

**NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE**

**Health Technology Appraisal**

**Pacritinib for treating myelofibrosis**

**Draft scope**

**Draft remit/appraisal objective**

To appraise the clinical and cost effectiveness of pacritinib within its marketing authorisation for treating myelofibrosis.

**Background**

Myelofibrosis is a cancer of the bone marrow in which the marrow is replaced by scar (fibrous) tissue. 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) or essential thrombocythaemia (a disorder in which the bone marrow makes too many platelets).

The early stages of myelofibrosis may be asymptomatic in some people while others may have severe symptoms from the onset. 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 25% 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.

The annual incidence of myelofibrosis is approximately 0.75 per 100,000. The median survival is 5 years from onset, but variation is wide; some patients have a rapidly progressing disorder with short survival. The peak incidence of primary myelofibrosis is between 50 and 70 years of age.

To guide treatment, myelofibrosis is classified into low, intermediate and high risk categories based on various prognostic factors such as age, presence of constitutional symptoms, haemoglobin level, white blood cell count, platelet count, circulating blast cells, transfusion dependence, and presence of unfavourable karyotype.

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. Other treatment options aim to relieve symptoms and improve quality of life. These include hydroxycarbamide, other chemotherapies, androgens, splenectomy, radiation therapy, erythropoietin and red blood cell transfusion.

Ruxolitinib, a protein kinase inhibitor that targets Janus-associated kinase (JAK) signalling, has a marketing authorisation in the UK for 'the treatment of disease-related splenomegaly or symptoms in adult patients with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis'. [NICE technology appraisal guidance 386](#) recommends ruxolitinib as an option for treating disease-related splenomegaly or symptoms in adults with primary myelofibrosis (also known as chronic idiopathic myelofibrosis), post polycythaemia vera myelofibrosis or post essential thrombocythaemia myelofibrosis, only in people with intermediate-2 or high-risk disease.

### The technology

Pacritinib (EPJEVY, CTI Biopharma) is a small molecule inhibitor of Janus-associated kinase 2 (JAK2) and FMS-like tyrosine kinase 3. It is administered orally.

Pacritinib does not have a marketing authorisation in the UK for treating myelofibrosis. It is currently being studied in clinical trials compared with best available therapy (which may or may not include other JAK2 inhibitors) in adults with or without thrombocytopenia and primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis with intermediate -1 or -2 or high-risk.

<b>Intervention</b>	Pacritinib
<b>Population</b>	People with primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis
<b>Comparators</b>	<ul style="list-style-type: none"> <li>• Ruxolitinib</li> <li>• Established clinical practice (including but not limited to hydroxycarbamide, other chemotherapies, androgens, splenectomy, radiation therapy, erythropoietin and red blood cell transfusion)</li> </ul>

<b>Outcomes</b>	<p>The outcome measures to be considered include:</p> <ul style="list-style-type: none"> <li>• spleen size</li> <li>• symptom release (including itch, pain and fatigue)</li> <li>• overall survival</li> <li>• progression-free survival</li> <li>• response rate</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 patient access schemes for the intervention or comparator technologies will be taken into account.</p>
<b>Other considerations</b>	<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>If evidence allows, consideration should be given to subgroups according to prognostic factors (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 (&lt;50,000/uL).</p>
<b>Related NICE recommendations and NICE Pathways</b>	<p><b>Related Technology Appraisals:</b>  <a href="#">‘Ruxolitinib for disease-related splenomegaly or symptoms in adults with myelofibrosis’</a> (Rev TA289) (2016) NICE technology appraisal guidance 386. Review date March 2019.</p> <p><b>Related Cancer Service Guidance:</b>  <a href="#">‘Haematological cancers: improving outcomes’</a> (2016). NICE guideline 47. Review date to be confirmed.</p> <p><b>Related NICE Pathways:</b></p>

	<p>NICE Pathway: Blood and bone marrow cancers, Pathway last updated: September 2016,  <a href="http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers">http://pathways.nice.org.uk/pathways/blood-and-bone-marrow-cancers</a></p>
<p><b>Related National Policy</b></p>	<p>Blood and marrow transplantation services (adults and children), Chapter 29, Manual for Prescribed Specialised Services 2016/17  <a href="https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf">https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2016/06/pss-manual-may16.pdf</a></p> <p>Department of Health (April 2016) NHS Outcomes Framework 2016-2017. Domain 1.  <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a></p> <p>Department of Health (April 2016) NHS Outcomes Framework 2016-2017. Domain 1.  <a href="https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017">https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017</a></p> <p>Independent Cancer Taskforce (2015) Achieving world-class cancer outcomes: a strategy for England 2015-2020  <a href="http://www.cancerresearchuk.org/about-us/cancer-strategy-in-england">http://www.cancerresearchuk.org/about-us/cancer-strategy-in-england</a></p> <p>Department of Health (2014) The national cancer strategy: 4th annual report  <a href="https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report">https://www.gov.uk/government/publications/the-national-cancer-strategy-4th-annual-report</a></p>

### Questions for consultation

Is the population defined in the scope appropriate?

Have all relevant comparators for pacritinib been included in the scope?  
 Which treatments are considered to be established clinical practice in the NHS for myelofibrosis (both primary and secondary)?

- How should established clinical practice be defined?
- Is best supportive care appropriately defined?
- Would treatment with pacritinib be considered only for people for whom haematopoietic stem cell transplant is inappropriate?

Will pacritinib be used to treat myelofibrosis or the symptoms of myelofibrosis?

Are the outcomes listed appropriate?

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

Where do you consider pacritinib will fit into the existing NICE pathway, [Blood and bone marrow cancers?](#)

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 pacritinib will be 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 pacritinib 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 pacritinib 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.

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>)

NICE has published an addendum to its guide to the methods of technology appraisal (available at <https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-technology-appraisals/methods-guide-addendum->

[cost-comparison.pdf](#)), which states the methods to be used where a cost comparison case is made.

- Would it be appropriate to use the cost comparison methodology for this topic?
- Is the new technology likely to be similar in its clinical efficacy and resource use to any of the comparators?
- Is the primary outcome that was measured in the trial or used to drive the model for the comparator(s) still clinically relevant?
- Is there any substantial new evidence for the comparator technology/ies that has not been considered? Are there any important ongoing trials reporting in the next year?

### References

1 MPD Voice (2015) Myelofibrosis. Accessed October 2016.  
<http://www.mpdvoice.org.uk/about-mpds/myelofibrosis/>