

# INPLASY

## Safety Analysis of Upadacitinib in the Management of Inflammatory Bowel Diseases: A Meta-Analysis of Randomized Clinical Trial

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### ADMINISTRATIVE INFORMATION

**Support** - None.

**Review Stage at time of this submission** - Data extraction.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202450040

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 May 2024 and was last updated on 09 May 2024.

### INTRODUCTION

**Review question / Objective** To assess the safety profile and the incidence of adverse events associated with the use of upadacitinib compared to placebo in adult patients with inflammatory bowel diseases (IBD), specifically Crohn's disease (CD) and ulcerative colitis (UC).

**Rationale** This review is in accordance to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

**Condition being studied** Inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis, causes chronic inflammation of the digestive tract and significantly impacts patient's quality of life. Current treatments aim to alleviate symptoms by inducing and maintaining

remission. However, many patients fail to respond to available treatments or lose response over time. Upadacitinib, a selective Janus kinase-1 (JAK-1) inhibitor has shown promising results regarding its efficacy. However, its use has raised concerns about the associated adverse events. Given that IBD requires long-term management, understanding these risks is crucial for clinical application.

### METHODS

**Search strategy** PubMed, Embase, and Cochrane Library were searched for relevant articles. The search was restricted to studies published in English. Key search terms for the intervention included "rinvoq" and "upadacitinib," which were used interchangeably with the Boolean operator "OR" to capture all relevant literature pertaining to the drug. For the condition of interest, terms

related to inflammatory bowel disease were extensively used, including "inflammatory bowel disease" OR "IBD" OR "Crohn's disease" OR "Crohn" OR "CD" OR "Ulcerative colitis" OR "UC". These terms were combined using the Boolean operator "AND" to ensure that the retrieved studies specifically focus on the application of upadacitinib in the treatment of IBD.

**Participant or population** Adult patients aged  $\geq$  18 years with inflammatory bowel disease (Crohn's disease or ulcerative colitis).

**Intervention** Upadacitinib.

**Comparator** Placebo.

**Study designs to be included** Randomized controlled trials.

**Eligibility criteria** Studies meeting the following inclusion criteria: (1) randomized controlled trials (RCTs); (2) published in English; (3) comparing upadacitinib with placebo; (4) for induction therapy; (5) in adult patients diagnosed with inflammatory bowel disease; (6) reporting at least one of the safety outcomes of interest; (7) without overlapping patient populations.

**Information sources** Electronic databases: PubMed, EMBASE, Cochrane. Trial registers: ClinicalTrials.gov. and European Union Clinical Trials Register (EudraCT). References of included studies and abstracts from conferences.

**Main outcome(s)** Incidence of any adverse events and serious adverse events in patients with inflammatory bowel disease receiving upadacitinib compared to placebo.

**Additional outcome(s)** Serious infections; herpes zoster; nasopharyngitis; upper respiratory tract infections; anemia; neutropenia; creatine kinase elevation; hepatic disorders; arthralgia; venous thromboembolic events; major cardiovascular events; malignancies of any kind.

**Quality assessment / Risk of bias analysis** Assessment using the Cochrane Collaboration's tool for the risk of bias in randomized trials. Categories include selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases.

**Strategy of data synthesis** Data analysis will be performed using Review Manager 5.4.1 software. Risk ratios (RRs) will be used to assess the

incidence of adverse events. Pooled estimates with 95% confidence intervals (CIs) will be calculated using the weighted variance technique. Heterogeneity among studies will be assessed using the  $I^2$  statistic. Depending on the level of heterogeneity, either random-effects or fixed-effects models will be employed.

**Subgroup analysis** Subgroup analyses will be performed to explore potential differences in the effects of upadacitinib on patients with ulcerative colitis (UC) and Crohn's disease (CD).

**Sensitivity analysis** Sensitivity analyses will be conducted by systematically removing each study one at a time, particularly when moderate or high heterogeneity is detected. This method will help determine whether any specific study disproportionately influences the overall results, ensuring the reliability of the findings.

**Language restriction** Studies published in English.

**Country(ies) involved** Brazil; Canada; United States.

**Keywords** Upadacitinib, inflammatory bowel diseases, ulcerative colitis, Crohn's disease, safety, adverse events, Janus kinase inhibitors.

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