Appendix B

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Ruxolitinib for treating polycythaemia vera (review of TA356)

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of ruxolitinib within its marketing authorisation for treating polycythaemia vera that is resistant or intolerant to hydroxycarbamide.

Background

Polycythaemia vera is a bone marrow disease that leads to an increase in the number of blood cells (primarily red blood cells). As more red blood cells are made, the blood becomes thicker which can lead to complications such as gout, bleeding problems and blood clots. Blood clots can cause strokes, heart attacks, or blockage of an artery in your lungs (pulmonary embolism) or in a vein deep within a muscle (deep vein thrombosis). Polycythaemia vera can also cause an increase in white blood cells which can lead to severe itching. In some cases, the extra cells collect in the spleen which may then become enlarged (splenomegaly). Polycythaemia vera can lead to other problems such as scarring of the bone marrow (myelofibrosis) and acute myeloid leukaemia.

Polycythaemia vera can affect people of any age, but is most prevalent in people aged over 60, and in men[1]. The UK prevalence based on the population enrolled in The Health Improvement Network is approximately 6.8 per 100,000. Approximately 5% to 15% of people with polycythaemia vera go on to have myelofibrosis[2]. No epidemiological data are available about the proportion of people receiving treatment for polycythaemia vera whose disease transforms into acute myeloid leukaemia.

Current treatments for polycythaemia vera aim to prevent symptoms and complications, and to minimise the risk of transformation to acute myeloid leukaemia or myelofibrosis, therefore improving survival. The British Committee for Standards in Haematology's guidelines for polycythaemia vera recommend a range of treatments including periodic phlebotomy (bloodletting), hydroxycarbamide, interferon, anagrelide, radioactive phosphorus or low dose busulphan. In addition, melphalan has a license for treating polycythaemia vera in the UK but is rarely used in clinical practice. NICE was previously unable to make a recommendation for ruxolitinib for treating polycythaemia vera because no evidence submission was received for the technology (TA356).

The technology

Ruxolitinib (Jakavi, Novartis) is an inhibitor of the Janus-associated kinases (JAKs), which are involved in blood cells differentiation. Ruxolitinib is administered orally.

Ruxolitinib has a marketing authorisation in the UK for the treatment of patients with polycythaemia vera, who are resistant to or intolerant of hydroxycarbamide, with or without splenomegaly.

Appendix B

Intervention(s)	Ruxolitinib with established clinical management
Population(s)	Adults with polycythaemia vera that is resistant or intolerant to hydroxycarbamide
Subgroups	• People with splenomegaly • People without splenomegaly
Comparators	Established clinical practice without ruxolitinib, comprising of treatment with phlebotomy and aspirin, and: • Hydroxycarbamide • Interferon alfa • Anagrelide • Busulfan • Radioactive phosphorus
Outcomes	The outcome measures to be considered include: • complete haematological remission (including reporting of haematocrit, white blood cell count and platelet count separately) • mortality • symptom relief (including a reduction in spleen size, itching, fatigue and venesection) • thrombosis • progression to acute myeloid leukaemia or myelofibrosis • 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. If appropriate, 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:** Fedratinib for treating disease-related splenomegaly or symptoms in myelofibrosis (2021). NICE technology appraisal guidance 756. Review date December 2021. Ruxolitinib for treating disease-related splenomegaly or symptoms in adults with myelofibrosis (2016). NICE technology appraisal guidance 386. Review date March 2016. **Related appraisals in development:** Ropeginterferon alfa-2b for treating polycythaemia vera without symptomatic splenomegaly [ID1596] NICE technology appraisal guidance. Publication date to be confirmed.
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)

Questions for consultation

Have all relevant comparators for ruxolitinib been included in the scope? Which treatments are considered to be established clinical practice in the NHS for polycythaemia vera?

Is splenomegaly a clinically relevant subgroup for polycythaemia vera? Are there any other subgroups of people in whom ruxolitinib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider ruxolitinib will fit into the existing care pathway for polycythaemia vera?

Would ruxolitinib be a candidate for managed access?

Do you consider ruxolitinib 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 ruxolitinib 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 ruxolitinib 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 ruxolitinib 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 ruxolitinib 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 intends to evaluate this technology through its Single Technology Appraisal process. We welcome comments on the appropriateness of appraising this topic through this 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. Macmillan (2019) Polycythaemia vera [accessed 1 June 2022

2. NICE (2015) Ruxolitinib for treating polycythaemia vera that is resistant or intolerant to hydroxycarbamide: Final scope [accessed 30 June 2022]