NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Larotrectinib for treating advanced solid tumours with TRK fusions

Draft scope

Draft remit/appraisal objective

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

Background

Solid tumours are abnormal localised masses of tissue. They can be cancerous or not cancerous 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 genes, NTRK1, NTRK2 and NTRK3, respectively. TRKs are exclusively expressed in human neuronal tissue and play an essential role in nervous system development and maintenance through activation by neurotrophins. TRK 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 adult and paediatric cancerous solid tumours.

In 2015, there were 359,960 new cases of cancer recorded in the UK with 163,444 cancer deaths[2]. Breast, prostate, lung and bowel cancer together accounted for more than half (53%) of all new cancers in the UK in 2015[2]. The prevalence of TRK fusions in cancer is estimated to range from 0.5% in common solid tumour types such as colon, lung and breast to 90% in rare tumour types such as mammary analogue secretory carcinoma and infantile fibrosarcoma[3].

There are currently no treatment options available in the NHS that specifically target solid tumours with TRK-fusions. Current treatments for different solid tumour cancers generally include surgery, chemotherapy, radiotherapy, hormone therapy, immunotherapy, or molecularly targeted treatment.

The technology

Larotrectinib (brand name unknown, Bayer) is an oral and selective inhibitor of the TRK family (TRKA, TRKB and TRKC). Larotrectinib turns off the signalling pathway that allows TRK fusion cancers to grow. It is administered orally as a capsule or as a liquid.

Larotrectinib does not have a marketing authorisation in the UK for treating advanced solid tumours with TRK fusions. It is being studied in single-arm Phase I and 2 basket trials in children, young people and adults with TRK fusion-positive advanced or metastatic solid tumours who have either progressed or not responded to standard therapies, are unfit for standard therapy or for whom no standard or available curative therapy exists.

Intervention(s)	Larotrectinib
Population(s)	People with TRK fusion-positive advanced solid tumours who; • have either progressed on or not responded to prior therapies • are unfit for chemotherapy or for whom no curative therapy exists
Comparators	Standard of care
Outcomes	The outcome measures to be considered include: • overall survival • progression-free survival • response rate • 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 use of larotrectinib is conditional on the presence of TRK fusion. The economic modelling should include the costs associated with diagnostic testing for TRK 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 5.9 of the Guide to the Methods of Technology Appraisals.
Other considerations	If evidence allows, subgroup analyses by: • tumour site • previous therapy will be considered. 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 National Policy	National Service Frameworks: Cancer National Service Frameworks: Children, Young People and Maternity Services Department of Health (2016) NHS outcomes framework 2016 to 2017 Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020 Department of Health (2014) The national cancer strategy: 4th annual report Department of Health (2011) Improving outcomes: a strategy for cancer Department of Health (2009) Cancer commissioning guidance

	Department of Health (2007) Cancer reform strategy

Questions for consultation

What is the population size for TRK fusion-positive advanced solid tumours?

Which solid tumour sites are most commonly associated with TRK fusion mutation?

How will larotrectinib be used in clinical practice?

- Would larotrectinib be used differently based on tumour site?

Have all relevant comparators for larotrectinib been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for TRK fusion-positive advanced solid tumours who

- have either progressed on or not responded to prior therapies or
- are unfit for chemotherapy or for whom no curative therapy exists?

How should standard of care be defined?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom larotrectinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Is testing for TRK fusion expression routine in the NHS for advanced solid tumours?

Where do you consider larotrectinib will fit into the existing NICE pathway?

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 will be 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.

Do you consider larotrectinib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of larotrectinib can result in any potential significant and 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 Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction)

References

1. Cancer Research UK 'Cancer Statistics for the UK'. Accessed July 2018.

2. Cancer Research UK 'Cancer Incidence Statistics'. Accessed July 2018.

3. American Society of Clinical Oncology (ASCO) 'New drug shows durable efficacy across diverse pediatri and adult cancers'. Accessed July 2018