detect the presence of this specific oncogenic driver. For this purpose, diagnostic testing for NTRK gene fusions is routinely available in the NHS, primarily via the National Genomic Test directory[10]. The test is nationally approved, funded and available for adult and paediatric patients with solid tumours to support the use of precision medicine and harmonise access across the country as part of the NHS Genomic Laboratory Hub (GLH). However, as discussed with clinicians, in routine clinical practice, the extent to which this testing is actively performed may vary based on some factors. Testing is generally prioritised for selected tumour types where NTRK fusions are either more prevalent or where standard treatments options are limited (e.g., rare cancers, paediatric tumours). In common tumour types (e.g., colorectal, lung, breast), broad panel Next-Generation Sequencing (NGS) assays may incidentally detect NTRK fusions if NGS is performed for other molecular markers[11] (e.g., KRAS, EGFR). However, it is not uniformly applied across all patients or tumour types and dependent on local genomic strategies, availability of comprehensive genomic profiling, tissue availability, clinical indications, clinicians' awareness or clinical urgency (in late-stage disease, rapid decisions may prevent full testing). This is primarily due to the fact that NTRK fusions are extremely rare in common cancers. Due to this rarity, oncologists may not prioritise NTRK testing unless common options have been ruled out (e.g., no common driver mutation, tumour has an unusual histology). Testing capability exists within the NHS infrastructure and is expanding according to NHS genomic medicine plan of "making genomics commonplace	

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		in the NHS". In 2024, NHS genomic medicine delivered 810,000 genomic tests, an increase of 8% since 2023[12]. Even with these encouraging numbers, systematic routine testing for all patients with advanced solid tumours is not currently standard practice, and testing is determined by histology, clinical context, and test access. **3. Please select from the following, will larotrectinib be:** A. Prescribed in primary care with routine follow-up in primary care B. Prescribed in secondary care with routine follow-up in primary care **C. Prescribed in secondary care with routine follow-up in secondary care** D. Other (please give details) **4. For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.** The setting for prescribing and routine follow-up for larotrectinib differs in several respects from standard comparators and subsequent treatments, particularly regarding the route of administration, monitoring, and toxicity management. An important distinction is that the use of larotrectinib requires prior confirmation of an NTRK gene fusion through molecular diagnostic testing, such as NGS or other validated molecular assays. This step is not required for most conventional chemotherapy regimens, which are typically selected based on histology and staging alone. However, as highlighted above, genomic testing is already established in NHS care pathways for advanced or	Comment noted. No action needed. Comments noted. No action needed.

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		rare tumours under the NHS Genomic Medicine Service and Genomic Test Directory, particularly for cancers such as non-small cell lung cancer and colorectal cancer, where biomarker-driven therapies are standard. Therefore, this testing requirement reflects the evolution of precision oncology in the NHS rather than a wholly new or exceptional resource need. Larotrectinib is an oral therapy administered in an outpatient setting, with no requirement for intravenous infusions or inpatient stay for drug delivery. Routine follow-up primarily involves clinical assessment, radiological imaging for disease monitoring, and standard laboratory tests, consistent with the monitoring required for most systemic anticancer therapies. The low incidence of treatment-related severe adverse events and associated toxicities (grade 3/4) typically reduces the need for intensive supportive care, hospital admissions, or management of severe adverse events. In the 2024 data cut-off of larotrectinib's pooled trials, the three most common adverse events with severity grade 3/4 related to study drug are decreased neutrophil count, ALT increase and weight gain which occurred in only (20/444) 5%, (19/444) 4% and (14/444) 3% of patients, respectively, based on the overall safety dataset. Based on the same data, only 9 patients (2%) had a treatment-emergent adverse event related to the study drug, which led to permanently discontinue larotrectinib. In contrast, standard comparators, depending on tumour histology, may include: - Cytotoxic chemotherapy (e.g., platinum-based chemotherapy), often administered intravenously in hospital or day-unit settings requiring pre-medication, an infusion chair, and post-infusion observation.	

