SUMMARY

danicopan

VOYDEYA 50 mg and 100 mg

film-coated tablet

First listing

Adopted by the Transparency Committee on 9 October 2024

Summary of opinion

Favourable opinion for reimbursement only "as an add-on to ravulizumab or eculizumab in the treatment of adult patients with paroxysmal nocturnal haemoglobinuria who have symptomatic haemolytic anaemia after treatment with a C5 inhibitor for at least 6 months".

Unfavourable opinion for reimbursement in the other situations covered by the MA indication.

Transparency Committee's conclusions

Clinical Benefit

- Paroxysmal nocturnal haemoglobinuria (PNH) is a rare (orphan disease) and serious condition caused by an acquired clonal mutation affecting all the haematopoietic cell lines. The disease is polymorphous but is usually manifested (90% of patients) by haemolysis due to the sensitivity of red blood cells to the haemolytic action of the complement. Episodes of haemolysis with haemoglobinuria occur primarily at night, as a result of a reduction in blood pH. The disease course is variable and can be life-threatening due to its complications: thromboembolic events (responsible for 40 to 67% of deaths), haemorrhages, infections, kidney and bone marrow failure.
- The proprietary medicinal product VOYDEYA (danicopan) is a preventive medicinal product.
- The efficacy/adverse effects ratio of VOYDEYA (danicopan) in the treatment of PNH in adult patients with haemolytic anaemia is:
  - High only in patients with residual symptomatic haemolytic anaemia after treatment with a C5 inhibitor for at least 6 months;
  - Not established in the other clinical situations due to a lack of clinical data.
- There is a therapeutic alternative that is already reimbursed: ASPAVELI (pegcetacoplan). FABHALTA (iptacopan) is not currently reimbursed (see section 2.2 of the opinion).
- In the treatment of PNH in adult patients with haemolytic anaemia, VOYDEYA (danicopan):
  - Is a second-line treatment only in patients with residual symptomatic haemolytic anaemia after treatment with a C5 inhibitor for at least 6 months,
  - Has no role in the treatment of PNH in the other clinical situations of the MA.

➔ **Public health benefit**

Considering:

- the seriousness of the disease, which is life-threatening due to its complications,
- its low prevalence (orphan disease),
- the partially met medical need,
- the partial response to the identified need only in the event of residual haemolytic anaemia after treatment with a C5 inhibitor for at least 6 months, given:
  - evidence of an additional impact in this population only on morbidity and compared to continuation of treatment with a C5 inhibitor, with no evidence versus ASPAVELI (pegcetacoplan), noting that they were developed concomitantly,
  - the lack of evidence of an impact on mortality or quality of life. Although a significant difference in favour of danicopan was demonstrated for the FACIT-Fatigue score, there are uncertainties with respect to the clinical relevance of this difference,
  - the lack of evidence of an impact on the organisation of care or the patient's care pathway;

VOYDEYA (danicopan) is unlikely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of VOYDEYA 50 mg and 100 mg (danicopan) film-coated tablet is:

- **substantial only "as an add-on to ravulizumab or eculizumab in the treatment of adult patients with PNH who have symptomatic haemolytic anaemia after treatment with a C5 inhibitor for at least 6 months";**
- **insufficient to justify public funding in the other MA situations.**

The Committee issues the following opinions:

- **a favourable opinion for inclusion of VOYDEYA 50 mg and 100 mg (danicopan) film-coated tablet in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use only within the scope retained and at the MA dosages;**
- **an unfavourable opinion for inclusion of VOYDEYA 50 mg and 100 mg (danicopan) film-coated tablet in both the list of covered drugs for outpatients and the list of covered drugs for inpatients approved for use in the other situations covered by the MA indication.**

➔ **Recommended reimbursement rate for inclusion in the list of covered drugs for outpatients: 65%**

Clinical Added Value

Considering:

- evidence of the superiority of VOYDEYA (danicopan) in combination with a C5 inhibitor (ravulizumab or eculizumab) versus continuation of a C5 inhibitor alone, in terms of increase in haemoglobin levels, reduction in transfusion needs and change in the FACIT-fatigue score after 12 weeks, in adults with PNH who have residual haemolytic anaemia after treatment with a C5 inhibitor for at least 6 months,
- the clinical relevance of these assessment criteria,
- the high effect size observed for haemoglobin levels and reduction in transfusion needs,

And despite:

- uncertainties with respect to the clinical relevance of the benefit observed for the FACIT-fatigue score and the absence of a benefit demonstrated on a quality of life score,
- the absence of comparative data beyond 12 weeks in a context of chronic disease with potentially lifelong treatment, in order to be able to assess maintenance of the benefits and the safety profile of danicopan in the long term, along with its impact on the incidence of thrombotic events, the leading cause of death in patients,
- the absence of robust comparative data versus pegcetacoplan, a treatment already available as second-line therapy after a C5 inhibitor, in particular the absence of a direct comparison, which would nonetheless have been justified on the date of the present assessment given their concomitant development; to date, it cannot be assumed that there is a lower risk of serious haemolysis with danicopan in combination with a C5 inhibitor than with pegcetacoplan, in view of their similar mechanisms of action,

the Committee deems that VOYDEYA 50 mg and 100 mg (danicopan) film-coated tablet provides a moderate clinical added value (CAV III) as an adjunct to ravulizumab or eculizumab in the treatment of adult patients with PNH who have symptomatic haemolytic anaemia after treatment with a C5 inhibitor for at least 6 months, in the same way as ASPAVELI (pegcetacoplan).

In the other situations of the MA: not applicable.