NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Pemigatinib for treating myeloproliferative neoplasms with an FGFR1 rearrangement

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of pemigatinib within its marketing authorisation for treating myeloproliferative neoplasms with an FGFR1 rearrangement.

Background

Myeloproliferative neoplasms are a group of blood cancers that occur when the bone marrow makes too many of one or more types of blood cells. Red blood cells, white blood cells and platelets may be affected. As more blood cells are made, they build up in the bone marrow and reduce its ability to produce enough healthy blood cells. This can also cause the blood to become thicker or not function properly, leading to complications such as blood clots. Types of myeloproliferative neoplasms differ by the type of blood cell affected and include essential thrombocythaemia, polycythaemia vera, primary myelofibrosis and chronic myeloid leukaemia (CML).[1] The early stages of myeloproliferative neoplasms may be asymptomatic in some people, while others may have symptoms from the onset. They can include tiredness, bruising or bleeding problems, having more infections, eye or vision problems, ringing in the ears, night sweats, itching, weight loss and frequent headaches.

Around 4,180 people are diagnosed with essential thrombocythaemia, polycythaemia vera and primary myelofibrosis each year in the UK.[2] A further 750 to 830 people are diagnosed with CML.[3,4] Most people who develop myeloproliferative neoplasms are over the age of 60 years.[1] Myeloproliferative neoplasms usually develop and progress slowly. But rare types with a genetic change called a fibroblast growth factor receptor 1 (FGFR1) rearrangement can be extremely aggressive with a poor prognosis.[5]

Bone marrow or stem cell transplant is a potential curative treatment for myeloproliferative neoplasms with an FGFR1 rearrangement. But this may not be suitable for all people. Other treatments for myeloproliferative neoplasms vary by disorder, symptoms and individual risk factors.[1]

For essential thrombocythaemia, low-dose aspirin is used to lower the risk of blood clots. Chemotherapy agents such as hydroxycarbamide or anagrelide are used to reduce the number of platelets. Targeted immunotherapy with peginterferon alfa 2a is used to slow blood cell growth.

For polycythaemia vera, venesection (therapeutic removal of blood) and low-dose aspirin are used to lower the risk of blood clots. Chemotherapy agents such as hydroxycarbamide or busulfan are used to reduce the number of red blood cells. Targeted treatment options include peginterferon alfa 2a and a Janus kinase inhibitor:

- NICE technology appraisal guidance 921 recommends ruxolitinib for treating polycythaemia vera in people who cannot tolerate hydroxycarbamide or when the condition is resistant to it.

For primary myelofibrosis, blood transfusions are given to treat anaemia and low-dose aspirin is used to lower the risk of blood clots. Chemotherapy agents such as hydroxycarbamide, busulfan or melphalan are used to reduce the number of white blood cells and platelets. Targeted treatment options include peginterferon alfa 2a and Janus kinase inhibitors:

- NICE technology appraisal guidance 386 recommends ruxolitinib as an option for treating disease-related splenomegaly or symptoms in people with primary myelofibrosis, post-polycythaemia vera myelofibrosis or post-essential thrombocythaemia myelofibrosis with intermediate-2 or high-risk disease.

- NICE technology appraisal guidance 756 recommends fedratinib for use within the Cancer Drugs Fund as an option for treating disease-related splenomegaly or symptoms in people with primary myelofibrosis, post-polycythaemia vera myelofibrosis or post-essential thrombocythaemia myelofibrosis who have previously had ruxolitinib.

For CML, targeted anti-cancer drugs called tyrosine kinase inhibitors (asciminib, bosutinib, dasatinib, imatinib, nilotinib and ponatinib) are used to control the growth of white blood cells. Chemotherapy drugs such as fludarabine, idarubicin and cytarabine are used in more advanced-stage disease.