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		- Immunotherapies (e.g., checkpoint inhibitors) are also typically delivered intravenously, with potential immune-related adverse events that could require hospitalisation. - In paediatric oncology, a standard regimen may involve prolonged inpatient stays and high toxicity monitoring, placing greater burden on hospital resources and caregivers. In this population, larotrectinib can be used as a means to shrink the tumour and make it operable; thus, it eliminates the need for disfiguring surgeries, such as amputation, along with all the associated long-term effects on the patient and significant costs to the healthcare system. For subsequent treatments, patients may return to the standard of care for their tumour histology, which would reintroduce the need for intravenous therapies, hospital visits or more intensive interventions. Of note, only 8/60 (13%) of patients treated with larotrectinib via the CDF (cut-off December 2024) received a subsequent treatment. Overall, larotrectinib's oral administration and favourable safety profile offer a less resource-intensive treatment setting, potentially reducing healthcare utilisation (e.g., infusion suite demand) and associated costs compared to intravenous chemotherapies or immunotherapies. **5. Do you consider that the use of larotrectinib can result in any potential 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 committee to take account of these benefits.**	Comments noted. No action needed.

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		Yes, the use of larotrectinib may provide substantial health-related benefits that are unlikely to be fully captured within the QALY calculation. In terms of prognosis, a Matching-Adjusted Indirect Comparison (MAIC)[13] suggests a 78% lower risk of death with larotrectinib compared with non-TRK inhibitor standard of care (SoC) in adult patients with NTRK fusion-positive solid tumours. This can translate into emotional and psychological benefits, explained by a reduced anxiety and sense of hope which goes beyond QALY metrics but deeply matters to patients. In addition, larotrectinib's oral administration constitutes a strong advantage over injectable treatments as evidence suggests[14] that oncology patients prefer oral treatment over intravenous (IV) for various reasons, including the absence of pain from needles, the possibility of working during the treatment, and the autonomy it provides to patients. The risk of serious complications, including fatal outcomes, associated with chemotherapy administration is often overlooked. In their review, Eek et al. (2016)[15] found that cancer patients also reported a general preference for the convenience of treatment intake. Indeed, outpatient management of larotrectinib reduces the logistical and emotional burden of treatment, which may result in lower caregiver burden – particularly important in paediatric populations, where parents or family members are heavily involved in managing hospital visits, toxicities, and supportive care. The reduction in caregiver time, stress, and potential income loss is not captured within the QALY framework but represents a meaningful health and social benefit.	

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		For paediatric patients specifically, avoiding intensive chemotherapy or radiotherapy may also reduce the risk of late effects on growth, cognitive development, and long-term organ function, with implications for lifetime health outcomes not fully captured within the model. In 2016, a meta-analysis of the neuropsychological effects of chemotherapy in the treatment of childhood cancer[16] demonstrated deficits in attentional capacity among children with cancer who received chemotherapy. Disutility caused by mutilating surgery can partially be captured in QALYs, but the impact of its avoidance is likely not, especially the impact on future productivity gains in adulthood. These hidden benefits will be further explored with NTRK-fusion-positive patients and their caregivers during interviews. **References** 1. European Medicines Agency. *Vitrakvi (larotrectinib) [updated EPAR]*. European Medicines Agency. Accessed June 19, 2025. https://www.ema.europa.eu/en/medicines/human/EPAR/vitrakvi 2. U.S. Food and Drug Administration**.** FDA approves larotrectinib for solid tumors with NTRK gene fusions. FDA; November 26, 2018. Accessed June 19, 2025. https://www.fda.gov/drugs/fda-approves-larotrectinib-solid-tumors-ntrk-gene-fusions-0 3. Westphalen, C.B. et al. The ESMO Tumour-Agnostic Classifier and Screener (ETAC-S): a tool for assessing tumour-agnostic potential of molecularly guided therapies and for steering drug development, 2024, Annals of Oncology, Volume 35, Issue 11, 936 – 953	

