

# NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

## Single Technology Appraisal

### Avapritinib for treating advanced systemic mastocytosis [ID3770]

#### Final scope

#### Remit/evaluation objective

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

#### Background

Mastocytosis is a condition caused by excessive amounts of neoplastic mast cells gathering in body tissues, such as the skin, gastro-intestinal tract, bone marrow, spleen, liver and lymph nodes. 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, blood pressure changes, syncope, tachycardia, vomiting, headache, diarrhoea, cognitive disturbances described as 'brain fog', organ failure and anaphylaxis.

There are various subtypes of systemic mastocytosis defined by level of disease. These include indolent systemic mastocytosis (a highly symptomatic form of systemic mastocytosis that accounts for about 90% of cases of systemic disease)<sup>1</sup>, smouldering systemic mastocytosis and advanced systemic mastocytosis.<sup>2</sup> 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 and lead to shortened life expectancy. Advanced systemic mastocytosis includes aggressive systemic mastocytosis, systemic mastocytosis with associated haematologic neoplasm and mast cell leukaemia.<sup>3</sup>

It is estimated that between 1 in 7,700 to 10,400 people have systemic mastocytosis.<sup>4</sup> Less than 10% of people with systemic mastocytosis will have advanced systemic mastocytosis.

There is no cure for advanced systemic mastocytosis, treatment aims to reduce the mast cell burden, reduce or reverse end organ damage and 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 and imatinib (for disease without the KIT mutation).<sup>5</sup>

#### 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.

<b>Intervention(s)</b>	Avapritinib
<b>Population(s)</b>	Adults with advanced systemic mastocytosis
<b>Subgroups</b>	<p>If evidence allows, subgroup analysis by disease type to include:</p> <ul style="list-style-type: none"> <li>• aggressive systemic mastocytosis</li> <li>• systemic mastocytosis with associated haematological neoplasm</li> <li>• mast cell leukaemia</li> </ul>
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• Midostaurin</li> <li>• Cladribine</li> <li>• Imatinib</li> <li>• Interferon alpha</li> </ul>
<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rate</li> <li>• symptom severity</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<b>Economic analysis</b>	<p>The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year.</p> <p>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.</p> <p>Costs will be considered from an NHS and Personal Social Services perspective.</p> <p>The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account.</p> <p>The availability and cost of biosimilar and generic products should be taken into account.</p>

<b>Other considerations</b>	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.
<b>Related NICE recommendations</b>	<b>Related technology appraisals:</b> Midostaurin for treating advanced systemic mastocytosis (2021) <a href="#">NICE technology appraisal guidance 728</a> .
<b>Related National Policy</b>	The NHS Long Term Plan (2019) <a href="#">NHS Long Term Plan</a> NHS England (2018) <a href="#">NHS manual for prescribed specialist services (2018/2019)</a> . Chapter 59

## References

1. UK Masto (2019) [Systemic mastocytosis](#). Accessed July 2023.
2. Jackson CW, Pratt CM, Rupprecht CP, Pattanaik D, Krishnaswamy G. Mastocytosis and Mast Cell Activation Disorders: Clearing the Air. *Int J Mol Sci*. 2021;22(20).
3. Gilreath JA, Tchertanov L, Deininger MW (2019) Novel approaches to treating advanced systemic mastocytosis. *Clin Pharmacol*;11:77-92
4. Orphanet. [Systemic mastocytosis](#). Accessed August 2023
5. NHS (2022) [Mastocytosis – treatment](#). Accessed July 2023.