SUMMARY

Reassessment of JAK inhibitors in ulcerative colitis

JYSELECA (filgotinib) 100 mg and 200 mg, tablet
XELJANZ (tofacitinib) 5 mg and 10 mg, tablet
RINVOQ (upadacitinib) 15mg, 30mg and 45 mg, tablet

Reassessment at Transparency Committee's request

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

- Seriousness of the condition: UC is a chronic inflammatory bowel disease (CIBD) manifested as severe chronic bloody diarrhoea, progressing in flare-ups. It significantly impairs quality of life and exposes patients to severe complications: acute colitis, dysplasia and cancer of the colon.
- This is a symptomatic medicinal product for UC.
- In view of the lack of new efficacy data available and the excess risk in terms of safety (major cardiovascular events, cancer, venous thromboembolism, severe infections and death) in relation to TNF inhibitors, identified during the PRAC reassessment of JAK inhibitors, the efficacy/adverse effects ratio remains high for upadacitinib (RINVOQ) and tofacitinib (XELJANZ) and remains moderate for filgotinib (JYSELECA) in adult patients who have had an inadequate response, loss or response or intolerance, to conventional treatments, with at least one TNFα inhibitor and vedolizumab, and where the alternatives are less suitable. In the other contexts covered by the MA, the efficacy/adverse effects ratio is not defined.
- The role of janus kinase inhibitors (JAK inhibitors) is changing: they consist of third-line treatment in view of the therapies available i.e. after failure to respond to a conventional treatment, at least one TNF inhibitor and vedolizumab (ENTYVIO), and where ustekinumab (STELARA) is less suitable

➔ Public health benefit

In view of:

- the seriousness and prevalence of UC, an incapacitating chronic disease of high morbidity on account of the frequency of flare-ups, its complications and referral for surgery. UC also significantly impairs quality of life;
- the partially met medical need including as a third line of UC treatment;
- a lack of evidence of an additional impact on morbidity on account of:
  - a clinically relevant effect size versus placebo in induction and maintenance and findings showing a benefit of upadacitinib (RINVOQ) on quality of life up to 52 weeks only versus placebo;
  - 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 these orally administered medicinal products, 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;

XELJANZ (tofacitinib), JYSELECA (filgotinib) and RINVOQ (upadacitinib) are unlikely to have an additional impact on public health in treatment of UC in adults.

Considering all of these elements, the Committee deems that the clinical benefit is:

- **substantial for RINVOQ (upadacitinib) and XELJANZ (tofacitinib) in the treatment of moderate to severe active ulcerative colitis for adult patients who have had an inadequate response, loss of response or intolerance to conventional treatments, at least one TNFα inhibitor and vedolizumab, and where the alternatives are less suitable,**
- **moderate for JYSELECA (filgotinib) in the treatment of moderate to severe active ulcerative colitis for adult patients who have had an inadequate response, loss of response or intolerance to conventional treatments, at least one TNFα inhibitor and vedolizumab, 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 continued inclusion of these three medicinal products in the list of covered drugs for outpatients and in the list of covered drugs for inpatients only in the treatment of moderate to severe active ulcerative colitis for adult patients who have had an inadequate response, loss of response or intolerance to conventional treatments, at least one TNFα inhibitor and vedolizumab, and where the alternatives are less suitable.

The Committee disapproves inclusion in the list of covered drugs for outpatients and in the list of covered drugs for inpatients for adult patients in the other MA contexts.

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

Clinical Added Value

In view of:

- the latest clinical efficacy data not affecting the assessment of efficacy versus placebo;
- the lack of sound efficacy data comparing JAK inhibitors with each other or with medicinal alternatives (TNF inhibitor and vedolizumab as second-line treatment and ustekinumab as third-line treatment);
- the lack of established effects on long-term quality of life (apart from upadacitinib up to 52 weeks versus placebo), on complications and referral for colectomy;
- and the updated safety profile of the JAK inhibitor class, with in particular an increased risk of tumours, venous or arterial thromboembolic events and severe infections, or death, compared to TNF inhibitors, and the lack of clinical data making it possible to rule out these risks compared to medicinal alternatives;

the Committee deems that XELJANZ (tofacitinib), JYSELECA (filgotinib) and RINVOQ (upadacitinib) provide no clinical added value (CAV V) in the current therapeutic strategy of UC in adults.