Section	Consultee/ Commentator	Comments [sic]	Action
		4. Laetsch TW, Nagasubramanian R, Chugh R, et al. Efficacy and safety of larotrectinib in patients with TRK fusion lung cancer: an updated analysis. *J Clin Oncol.* 2025;43(suppl 16):8610. doi:10.1200/JCO.2025.43.16_suppl.8610 5. Brose MS et al. Efficacy and safety of larotrectinib in patients with TRK fusion thyroid carcinoma: an updated analysis. *J Clin Oncol.* 2025;43(suppl 16):6094. doi:10.1200/JCO.2025.43.16_suppl.6094 6. Hong DS, Xu RH, Shen L, et al. Efficacy and safety of larotrectinib as first-line treatment for patients with TRK fusion cancer. *ESMO Open*. Published online May 22, 2025. doi:10.1016/j.esmoop.2025.105110 7. Sarcoma UK**.** *Sarcoma UK Genomics Full Report 2024*. Sarcoma UK; October 2024. Accessed June 19, 2025. https://sarcoma.org.uk/wp-content/uploads/2024/10/Sarcoma-UK-Genomics-Full-Report-2024.pdf 8. Federal Joint Committee (G-BA). Benefit assessment procedure for the active substance larotrectinib (solid tumors, histology-independent). In: G-BA – Benefit Assessment Procedures; 502. Published April 2, 2020. Accessed July 8, 2025. http://www.g-ba.de/bewertungsverfahren/nutzenbewertung/502/#english 9. Medicinrådet**.** *Medicinrådets vurdering vedrørende larotrectinib (Vitrakvi) til behandling af NTRK-fusion-positiv kræft* [pdf]. København, Denmark: Medicinrådet; 2025. Version 1.0. Available at: medicinraadet.dk. Accessed July 1, 2025. 10. Murphy P, Glynn D, Dias S, et al. Modelling approaches for histology-independent cancer drugs to inform NICE appraisals: a systematic review and decision-framework. Health Technol Assess. 2021;25(76):1-228. doi:10.3310/hta25760	

Section	Consultee/ Commentator	Comments [sic]	Action
		11. National Comprehensive Cancer Network. *NCCN Clinical Practice Guidelines in Oncology: Non–Small Cell Lung Cancer (NSCLC)*. Version 4.2025. National Comprehensive Cancer Network; 2025. https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed June 20, 2025. Page 88. 12. Hendriks, L.E. et al., Oncogene-addicted metastatic non-small-cell lung cancer: ESMO Clinical Practice Guideline for diagnosis, treatment and follow-up, 2023, Annals of Oncology, Volume 34, Issue 4, 339 – 35 13. Getting It Right First Time (GIRFT) Programme. Getting It Right First Time: The GIRFT programme – Introduction. Getting It Right First Time. Accessed July 1, 2025. Available at: gettingitrightfirsttime.co.uk 14. NHS England. *National genomic test directory*. NHS England. Published August 3, 2018; updated June 12, 2025. Accessed June 19, 2025. https://www.england.nhs.uk/publication/national-genomic-test-directories/ 15. Zito Marino F, Pagliuca F, Ronchi A, et al. NTRK Fusions, from the Diagnostic Algorithm to Innovative Treatment in the Era of Precision Medicine. *Int J Mol Sci*. 2020;21(10):3718. Published 2020 May 25. doi:10.3390/ijms21103718 16. NHS England. The NHS Genomic Medicine Service: achievements in 2024. NHS England. Published February 6, 2025. Accessed June 19, 2025. https://www.england.nhs.uk/long-read/the-nhs-genomic-medicine-service-achievements-in-2024/	
	British Oncology Pharmacy Association	Larotrectinib's place in therapy is like at the end of line when patient has exhausted all available standard of care treatment options.	Comments noted. No action needed.

