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

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of larotrectinib within its marketing authorisation for treating NTRK fusion-positive advanced solid tumours.

Background

Solid tumours are abnormal localised masses of tissue. They can be cancerous (malignant) or not cancerous (benign) and are classified according to the type of cells that form them. The two major types of cancerous solid tumours are sarcomas and carcinomas. Sarcomas are developed from cells of muscles, bone or fat tissue and carcinomas start from the epithelial cells in the skin or tissues that line or cover internal organs. Advanced solid tumours can be locally advanced (tumour that has spread to surrounding tissues or lymph nodes but has not yet spread to other parts of the body) or metastatic (tumour that has spread to other parts of the body).

Tropomyosin-related kinase receptors (TRKs) belong to a family of growth receptors with tyrosine kinase activity. It contains three members, TRKA, TRKB and TRKC that are encoded by neurotrophic tyrosine kinase (NTRK) genes, NTRK1, NTRK2 and NTRK3, respectively. TRKs are exclusively expressed in human neuronal and extra-neuronal tissue and play an essential role in nervous system development and maintenance through activation by neurotrophins. NTRK fusions occur when one of the NTRK genes becomes abnormally connected to another unrelated gene. This results in uncontrolled TRK signalling that can lead to various cancerous solid tumours.

In 2022, there were 346,217 new cases of cancer recorded in England.[1] Breast, prostate, lung and bowel cancer together accounted for more than half (51%) of all these new cancers.[1] NTRK fusion-positive tumour prevalence is estimated to be 0.28% in people aged 18 years and over and 1.34% in people aged less than 18 years.[2] The highest NTRK gene fusion frequencies are reported in rare cancers including infantile or congenital fibrosarcoma, secretory breast cancer and congenital mesoblastic nephroma. Lower frequencies are reported in non-small cell lung cancer, colorectal adenocarcinoma, cutaneous melanoma and non-secretory breast carcinoma.[3]

Current treatments for different solid tumour cancers generally include surgery, chemotherapy, radiotherapy, hormone therapy, immunotherapy, or molecularly targeted treatment. Treatment options that specifically target solid tumours with NTRK-fusions are currently only available to the NHS through managed access:

- larotrectinib in adults and children if the disease is locally advanced or metastatic or surgery could cause severe health problems, and they have no satisfactory treatment options (NICE technology appraisal 630)

- entrectinib in adults and children 12 years and older if the disease is locally advanced or metastatic or surgery could cause severe health problems, and they have not had an NTRK inhibitor before and they have no satisfactory treatment options (NICE technology appraisal 644).

This evaluation will update TA630.

The technology

Larotrectinib (Vitrakvi, Bayer) is indicated for the treatment of solid tumours that display a NTRK gene fusion in adults and children whose condition is locally advanced, metastatic or where surgical resection is likely to result in severe morbidity, and when there are no satisfactory treatment options.

Intervention(s)	Larotrectinib
Population(s)	People with NTRK fusion-positive solid tumours that is locally advanced, metastatic or where surgery is likely to result in severe morbidity and when there are no satisfactory treatment options
Subgroups	If the evidence allows, the following subgroups will be considered: • tumour site • previous therapy will be considered
Comparators	Established clinical management without larotrectinib
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • duration of response • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability and cost of biosimilar and generic products should be taken into account. The use of larotrectinib is conditional on the presence of NTRK fusion. The economic modelling should include the costs associated with diagnostic testing for NTRK fusion in people with advanced solid tumours who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
Other considerations	Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations	**Related technology appraisals** Entrectinib for treating NTRK fusion-positive solid tumours (2020) NICE technology appraisal guidance 644. Larotrectinib for treating NTRK fusion-positive solid tumours (2020) NICE technology appraisal guidance 630. **Related technology appraisals in development** Trastuzumab deruxtecan for previously treated unresectable or advanced HER2-positive solid tumours. NICE technology appraisal guidance [ID6511] Publication date to be confirmed. **Related NICE guidelines** Suspected cancer: recognition and referral (2015, updated 2025) NICE guideline NG12. Improving outcomes for people with sarcoma (2006) NICE cancer service guideline CSG9. **Related quality standards**

	Suspected cancer (2016, updated 2017) NICE quality standard QS124.

Questions for consultation

Where do you consider larotrectinib will fit into the existing care pathway for NTRK fusion-positive advanced solid tumours?

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?

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):
For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention.

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.

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

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which 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.

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

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation).

References

1. NHS England. Cancer Registration Statistics, England, 2022. Accessed June 2025.

2. Westphalen CB, Krebs MG, Le Tourneau C, et al. (2021) Genomic context of *NTRK1/2/3* fusion-positive tumours from a large real-world population. NPJ Precision Oncology 5(69).

3. Forsythe A, Zhang W, Phillip Strauss U, et al. (2020) A systematic review and meta-analysis of neurotrophic tyrosine receptor kinase gene fusion frequencies in solid tumors. Therapeutic Advances in Medical Oncology 21(12).