OPINION ON MEDICINAL PRODUCTS

ruxolitinib
JAKAVI 5 mg, 10 mg, 15 mg, 20 mg
tablets

New indication(s)

Adopted by the Transparency Committee on 19 October 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement in the **treatment of patients aged 12 years and older with acute graft-versus-host disease or chronic graft-versus-host disease who have an inadequate response (resistant or dependent) to corticosteroids or other systemic therapies**.

Therapeutic improvement?

A therapeutic advance in the management of patients with acute graft-versus-host disease or chronic graft-versus-host disease who have an inadequate response (resistant or dependent) to corticosteroids or other systemic therapies.

Role in therapeutic strategy?

The therapeutic management of GvHD is currently based on systemic treatment with **corticosteroids for acute grade II to IV GvHD and for moderate to severe chronic GvHD,** due to the hyperinflammatory state of the patient. Apart from corticosteroids, which are used as the first-line treatment in a curative context, but for which approximately one in two patients are refractory, there is currently no single established and consensual therapeutic strategy for the treatment and management of these diseases, despite the existing therapeutic alternatives.

The European *Society for Blood and Marrow Transplantation* (EBMT) European guidelines, updated in 2020, indicate that there is no standard second-line treatment for acute or chronic drug-resistant GvHD.

Role of the medicinal product

JAKAVI (ruxolitinib) is a **first-line treatment** in the management strategy for patients aged 12 years and older with acute graft-versus-host disease or chronic graft-versus-host disease who have an inadequate response to corticosteroids or other systemic therapies.

The Summary of Product Characteristics (SPC) and the Risk Management Plan (RMP) must be followed.

Special recommendations

The Committee would like to receive the final overall survival data from the REACH 3 study as soon as it is available. On the basis of these results, it will decide whether to reassess this medicine.

Committee's conclusions

Clinical Benefit

- Acute graft-versus-host disease and chronic graft-versus-host disease, which have an inadequate response to corticosteroids or other systemic therapies are serious, life-threatening clinical situations.
- The proprietary medicinal product JAKAVI (ruxolitinib) is a curative/symptomatic medicine.
- Its efficacy/adverse effect ratio is substantial.
- Alternative medicinal products (see Section **Erreur ! Source du renvoi introuvable.**).
- JAKAVI (ruxolitinib) is a first-line treatment for patients with acute or chronic GvHD who are resistant to or dependent on corticosteroids.

Public health benefit

Considering:

- the severity of the diseases concerned,
- the partially met medical need,
- the partial response to the identified need, given:
  - a demonstrated additional impact on morbidity but not on mortality,
  - an additional impact on the delivery of care,
  - an additional impact /a lack of expected impact on the care and/or life pathway,

JAKAVI (ruxolitinib) is not likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the actual clinical benefit of JAKAVI (ruxolitinib) is SUBSTANTIAL in the marketing authorisation indication.

The Committee approves inclusion in the list of proprietary medicinal products qualifying for reimbursement under social security and in the list of proprietary products approved for community use for the marketing authorisation indication and at the marketing authorisation dosages.

Recommended reimbursement rate: 65%

Clinical Added Value

Considering:

- the new means of management provided by JAKAVI (ruxolitinib),
- the simplicity of its administration due to its tablet form (oral route), enabling the product to be used on an outpatient basis,
- the results of the available clinical studies supporting the presumption of a benefit for the patient, including
  - short-term efficacy data from a randomised, open-label, comparative phase III study that demonstrated the superiority of ruxolitinib over comparator therapies for the 28-day overall response rate (OR=2.64 [95% CI: 1.65-4.22]) and 56-day overall response rate (OR=2.38 [95% CI: 1.43-3.94]) in patients over 12 years of age with grade II-IV corticosteroid-resistant acute GVHD (REACH 2 study),
  - efficacy data from a phase III, comparative, randomised, multi-centre, open-label study that demonstrated the superiority of ruxolitinib for the 24-week overall response rate (OR=2.99 [95% CI: 1.86-4.80]) and survival without treatment failure (HR=0.37 [95% CI: 0.27-0.51]) in patients over 12 years of age with moderate to severe corticosteroid-refractory or cortico-steroid-dependent chronic GVHD (REACH study 3),
- the medical need for effective medicines to treat patients with acute or chronic graft-versus-host disease who have an inadequate response to corticosteroids or other systemic therapies,
- the known acceptable safety profile of ruxolitinib with a majority of haematological adverse events related to its mechanism of action,

and despite:

- the lack of robust evidence of an effect on overall survival assessed on an exploratory basis in life-threatening clinical situations,
- the low number of adolescent patients aged 12 to 18 years included (approximately 3% in each study), which does not ensure the transposability of the results of the clinical studies in this population,

the Committee deems that JAKAVI (ruxolitinib) provides minor clinical added value (CAV IV) in the therapeutic strategy.