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		Other than larotrectinib, entrectinib is the only other treatment currently available that offer potential clinical benefits to NTRK fusion-positive advanced solid tumour patients. NTRK is currently available on the national genmoic test directory for cancer. The comparator for this evaluation is likely to be best supportive care as the licensed indication specifies “no satisfactory treatment options”	
	British Thoracic Oncology Group	Testing for NTRK is standard for thoracic tumours via genomic hubs	Comment noted. No action needed.
	Sarcoma UK	**Where do you consider larotrectinib will fit into the existing care pathway for NTRK fusion-positive advanced solid tumours?** Within treatment for sarcoma, there will be a breadth of uses for larotrectinib throughout the pathway, from neoadjuvant use at beginning of treatment, as first line treatment, to administration at the point of exhaustion of other treatment options. This will be determined primarily by age of population and subtype. It is important to note that while use will be more common in paediatric sarcoma pathways, use in adult pathways is highly significant. While only 1.27% of adult sarcoma are NTRK fusion-positive, the effectiveness of Larotrectinib in these cases merits access to the drug for adult sarcoma patients. **What treatments are established clinical management for NTRK fusion-positive advanced solid tumours?** For sarcomas, including NTRK fusion-positive sarcomas, standard treatments as mandated in British Sarcoma Group Guidelines are: Doxorubicin;	Comments noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		Gemcitabine; Docetaxol; surgery. Where accessible by individual requests, larotrectinib has been used. This is not an exhaustive list of treatments.	Comments noted. No action needed.
		Is diagnostic testing for NTRK fusion routinely used in the NHS for people with advanced solid tumours? If so, is it routinely done in the NHS for all solid tumours? Whether a sarcoma is NTRK fusion-positive will be determined by genomic testing. Routine Whole Genome Sequencing is commissioned for paediatric sarcoma patients. Routine Whole Genome Sequencing testing is no longer funded for adult sarcoma patients but is still available on clinical request.	Comments noted. No action needed.
		Please select from the following, will larotrectinib be: ***A. Prescribed in primary care with routine follow-up in primary care*** ***B. Prescribed in secondary care with routine follow-up in primary care*** ***C. Prescribed in secondary care with routine follow-up in secondary care*** ***D. Other (please give details):*** Other: prescribed in quaternary care with routine follow-up primarily in quaternary care. All patients with sarcomas must have their care overseen by a Sarcoma Multidisciplinary Team (MDT), which is a Quaternary-level service. Sarcoma MDTs would therefore prescribe larotrectinib, as they are responsible for determining patients' care plans and are responsible for delivery in Specialist Sarcoma Centres or by designated practitioners in Local Sarcoma Units, in line with pathways agreed with the Sarcoma Advisory Group, NICE and British Sarcoma Group guidelines, and as mandated by NHS England's 2019 *Sarcoma Service Specification*. Follow-up care may be	Comments noted. No action needed.

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		delivered in secondary services under supervision of specialist services, but would typically be followed up by specialist services themselves. **For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.** Does not differ. **Do you consider that the use of larotrectinib can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** QALY calculation is unlikely to measure broader psycho-social effects of larotrectinib on the mental health of carers. QALY calculation may not also effectively capture neoadjuvant usage of larotrectinib, whereby it increases quality and quantity of health in conjunction with other treatments, more than use as a standalone treatment. *Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.* There are multiple UK and US journal articles detailing trials of the effectiveness of neo-adjuvant usage of larotrectinib. **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:**	Comment noted. No action needed. Comments noted. No action needed.

Section	Consultee/ Commentator	Comments [sic]	Action
		-could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which larotrectinib is 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.** Answered above. **Please tell us what evidence should be obtained to enable the committee to identify and consider such impacts.** There are multiple journal articles showing difference in usage of larotrectinib in adult and paediatric populations.	Comment noted. No action needed. Comment noted. No action needed.
	British Thoracic Oncology Group	None	Comment noted. No action needed.