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MPN Alliance Australia
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Dear Ken and Nathalie,

Novartis have lodged a submission to the Pharmaceutical Benefits Advisory Committee (PBAC) for consideration at the November 2019 PBAC Meeting for Jakavi® (ruxolitinib) for the treatment of polycythemia vera (PV). Consumers have the opportunity to submit comments to be taken into account when PBAC considers the submission. Consumer comments can be submitted by a patient, carer, member of the public, health professional or member of a consumer interest group for consideration by the PBAC. The website is open for comments from **28 August to 9 October 2019**, and may be accessed via the following link: https://www1.health.gov.au/internet/main/publishing.nsf/Content/PBAC_online_submission_form

Provided below is some key information on the submission, including the proposed PBS listing, potential issues, key publications and suggested areas for comment.

Proposed listing for ruxolitinib for PV on the Pharmaceutical Benefits Schedule (PBS)
The proposed listing on the PBS is for the treatment of PV patients who are resistant (i.e. inadequate response) to or intolerant (i.e. unacceptable side effects) of hydroxycarbamide (also known as hydroxyurea). This is consistent with the Therapeutic Goods Administration (TGA) registered indication for ruxolitinib for PV. Additionally, to continue treatment with ruxolitinib, patients may be required to demonstrate a response to treatment within the first six months of initiating treatment, and on an ongoing basis. The proposed criteria for response are a modification of the European LeukemiaNet (ELN) criteria[1]:

- Haematocrit < 45% without phlebotomy (at least 3 months since last phlebotomy), OR
- Both of the following; platelet count ≤ 400 x 109/L AND absence of palpable splenomegaly.

Potential submission issues
One of anticipated key issues for the submission is assessing the benefit of treatment with ruxolitinib on patient-relevant outcomes. Clinical study endpoints are generally based on European LeukemiaNet criteria for response, and may not necessarily translate to patient relevant outcomes, including quality of life (QoL). As a result:

[1] Barosi, G., Birgegard, G., Finazzi, G., Griesshammer, M., Harrison, C., Hasselbach, H. C., Kiladjian, J. J., Lengfelder, E., McMullin, M. F., Passamonti, F., Reilly, J. T., Vannucchi, A. M. & Barbui, T. 2009. Response criteria for essential thrombocythemia and polycythemia vera: result of a European LeukemiaNet consensus conference. *Blood,* 113**,** 4829-33

- Patients may be required to discontinue ruxolitinib treatment for PV prematurely on the PBS if patients are required to meet modified ELN criteria for response to continue treatment beyond the initial six months and on an ongoing basis
- The impact of PV and benefit of treatment on QoL may not be adequately captured because data used in the economic evaluation are from generic (non-disease specific) questionnaires, and therefore may not capture the full burden of disease symptoms.

Publications of key clinical studies included in the submission

- Vannucchi et al. (2015) Ruxolitinib versus Standard Therapy for the Treatment of Polycythaemia Vera. The New England Journal of Medicine 2015; 372(5): 426-435.
- Passamonti et al. (2017) Ruxolitinib for the treatment of inadequately controlled polycythaemia vera without splenomegaly (RESPONSE-2): a randomised, open-label, phase 3b study. Lancet Oncology 2017; 18(1): 88-99
- Harrison et al. (2018a) Ruxolitinib compared with best available therapy for polycythaemia vera patients resistant or intolerant to hydroxycarbamide in MAJIC-an investigator-led trial. Poster at 23rd Congress of the European Hematology Association, Stockholm, June 14-17, 2018

Suggested areas for comment

The PBS website provides the following points as guidance, to consider when commenting on a medicine to be considered by PBAC;

- How does this condition/disease affect quality of life?
- What would you most like to see from this treatment? Improved side effects? Slowing disease progression? More mobility? Other benefits?
- If you have used or prescribed this new medicine, what was your experience of the beneficial effects?
- If you have used or prescribed this new medicine, what side effects or toxicities did you experience or observe?
- If you haven't used the new medicine yet, what are your expectations of it?
- If you use other currently available therapies or medicines you use to manage your condition (or for prescribers, for your patient’s condition), what are the benefits and/ or the challenges?

If you require further information or have any questions, do not hesitate to contact me on 0427 588 225 or via email: amy.gye@novartis.com.

Warm regards,

Amy Gye
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