

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Fedratinib for treating disease-related splenomegaly or symptoms in myelofibrosis (Review of TA756) (ID5115)

Draft scope

**Remit/evaluation objective**

To appraise the clinical and cost effectiveness of fedratinib 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.<sup>1</sup> 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<sup>2</sup>; known as post polycythaemia vera myelofibrosis) or essential thrombocythaemia (a disorder in which the bone marrow makes too many platelets<sup>3</sup>; 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.<sup>4</sup> 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 and 20% of people with myelofibrosis develop acute myeloid leukaemia.<sup>1</sup>

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.<sup>5</sup> Around 2 to 3 people per 100,000 are diagnosed with myelofibrosis every year.<sup>4</sup> The average age at diagnosis is 65 years.<sup>1</sup> Median survival for people with myelofibrosis is around 5 years.<sup>6</sup>

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.<sup>7</sup>

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. This recommendation is the subject of this evaluation. Other treatment options include hydroxycarbamide, other chemotherapies, androgens, splenectomy, radiation therapy, erythropoietin and red blood cell transfusion.

**The technology**

Fedratinib (Inrebic, Bristol Myers Squibb) has a UK marketing authorisation for ‘the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis, post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis who are Janus Associated Kinase (JAK) inhibitor naïve or have been treated with ruxolitinib.

<b>Intervention(s)</b>	Fedratinib
<b>Population(s)</b>	Adults with disease-related splenomegaly or symptoms of: <ul style="list-style-type: none"> <li>• primary myelofibrosis (also known as chronic idiopathic myelofibrosis),</li> <li>• post polycythaemia vera myelofibrosis, or,</li> <li>• post essential thrombocythemia myelofibrosis.</li> </ul>
<b>Subgroups</b>	<ul style="list-style-type: none"> <li>• People whose disease was previously treated with a JAK inhibitor</li> <li>• Prognostic factors such as haemoglobin &lt;10 g/dL, leukocyte count &gt;25 x 10<sup>9</sup>/L, circulating blasts (immature blood cells) ≥ 1%, presence of constitutional symptoms or platelet count</li> </ul>
<b>Comparators</b>	<p>For people eligible for treatment with ruxolitinib:</p> <ul style="list-style-type: none"> <li>• ruxolitinib.</li> </ul> <p>For people whose disease was previously treated with ruxolitinib or if ruxolitinib is not appropriate (including people with low or intermediate-1 risk disease):</p> <ul style="list-style-type: none"> <li>• established clinical practice (including but not limited to hydroxycarbamide, other chemotherapies, androgens, splenectomy, radiation therapy, erythropoietin and red blood cell transfusion).</li> <li>• Momelotinib (subject to NICE evaluation)</li> </ul>

<p><b>Outcomes</b></p>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• spleen size</li> <li>• symptom relief (including itch, pain and fatigue)</li> <li>• overall survival</li> <li>• leukaemia-free survival</li> <li>• response rate</li> <li>• hematologic parameters (including red blood cell transfusion and blood count)</li> <li>• adverse effects of treatment</li> <li>• health-related quality of life.</li> </ul>
<p><b>Economic analysis</b></p>	<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>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.</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>
<p><b>Other considerations</b></p>	<p>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.</p>
<p><b>Related NICE recommendations</b></p>	<p><b>Related technology appraisals:</b></p> <p><a href="#">‘Fedratinib for treating disease-related splenomegaly or symptoms in myelofibrosis’</a> (2021) NICE technology appraisal guidance 756. Currently under review.</p> <p><a href="#">‘Ruxolitinib for treating disease-related splenomegaly or symptoms in adults with myelofibrosis’</a> (Rev TA289) (2016)</p>

	<p>NICE technology appraisal guidance 386. Review date March 2019.</p> <p><b>Related technology appraisals in development:</b></p> <p><a href="#">‘Momelotinib for treating disease-related splenomegaly or symptoms in adults with myelofibrosis’</a>. NICE technology appraisal guidance [ID6141] Publication expected March 2024.</p> <p><a href="#">Navitoclax with ruxolitinib for treating myelofibrosis when stem cell transplant is unsuitable</a>. NICE technology appraisal guidance [ID5096]. Publication date to be confirmed.</p> <p><a href="#">Ropeginterferon alfa-2b for treating polycythaemia vera without symptomatic splenomegaly</a>. NICE technology appraisal guidance [ID1596]. Publication date to be confirmed.</p> <p><a href="#">‘Pacritinib for treating myelofibrosis’</a> NICE technology appraisals guidance [ID880]. Suspended.</p>
<p><b>Related National Policy</b></p>	<p>The NHS Long Term Plan (2019) <a href="#">NHS Long Term Plan</a></p> <p>NHS England (2018) <a href="#">NHS manual for prescribed specialist services (2018/2019)</a> Chapter 105.</p>

**Questions for consultation**

Where do you consider fedratinib will fit into the existing care pathway for myelofibrosis?

Do you consider that the use of fedratinib can result in any potential 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 committee to take account of these benefits.

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 fedratinib 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.

NICE intends to evaluate this technology through its Single Technology Appraisal process. (Information on NICE's health technology evaluation processes is available at <https://www.nice.org.uk/about/what-we-do/our-programmes/nice-guidance/nice-technology-appraisal-guidance/changes-to-health-technology-evaluation>).

### References

1. [What is myelofibrosis?](#) (2020). Cancer Research UK. Accessed August 2023.
2. [What is polycythaemia?](#) (2020). Cancer Research UK. Accessed August 2023.
3. [What is thrombocythaemia?](#) (2020). Cancer Research UK. Accessed August 2023.
4. [Myelofibrosis](#). Myeloproliferative Neoplasms Support Voice. Accessed August 2023.
5. [Myelofibrosis](#). Leukaemia and Lymphoma Society. Accessed August 2023
6. [Life expectancy and prognostic factors in the classic \*BCR/ABL\*-negative myeloproliferative disorders](#). Cervantes. F, Passamonti. F et al (2008). *Leukemia* 22, 905-914. Accessed August 2023.
7. [Tests and treatment for myelofibrosis](#) (2020). Cancer Research UK. Accessed August 2023.