NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Midostaurin for treating advanced systemic mastocytosis [ID1573]

Final scope

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 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. 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.

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 systemic condition mainly affects adults. It is estimated that around 1 in 10,000 people have systemic mastocytosis.[2,3]

The aim of treatment for advanced systemic mastocytosis is to decrease the number of mast cells and to control symptoms. Therefore, treatment depends on the symptoms experienced by each person. Treatment may include interferon alpha, cladribine, imatinib (for disease without the KIT mutation), nilotinib or dasatinib.[4] 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)	Adults 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 (these 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	If evidence allows, subgroup analysis by disease type to include: • aggressive systemic mastocytosis • systemic mastocytosis with associated haematological neoplasm • mast cell leukaemia 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

References

1 UK Masto (2019) Systemic mastocyctosis. Accessed April 2019.

2 Cohen SS, Skovbo S, Vestergaard H et al. (2014) Epidemiology of systemic mastocytosis in Denmark. British Journal of Haematology 166(4): 521-8.

3 van Doormaal J, Arends S, Brunekreeft KL et al. (2013) Prevalence of indolent systemic mastocytosis in a Dutch region. Journal of allergy and clinical immunology 131(5): 1429-1430.

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