NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Evaluation

Ruxolitinib for treating acute graft versus host disease refractory to corticosteroids in people aged 12 and over ID6377

Draft scope

Draft remit/evaluation objective

To appraise the clinical and cost effectiveness of ruxolitinib within its marketing authorisation for treating acute graft versus host disease refractory to corticosteroids in people aged 12 and over.

Background

Graft versus host disease (GvHD) usually occurs after an allogeneic haematopoietic stem cell transplant (HSCT) when donated T-cells attack the recipient's own cells.[1] Rarely, GvHD can develop after transplant of solid organs that are rich in lymphoid cells (such as the liver).[1] Differentiation of acute and chronic GvHD is based on the clinical features of disease and the timing of presentation.[1,2] Acute GvHD usually occurs within 100 days after a HSCT (whereas chronic GvHD usual occurs more than 100 days after). Acute GvHD is characterised by damage to the skin, gastrointestinal tract and liver, with symptoms including generalised patchy skin rash, sickness, weight loss, loss of appetite, diarrhoea, severe abdominal pain and jaundice.[3] Acute GvHD can be graded in severity from grade I (mild) through II (moderate), III (severe) to IV (very severe) according to the modified Seattle Glucksberg criteria.[3] The grade correlates to survival prognosis, with 5-year survival of 25% for grade III and 5% for grade IV disease.[3]

In 2022, there were 1,535 allogeneic transplants in the UK.[4] Up to 50% of people who have a HSCT from a human leukocyte antigen-matched sibling develop acute GvHD, and the risk is typically higher for unmatched donors.[1]

For first-line treatment, the European Society for Blood and Marrow Transplantation recommends topical corticosteroids for grade I acute GvHD and systemic corticosteroids for grade II to IV.[5] For acute GvHD that is refractory to steroids, the recommendations note that there is no standard second-line treatment, and that clinicians should follow institutional guidelines. NHS England's clinical commissioning policy recommends combination therapy (including sirolimus and/or mycophenolate mofetil) as second-line treatment for steroid-refractory acute GvHD.[4] The policy also recommends extracorporeal photopheresis for steroid-refractory acute GvHD, or for people who have developed significant adverse effects to first-line treatments, or are steroid-dependent.[3]

The technology

Ruxolitinib (Jakavi, Novartis Pharmaceuticals UK Ltd) is indicated for the treatment of patients aged 12 years and older with acute graft versus host disease who have inadequate response to corticosteroids or other systemic therapies.

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Intervention(s)	Ruxolitinib
Population(s)	People aged 12 years and older with acute graft versus host disease who have inadequate response to corticosteroids.
Comparators	Established clinical management without ruxolitinib, including but not limited to: • Extracorporeal photopheresis • Combination therapy with mammalian target of rapamycin inhibitors (for example, sirolimus) and/or mycophenolate mofetil
Outcomes	The outcome measures to be considered include: • response to treatment (including complete response and overall response) • mortality • 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.
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** Belumosudil for treating chronic graft versus host disease after 2 or more lines of systemic therapy (2024) NICE technology appraisal guidance 924

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Related National Policy	NHS England (2019) The NHS long term plan NHS England (2017) NHS Medicines for Children's Policy NHS England (2023) Prescribed specialised services manual (version 6) Chapter 29. Haematopoietic stem cell transplantation services (adults and children), Chapter 100. Severe combined immunodeficiency and related disorders service (children) NHS England (2019) Clinical Commissioning Policy: Allogeneic Haematopoietic Stem Cell Transplant for Primary Immunodeficiencies (all ages) NHS England Reference: 170129P NHS England (2017) Clinical Commissioning Policy: Treatments for Graft versus Host Disease (GvHD) following Haematopoietic Stem Cell Transplantation

Questions for consultation

Where do you consider ruxolitinib will fit into the existing care pathway for acute graft versus host disease?

Have all relevant comparators for ruxolitinib been included in the scope? Which treatments are established clinical practice in the NHS for acute GVHD?

Would ruxolitinib ever be given in combination with other treatments? If so, which treatments?

Would acute graft-versus-host disease be more likely to occur in people for whom tissue-type matched donors may be more difficult to identify, for example people from a Black, Asian or minority ethnic family background?

Are the outcomes listed appropriate?

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

Would ruxolitinib be a candidate for managed access?

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 is licensed;

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- 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. Justiz Vaillant AA, Modi P, Mohammadi O. (2022) Graft-Versus-Host Disease. StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK538235/

2. Malard F, Holler E, Sandmaier BM et al. (2023) Acute graft-versus-host disease. Nat Rev Dis Primers 9, 27 (2023).

3. NHS England (2017) Clinical Commissioning Policy: Treatments for Graft versus Host Disease (GvHD) following Haematopoietic Stem Cell Transplantation

4. British Society for Blood and Marrow Transplantation (2022) https://bsbmtct.org/activity/2022/

5. Penack O, Marchetti M, Ruutu T, et al. (2020) Prophylaxis and management of graft versus host disease after stem-cell transplantation for haematological malignancies: updated consensus recommendations of the European Society for Blood and Marrow Transplantation. Lancet Haematol. 2020;7(2):e157-e167.

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