Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Avapritinib for treating inadequately controlled moderate to severe indolent systemic mastocytosis

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of avapritinib within its marketing authorisation for treating inadequately controlled moderate to severe indolent systemic mastocytosis.

Background

Mastocytosis is a rare condition caused by an excess number of mast cells gathering in the body's tissues. The cause or causes of mastocytosis are not fully known, but there's thought to be an association with a change in genes, known as the KIT mutation. The KIT mutation means too many mast cells are produced, and it can lead to them surviving for longer. The mast cells release large amounts of histamine and other mediators into the blood, causing symptoms such as skin rash, itchy skin, fatigue, trouble with cognition and memory, hot flushes, blood pressure changes, fainting, tachycardia, headache, vomiting, diarrhoea, organ failure and anaphylaxis. People can have some or all of these symptoms, which can be mild or severe, may be episodic or chronic and may be unpredictable.

There are 2 main types of mastocytosis, cutaneous mastocytosis, which affects the skin (mainly in children), and systemic mastocytosis, which affects the skin, internal organs and bones (mainly in adults). Systemic mastocytosis has subtypes defined by level of disease: indolent (the most common, about 90% of cases[1]), smouldering, and advanced systemic mastocytosis. Symptoms of indolent systemic mastocytosis vary from person to person. A recent study found that 4.9% of indolent systemic mastocytosis cases progressed to more advanced types.[2] The KIT D816V mutation has been found in around 95% of indolent systemic mastocytosis cases.[3]

According to clinical expert opinion, 1 in 10,000 people in the UK may have indolent systemic mastocytosis.

There is no cure for indolent systemic mastocytosis. Treatment aims to relieve symptoms and includes antihistamines, including H1 and H2 receptor antagonists, leukotriene inhibitors, sodium cromoglicate (primarily for bowel symptoms), proton-pump inhibitors and, rarely, oral corticosteroids. Phototherapy and photochemotherapy may be used to temporarily relieve symptoms. Phototherapy cannot be used long term because of the risk of skin damage and cancer.

The technology

Avapritinib (Ayvakyt, Blueprint Medicines) does not currently have a marketing authorisation in the UK for treating inadequately controlled moderate to severe indolent systemic mastocytosis.

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Avapritinib as an add-on to standard care is being studied in a clinical trial compared with placebo as an add on to standard care in adults with moderate to severe indolent systemic mastocytosis whose symptoms are not adequately controlled by standard care.

Avapritinib has a marketing authorisation to treat aggressive systemic mastocytosis, systemic mastocytosis with an associated haematological neoplasm, or mast cell leukaemia in adults.

Intervention(s)	Avapritinib as an add-on to standard care
Population(s)	Adults with inadequately controlled moderate to severe indolent systemic mastocytosis
Comparator	Established clinical management without avapritinib
Outcomes	The outcome measures to be considered include: • symptom severity • mast cell burden • response rate • adverse effects of treatment • health-related quality of life • mortality
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.
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.

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Related NICE recommendations	**Related technology appraisals:** Avapritinib for treating advanced systemic mastocytosis (2024) NICE technology appraisal guidance 1012. Midostaurin for treating advanced systemic mastocytosis (2021) NICE technology appraisal guidance 728.

References

1. NHS.UK: mastocytosis [accessed July 2025].

2. Trizuljak J, Sperr WR, Nekvindová L, et al. (2020) Clinical features and survival of patients with indolent systemic mastocytosis defined by the updated WHO classification. Allergy 75(8):1927–1938.

3. George T, Hoehn G, Lin H-M, et al. (2020) Increased detection of KIT D816V mutation in peripheral blood samples from patients with indolent systemic mastocytosis (ISM) in the phase 2 pioneer study using a high sensitivity droplet digital (dd) PCR assay compared with next generation sequencing (NGS). Blood 136: 7–8.

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