- NICE technology appraisal guidance 401 recommends bosutinib as an option for chronic, accelerated and blast phase Philadelphia chromosome positive CML in people who have previously had 1 or more tyrosine kinase inhibitor and imatinib, nilotinib and dasatinib are not appropriate.

- NICE technology appraisal guidance 425 recommends dasatinib and nilotinib as options for treating only chronic- or accelerated-phase Philadelphia-chromosome-positive CML in people who cannot have imatinib, or their disease is imatinib-resistant.

- NICE technology appraisal guidance 426 recommends dasatinib, nilotinib and imatinib as options for untreated chronic-phase Philadelphia-chromosome-positive CML.

- NICE technology appraisal guidance 451 recommends ponatinib as an option for treating chronic-, accelerated- or blast-phase CML in people with disease that is resistant to dasatinib or nilotinib or they cannot tolerate dasatinib or nilotinib and for whom subsequent treatment with imatinib is not clinically appropriate or the T315I gene mutation is present.

- NICE technology appraisal guidance 813 recommends asciminib as an option for treating chronic-phase Philadelphia-chromosome-positive CML without a T315I gene mutation in people who have previously had 2 or more tyrosine kinase inhibitors.

The technology

Pemigatinib (Pemazyre, Incyte) does not currently have a marketing authorisation in the UK for treating myeloproliferative neoplasms. It has been studied in a single arm clinical trial as monotherapy in people with myeloproliferative neoplasms with an FGFR1 rearrangement.

Intervention(s)	Pemigatinib
Population(s)	People with myeloproliferative neoplasms with a fibroblast growth factor receptor 1 (FGFR1) rearrangement

Comparators	Established clinical management without pemigatinib, which may include bone marrow or stem cell transplant, or
	• For essential thrombocythaemia:
	  ○ low-dose aspirin
	  ○ chemotherapy (such as hydroxycarbamide or anagrelide)
	  ○ targeted immunotherapy (such as peginterferon alfa 2a)
	• For polycythaemia vera:
	  ○ venesection
	  ○ low-dose aspirin
	  ○ chemotherapy (such as hydroxycarbamide or busulfan)
	  ○ targeted immunotherapy (such as peginterferon alfa 2a and ropeginterferon alfa 2b [subject to a NICE evaluation])
	  ○ Janus kinase inhibitor (such as ruxolitinib)
	• For primary myelofibrosis:
	  ○ blood transfusions
	  ○ low-dose aspirin
	  ○ chemotherapy (such as hydroxycarbamide, busulfan or melphalan)
	  ○ targeted immunotherapy (such as peginterferon alfa 2a)
	  ○ Janus kinase inhibitors (such as ruxolitinib, fedratinib [subject to a NICE evaluation] and momelotinib [subject to a NICE evaluation])
	• For chronic myeloid leukaemia:
	  ○ tyrosine kinase inhibitors (asciminib, bosutinib, dasatinib, imatinib, nilotinib and ponatinib)
	  ○ chemotherapy (such as fludarabine, idarubicin and cytarabine)

Outcomes	The outcome measures to be considered include: • response rates • duration of response • progression-free survival • overall survival • 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. The availability and cost of biosimilar and generic products should be taken into account. The use of pemigatinib is conditional on the presence of FGF/FGFR gene alteration. The economic modelling should include the costs associated with diagnostic testing for the FGF/FGFR gene alteration in people with myeloproliferative neoplasms who would not otherwise have been tested. A sensitivity analysis should be provided without the cost of the diagnostic test. See section 4.8 of the guidance development manual (available here: https://www.nice.org.uk/process/pmg36/chapter/introduction-to-health-technology-evaluation).
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 treating polycythaemia vera. (2023) NICE technology appraisal guidance 921

