NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Momelotinib for treating disease-related splenomegaly or symptoms in adults with myelofibrosis

Final scope

Remit/evaluation objective

To appraise the clinical and cost effectiveness of momelotinib within its marketing authorisation for treating disease-related splenomegaly or symptoms from myelofibrosis.

Background

Myelofibrosis is a cancer of the bone marrow in which the marrow is replaced by scar (fibrous) tissue.[1] Myelofibrosis may be primary (known as chronic idiopathic myelofibrosis), or secondary to either polycythaemia vera (a disorder in which the bone marrow makes too many red blood cells[2]; known as post polycythaemia vera myelofibrosis) or essential thrombocythaemia (a disorder in which the bone marrow makes too many platelets[3]; known as post essential thrombocythemia myelofibrosis).

The early stages of myelofibrosis may be asymptomatic in some people while others may have severe symptoms from the onset.[4] As the bone marrow becomes more scarred, it is less able to produce blood cells. To compensate for this, blood cell production occurs in the spleen and liver, causing these organs to enlarge. Enlargement of spleen (splenomegaly) may cause abdominal pain, dyspnoea (shortness of breath), early satiety (feeling full) and faecal incontinence, along with progressive anaemia. Splenomegaly can also lead to problems with blood circulation in the liver and spleen. Other symptoms include incurable itch, general malaise, weight loss, night sweats, low grade fever, anaemia, fatigue, and pallor. Between 10 to 20% of people with myelofibrosis develop acute myeloid leukaemia.[1]

Many people with myelofibrosis have mutations in a gene known as Janus-associated kinase 2 (JAK2) gene. JAK signalling controls cytokines and growth factors that are important for blood cell production and immune function. Regardless of mutational status, loss of regulation of the JAK signalling pathway is thought to be the underlying mechanism of the disease in myelofibrosis.[5] Around 2 to 3 people per 100,000 are diagnosed with myelofibrosis every year.[5] The average age at diagnosis is 65 years.[1] Median survival for people with myelofibrosis is around 5 years.[6]

To help guide treatment, myelofibrosis is classified into 4 risk groups: low, intermediate (1 or 2) or high-risk, based on various prognostic factors such as age, presence of constitutional symptoms, haemoglobin level, white blood cell count and number of blast cells in the blood.[7]

Allogeneic stem cell transplant is the only potentially curative treatment for myelofibrosis, however, it is only suitable for people who are fit enough to undergo treatment. For adults with intermediate-2 or high-risk primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis, NICE technology appraisal guidance 386 recommends ruxolitinib as a treatment option and NICE technology appraisal guidance 756 recommends fedratinib for use

within the Cancer Drugs Fund for people who have previously had ruxolitinib. Other treatment options include hydroxycarbamide, other chemotherapies, androgens, splenectomy, radiation therapy, erythropoietin and red blood cell transfusion.

The technology

Momelotinib (Omjjara, GSK) does not have a marketing authorisation in the UK for treating myelofibrosis. It has been studied in clinical trials compared with ruxolitinib, danazol (an androgen therapy) or best available therapy in adults with primary myelofibrosis, post polycythaemia vera myelofibrosis, or post essential thrombocythaemia myelofibrosis, with splenomegaly and with or without anaemia.

Intervention	Momelotinib
Population	Adults with disease-related splenomegaly or symptoms of: • primary myelofibrosis (also known as chronic idiopathic myelofibrosis), • post polycythaemia vera myelofibrosis, or, • post essential thrombocythemia myelofibrosis.
Subgroups	• People whose disease was previously treated with a JAK inhibitor • Prognostic factors such as haemoglobin <10 g/dL, leukocyte count >25 x 109/L, circulating blasts (immature blood cells) ≥ 1%, presence of constitutional symptoms or platelet count
Comparators	For people eligible for treatment with ruxolitinib: • ruxolitinib. For people whose disease was previously treated with ruxolitinib or if ruxolitinib is not appropriate (including people with low or intermediate-1 risk disease): • established clinical practice (including but not limited to hydroxycarbamide, other chemotherapies, androgens, splenectomy, radiation therapy, erythropoietin and red blood cell transfusion).

Outcomes	The outcome measures to be considered include: • spleen size • symptom relief (including itch, pain and fatigue) • overall survival • leukaemia-free survival • response rate • haematologic parameters (including red blood cell transfusion and blood count) • 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:** Ruxolitinib for disease-related splenomegaly or symptoms in adults with myelofibrosis (Rev TA289) (2016) NICE technology appraisal guidance 386.

	Fedratinib for treating disease-related splenomegaly or symptoms in myelofibrosis (2021) NICE technology appraisal guidance 756. **Related technology appraisals in development:** Navitoclax with ruxolitinib for treating myelofibrosis when stem cell transplant is unsuitable. NICE technology appraisal guidance [ID5096]. Publication date to be confirmed. Ropeginterferon alfa-2b for treating polycythaemia vera without symptomatic splenomegaly. NICE technology appraisal guidance [ID1596]. Publication date to be confirmed.
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan

References

1. Cancer Research UK, Myelofibrosis, What is myelofibrosis? (2020) Accessed November 2022
2. Cancer Research UK, Polycythaemia, What is polycythaemia? (2020) Accessed November 2022
3. Cancer Research UK, Thrombocythaemia, What is thrombocythaemia? (2020) Accessed November 2022
4. Myelofibrosis (MF) – MPN Voice. Accessed November 2022.
5. Leukaemia and Lymphoma Society, Myelofibrosis. Accessed November 2022
6. Cervantes et al. Life expectancy and prognostic factors in the classic *BCR/ABL*-negative myeloproliferative disorders. *Leukemia* 22, 905-914 (2008)
7. Cancer Research UK, Myelofibrosis, Tests and treatment for myelofibrosis (2020). Accessed November 2022.