NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Midostaurin for treating advanced systemic mastocytosis

Draft scope

Draft remit/appraisal objective

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

Background

Mastocytosis is a rare 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). 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. Advanced systemic mastocytosis includes aggressive systemic mastocytosis, mast cell leukaemia and systemic mastocytosis with an associated blood (haematological) disease.

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. 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. The systemic condition mainly affects adults. It is estimated that between 1 in 20,000 and 1 in 40,000 worldwide have systemic mastocytosis[2].

The aim of treatment for advanced systemic mastocytosis is to decrease the number of mast cells. Treatment may include interferon alpha, cladribine, imatinib (for disease without the KIT mutation), nilotinib or dasatinib[3]. Treatment for systemic mastocytosis with an associated blood (haematological) disease will also include treatment for the associated condition.

The technology

Midostaurin (Rydapt, Novartis) is a multi-targeted kinase inhibitor, which inhibits FLT3, KIT and other receptor tyrosine kinases. It is administered orally. Midostaurin has a marketing authorisation for treating adults with aggressive systemic mastocytosis, systemic mastocytosis with associated haematological neoplasm or mast cell leukaemia.

Intervention(s)	Midostaurin
Population(s)	People with aggressive systemic mastocytosis, systemic mastocytosis with associated haematological neoplasm or mast cell leukaemia.
Comparators	Current clinical management including but not limited to interferon alpha, cladribine, imatinib, nilotinib, or dasatinib (treatments do not currently have a marketing authorisation in the UK for this indication).
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 availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will 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 and NICE Pathways	Appraisals in development (including suspended appraisals): Masitinib for treating systemic mastocytosis. NICE technology appraisals guidance [ID781]. Suspended.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018/2019) NHS manual for prescribed

	specialist services (2018/2019) Chapter 59. Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017

Questions for consultation

Have all relevant comparators for midostaurin been included in the scope? Which treatments are considered to be established clinical practice in the NHS for advanced mastocytosis?

Are the outcomes listed appropriate?

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

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 midostaurin 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.

Do you consider midostaurin 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 midostaurin 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 UK Masto (2019) Systemic mastocyctosis. Accessed April 2019.

2 Orphanet (2008) Systemic mastocytosis. Accessed April 2019.

3 NHS (2016) Mastocytosis – treatment. Accessed April 2019.