OPINION ON MEDICINAL PRODUCTS

upadacitinib

RINVOQ 15 mg, 30 mg, 45 mg,

sustained-release tablets

New(s) indication(s)

Adopted by the Transparency Committee on 4 January 2023

SUMMARY

The legally binding text is the original French opinion version

Key points

Approval of reimbursement of RINVOQ (upadacitinib) for the treatment of moderate to severe active UC in adults in cases of failure (poor response, loss of response, intolerance or contraindication) of conventional treatments (amino-5 salicylates, corticosteroids and immunosuppressants) with at least one TNFα inhibitor and vedolizumab.

Disapproval of reimbursement in other contexts covered by the marketing authorisation indication, i.e. adult patients exhibiting a poor response, loss of response or intolerance to conventional treatment but treatment-naive in respect of at least one TNFα inhibitor and vedolizumab.

Therapeutic improvement?

No therapeutic improvement in the care pathway.

Transparency Committee's Conclusions

Actual Clinical Benefit

- Disease severity: UC is a chronic inflammatory bowel disease (CIBD) manifested as severe chronic bloody diarrhoea, progressing in episodes. It significantly impairs quality of life and exposes patients to severe complications: acute colitis, dysplasia and cancer of the colon.
- The proprietary medicinal product RINVOQ (upadacitinib) is a symptomatic medicinal product for UC and intended to prevent recurrence.
- The efficacy/adverse effect ratio of upadacitinib in adults in the treatment of UC is significant, with in particular an established effect on endoscopic and quality-of-life outcome measures.
- Availability of alternative: clinically relevant comparators are available as second- and third-line treatments (see Section 2.3.1).
- This medicinal product is recommended for adults with UC exhibiting a poor response, loss of response or intolerance, to conventional treatments, with at least one TNFα inhibitor and vedolizumab. Furthermore, like other JAK inhibitors in UC, RINVOQ (upadacitinib) is only recommended if no suitable therapeutic alternative is available for patients aged over 65 years, smokers (current/former) and in cases of increased risk of major cardiovascular disorders and cancer. In addition, they should be used with caution in the case of other existing risk factors of venous thromboembolism. In the case of JAK inhibitor use, based on the clinical data available, upadacitinib (RINVOQ) is to be preferred as a first-line approach.

- **Public health benefit**

Considering:

- the severity and prevalence of UC, an incapacitating chronic disease of high morbidity on account of the frequency of episodes, its complications and referral for surgery. It also significantly impairs quality of life;
- the partially met medical need including as a third line of UC treatment;
- a clinically relevant effect size versus placebo in induction and maintenance;
- findings showing a benefit on patients' quality of life versus placebo particularly during the maintenance study;

but also the lack of response to the identified need, with:

- efficacy of upadacitinib only established versus placebo and the lack of evidence of an additional impact on morbidity compared to the clinically relevant comparators;
- the lack of elements making it possible to support an expected impact on the care pathway and colectomy;
- safety data for JAK inhibitors;

RINVOQ (upadacitinib) 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 RINVOQ (upadacitinib) is significant only for moderate to severe active UC in adult patients who have exhibited a poor response, loss or response or intolerance, to conventional treatments, with at least one TNFα inhibitor and vedolizumab.

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 in the indication extension (UC) and at the marketing authorisation dosages for these patients.

➔ **Recommended reimbursement rate: 65 %**

The Committee disapproves 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 adult patients in the other contexts covered by the marketing indication, i.e. adult patients exhibiting a poor response, loss of response or intolerance to conventional treatment but treatment-naive in respect of at least one TNFα inhibitor and vedolizumab.

Clinical Added Value

Considering:

- **the methodological quality of the pivotal studies (controlled, randomised, double-blind, relevant choices of outcome measures including quality of life, sample size), but given that the choice of placebo is regrettable in particular for biological treatment-naive patients, and the efficacy was assessed in a heterogenous population including biological treatment-naive and non-naive patients;**
- **the evidence of superiority of upadacitinib versus placebo, with a relevant effect size both in the induction phase and maintenance phase; the lack of evidence of an effect on referral for colectomy;**
- **the lack of comparative data versus TNFα inhibitors in patients exhibiting a poor response to a conventional basic treatment and TNFα inhibitor-naive, and versus vedolizumab (ENTYVIO), while these comparisons were possible;**
- **and the safety profile of upadacitinib;**

the Transparency Committee deems that RINVOQ (upadacitinib) provides no clinical added value (CAV V) in the therapeutic strategy of adult ulcerative colitis.

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