3770NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Avapritinib for treating advanced systemic mastocytosis

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of avapritinib within its marketing authorisation for treating systemic mastocytosis.

Background

Mastocytosis is a condition caused by excessive amounts of mast cells gathering in body tissues, such as the skin, organs and bones. In many cases, mastocytosis is caused by a mutation in the KIT gene. Mastocytosis is generally classified as cutaneous (affecting the skin) or systemic (affecting the internal organs). The mast cells release large amounts of histamine and other mediators into the blood, causing symptoms such as skin rash, itchy skin, hot flushes, vomiting, diarrhoea and anaphylaxis.

There are various subtypes of systemic mastocytosis defined by level of disease progression. These include indolent systemic mastocytosis (a non-progressive form of systemic mastocytosis that accounts for about 90% of cases of systemic disease)[1], and advanced systemic mastocytosis. In advanced systemic mastocytosis, mast cells accumulate in internal organs and can cause organ damage, bone fractures and anaemia. The wide-ranging symptoms can be disabling or even life-threatening. Advanced systemic mastocytosis includes aggressive systemic mastocytosis, systemic mastocytosis with associated haematologic neoplasm and mast cell leukaemia.[2]

It is estimated that between 1 in 10,000 to 30,000 people have mastocytosis.[1,3] Approximately 10% of people with systemic mastocytosis will have advanced systemic mastocytosis.[1]

There is no cure for advanced systemic mastocytosis, treatment aims to decrease the number of mast cells and to control symptoms. Therefore, treatment depends on the symptoms experienced by each person. NICE technology appraisal 728 recommends midostaurin as an option for treating aggressive systemic mastocytosis, systemic mastocytosis with associated haematological neoplasm, or mast cell leukaemia in adults. Other treatments for advanced systemic mastocytosis may include interferon alpha, cladribine, imatinib (for disease without the KIT mutation), nilotinib or dasatinib.[4]

The technology

Avapritinib (Ayvakyt, Blueprint Medicines) does not currently have a marketing authorisation in the UK for treating advanced systemic mastocytosis. It has been studied in a phase II clinical trial in adults with advanced systemic mastocytosis.

Intervention(s)	Avapritinib
Population(s)	Adults with advanced systemic mastocytosis
Subgroups	If evidence allows, subgroup analysis by disease type to include: • aggressive systemic mastocytosis • systemic mastocytosis with associated haematological neoplasm • mast cell leukaemia
Comparators	• Midostaurin • Cladribine • Dasatinib • Imatinib • Interferon alpha • Nilotinib
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. If the technology is likely to provide similar or greater health benefits at similar or lower cost than technologies recommended in published NICE technology appraisal guidance for the same indication, a cost comparison may be carried out. 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.
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:** Midostaurin for treating advanced systemic mastocytosis (2021) NICE technology appraisal guidance 728.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019). Chapter 59

Questions for consultation

Are the outcomes listed appropriate? Should change in symptom severity be included as an outcome?

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

Where do you consider avapritinib will fit into the existing care pathway for advanced systemic mastocytosis?

Would avapritinib be a candidate for managed access?

Do you consider that the use of avapritinib 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 avapritinib 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.

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).

NICE is considering evaluating this technology through its cost comparison evaluation process.
Please provide comments on the appropriateness of appraising this topic through this 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).

Technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost, compared with technologies that have been previously recommended (as an option) in published NICE guidance for the same indication. Companies can propose cost-comparison topics to NICE at any stage during topic selection and scoping. NICE will route technologies for evaluation through the cost-comparison process if it is agreed during scoping that the process is an appropriate route to establish the clinical and cost effectiveness of the technology.

NICE's health technology evaluations: the manual states the methods to be used where a cost comparison case is made.

- Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?

- Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.
- Will the intervention be used to treat the same population as the comparator(s)?
- Overall is the technology likely to offer similar or improved health benefits compared with the comparators?
- Would it be appropriate to use the cost-comparison methodology for this topic?

References

1. UK Masto (2019) Systemic mastocytosis. Accessed July 2023.

2. Gilreath JA, Tchertanov L, Deininger MW (2019) Novel approaches to treating advanced systemic mastocytosis. *Clin Pharmacol*;11:77-92

3. Brockow K (2014) Epidemiology, Prognosis, and Risk Factors in Mastocytosis. Immunology and allergy clinics of North America; 34,2: 283-295

4. NHS (2022) Mastocytosis – treatment. Accessed July 2023.