SUMMARY

upadacitinib

RINVOQ 15 mg, 30 mg and 45 mg,

prolonged-release tablet

Indication extension

Original French opinion adopted by the Transparency Committee on 29 November 2023

The legally binding text is the original French opinion version

Transparency Committee's Conclusions

Clinical Benefit

- Crohn's disease is a chronic inflammatory bowel disease (CIBD). It progresses in flare-ups interspersed by periods of remission. It is an incapacitating condition resulting in a marked impairment of quality of life and complications.
- This is a symptomatic medicinal product.
- The efficacy/adverse effects ratio in the treatment of moderate to severe active Crohn's disease in adults is high for adult patients who have had an inadequate response, loss of response or intolerance to conventional treatments and to at least one TNFα inhibitor, and where the alternatives are less suitable. For other patients, this ratio has not been defined.
- This is a third-line treatment in view of the therapies available, i.e. after failure to respond to a conventional treatment including an immunosuppressant (including azathioprine and 6-mercaptopurine) or a corticosteroid, at least one TNF inhibitor (adalimumab, infliximab), and where ustekinumab (STELARA), risankizumab (SKYRIZI) and vedolizumab (ENTYVIO) are less suitable.

- **Public health benefit**

In view of:

- the seriousness of Crohn's disease: an incapacitating severe chronic condition causing substantial impairment of quality of life and which has a high morbidity on account of the frequency of flare-ups, its complications and referral for surgery, the low prevalence of moderate to severe active forms failing to respond to conventional treatments and TNFα inhibitors,
- the partially met medical need including as a third line of Crohn's disease treatment;

- a lack of evidence of an additional impact on morbidity on account of:
  - the lack of robust data on colectomy and corticosteroid-free remission, fistulas, and on quality of life at 52 weeks,
  - the lack of robust comparison to the other second- and third-line treatments available,
  - a safety including high risks in certain at-risk populations and persisting uncertainties relating to the populations not studied in the ORAL Surveillance safety study;
- the lack of evidence of an impact, for this orally administered medicinal product, on the delivery of care and the patient's life pathway (particularly in terms of reducing the need for nursing care, hospital admissions required to administer biological medicines and the need for medical transport) and considering the need:
  - to monitor haematological and lipid parameters during treatment;
  - to set up effective contraception for women of reproductive age;

RINVOQ (upadacitinib) is unlikely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the clinical benefit of RINVOQ (upadacitinib) 15 mg, 30 mg and 45 mg, prolonged-release tablet, is:

- **substantial in the treatment of moderate to severe active Crohn's disease for adult patients who have had an inadequate response, loss of response or intolerance to conventional treatments and to at least one TNFα inhibitor, and where the alternatives are less suitable.**
- **insufficient to justify public funding in view of the alternatives available in the other MA contexts.**

The Committee approves inclusion of RINVOQ (upadacitinib) 15 mg, 30 mg and 45 mg, prolonged-release tablet, in the list of covered drugs for outpatients and in the list of covered drugs for inpatients in the treatment of moderate to severe active Crohn's disease for adult patients who have had an inadequate response, loss of response or intolerance to conventional treatments and to at least one TNFα inhibitor, and where the alternatives are less suitable.

The Committee disapproves the inclusion of RINVOQ (upadacitinib) 15 mg, 30 mg and 45 mg, prolonged-release tablet, in the list of covered drugs for outpatients and in the list of covered drugs for inpatients in the treatment of moderate to severe active Crohn's disease in the other marketing authorisation contexts.

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

Clinical Added Value

For patients failing to respond to conventional treatments (corticosteroids or immunosuppressants) and at least one TNF inhibitor, in view of:

- **the methodological quality of the evidence of the efficacy of RINVOQ (upadacitinib) in three randomised controlled studies versus placebo conducted on patients mostly failing to respond to at least one TNF inhibitor, especially having a moderate form of Crohn's disease (CD),**

- **the lower robustness of this evidence for the maintenance treatment,**
- **the clinically relevant effect size versus placebo on clinical remission and endoscopic response at W12 and W52, with an established effect on quality of life at W12 (fatigue and IBDQ score) and at W52 (IBDQ score),**

but also in view of:

- **the lack of established additional impact with upadacitinib (RINVOQ) on complications (fistulas, stenosis), extraintestinal manifestations of Crohn's disease and referral for surgery,**
- **the efficacy and safety data currently available not allowing positioning in relation to the clinically relevant comparators (STELARA and ENTYVIO in particular),**
- **and the updated safety profile of janus kinase inhibitors including that of RINVOQ (upadacitinib) in CIBD (UC and CD) with a risk of serious adverse events and death,**

the Committee deems that RINVOQ (upadacitinib) 15 mg, 30 mg and 45 mg, prolonged-release tablet, provides no clinical added value (CAV V) in the current therapeutic strategy.