	Asciminib for treating chronic myeloid leukaemia after 2 or more tyrosine kinase inhibitors. (2022) NICE technology appraisal guidance 813 Fedratinib for treating disease-related splenomegaly or symptoms in myelofibrosis. (2021) NICE technology appraisal guidance 756 Ponatinib for treating chronic myeloid leukaemia and acute lymphoblastic leukaemia. (2017) NICE technology appraisal guidance 451 Dasatinib, nilotinib and imatinib for untreated chronic myeloid leukaemia. (2016) NICE technology appraisal guidance 426 Dasatinib, nilotinib and high-dose imatinib for treating imatinib-resistant or intolerant chronic myeloid leukaemia. (2016) NICE technology appraisal guidance 425 Bosutinib for previously treated chronic myeloid leukaemia. (2016) NICE technology appraisal guidance 401 **Related technology appraisals in development:** Momelotinib for treating disease-related splenomegaly or symptoms in adults with myelofibrosis [ID6141] Publication expected March 2024 Navitoclax with ruxolitinib for treating myelofibrosis when stem cell transplant is unsuitable [ID5096] Publication date to be confirmed Fedratinib for treating disease-related splenomegaly or symptoms in myelofibrosis (Review of TA756) [ID5115] Publication date to be confirmed Ropeginterferon alfa-2b for treating polycythaemia vera without symptomatic splenomegaly [ID1596] Publication date to be confirmed **Related NICE guidelines:** Haematological cancers: improving outcomes (2016) NICE guideline NG47 **Related quality standards:** Haematological cancers (2017) NICE quality standard 150
Related National Policy	The NHS Long Term Plan (2019) NHS Long Term Plan NHS England (2018) NHS manual for prescribed specialist services (2018/2019)

Questions for consultation

Background

Does the broad term 'myeloproliferative neoplasms' include the following disorders: essential thrombocythaemia, polycythaemia vera and primary myelofibrosis and chronic myeloid leukaemia (CML)? Is CML generally considered a type myeloproliferative neoplasm? Are there other types of myeloproliferative neoplasms that can have a fibroblast growth factor receptor 1 (FGFR1) rearrangement that should be included in the scope?

What proportion of myeloproliferative neoplasms are likely to have an FGFR1 rearrangement? Are there any subtypes of myeloproliferative neoplasm that are more likely to have FGFR1 rearrangement than others?

Treatment pathway and comparators

Where do you consider pemigatinib will fit into the existing care pathway for myeloproliferative neoplasms?

Is "established clinical management without pemigatinib" appropriate to describe the comparator treatments for pemigatinib? If so, which treatments are considered to be established clinical management in the NHS for people with myeloproliferative neoplasms and an FGFR1 rearrangement including:

- essential thrombocythaemia
- polycythaemia vera
- primary myelofibrosis, and
- CML.

Would people with myeloproliferative neoplasms that have an FGFR1 rearrangement potentially be suitable for a bone marrow or stem cell transplant before or after treatment with pemigatinib? Would pemigatinib be used as a bridge to transplant?

Is genetic testing for an FGFR1 rearrangement done routinely in NHS clinical practice? At what stage in the treatment pathway for myeloproliferative neoplasms would genetic testing be performed?

Outcomes and subgroups

Are the outcomes listed appropriate? Are there other outcomes that should be listed?

Are there any subgroups of people with myeloproliferative neoplasms and an FGFR1 rearrangement in whom pemigatinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

How long is pemigatinib expected to be given to patients?

Would pemigatinib be a candidate for managed access?

Do you consider that the use of pemigatinib 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 pemigatinib 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.

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. Cancer Research UK (2023) Myeloproliferative neoplasms Accessed November 2023

2. Blood Cancer UK (2023) Myeloproliferative neoplasms Accessed November 2023

3. Blood Cancer UK (2023) Chronic myeloid leukaemia (CML) Accessed November 2023

4. Cancer Research UK (2023) What is chronic myeloid leukaemia (CML)? Accessed November 2023

5. Gotlib J. (2017) World Health Organization-defined eosinophilic disorders: 2017update on diagnosis, risk stratification, and management. Am J Hematol 92:1243–1259