Report RINVOQ® - Upadacitinib

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: upadacitinib **Brand Name:** Rinvoq **Originator/licensee:** AbbVie Deutschland GmbH & Co. KG **Classification:** NI **ATC code:** L04AA44 **Orphan Status:** **Eu:** No **Us:** - **Mechanism of action:** UPA is a selective and reversible JAK inhibitor. It preferentially inhibits signaling by JAK1 or JAK1/3 with functional selectivity over cytokine receptors that signal via pairs of JAK2. JAK1 is important in inflammatory cytokine signals while JAK2 is important for red blood cell maturation and JAK3 signals play a role in immune surveillance and lymphocyte function [1].	**Authorized Indication:** **EMA:** Upadacitinib is indicated for the treatment of active nr-axSpA in adult pts with objective signs of inflammation as indicated by elevated CRP and/or MRI, who have responded inadequately to NSAIDs [1]. **Route of administration:** OS **Licensing status** **EU CHMP P.O. date:** 23/06/2022 **FDA M.A. date:** / **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** / **ABBREVIATIONS:** **AE:** adverse event **AS:** Ankylosing spondylitis **CRP:** C-reactive protein **DMARD:** disease-modifying antirheumatic drug **IL-17i**: interleukin-17 inhibitor **JAK:** Janus Kinases **JAKi:** Janus Kinases inhibitors **M.A.:** Marketing Authorization **MRI:** Magnetic Resonance Imaging **nr-axSpA:** Non-radiographic axial spondyloarthritis **NSAID**: non-steroidal anti-inflammatory drug **OS:** oral administration **PTS:** patients **TEAE:** Treatment-Emergent Adverse Event **TNFi:** Tumor Necrosis Factor alpha inhibitor **UPA:** upadacitinib **VS.:** versus	**Summary of clinical EFFICACY:** **SELECT-AXIS 2 (NCT04169373)** is a double-blind, randomized, placebo-controlled, phase 3 trial conducted under a master protocol comprising two independent studies, one in an AS population with an inadequate response to biologic DMARDs and one in an nr-axSpA population. The nr-axSpA study enrolled adults pts with a clinical diagnosis of nr-axSpA, who had objective signs of active inflammation on MRI or based on high sensitivity CRP. Pts were randomized 1:1 to receive oral UPA 15 mg once daily (n=156) or placebo (n=157) during a 52-week double-blind treatment period. The primary endpoint was ASAS40* response at week 14. A significantly higher ASAS40 response rate at week 14 was achieved with UPA vs. placebo (45% vs 23%; P<0,0001) [2]. **Summary of clinical SAFETY:** The proportion of pts who experienced a TEAE was similar between treatment groups (UPA, 48%; placebo, 46%). Serious TEAEs were reported in 4 (2,6%) pts in the UPA group vs. 2 (1,3%) in the placebo group. TEAEs leading to discontinuation were reported in 4 (2,6%) pts treated with UPA and 2 (1,3%) pts treated with placebo. No deaths were reported in the study [2]. **Ongoing studies:** ● ***For the same indication:*** No ● ***For other indications:*** Yes **Discontinued studies (for the same indication):** No --- **References:** 1.https://www.ema.europa.eu/en/documents/product-information/rinvoq-epar-product-information_en.pdf 2. https://congress.eular.org/myUploadData/files/euroab_2022_book_final.pdf 3. https://gallery.farmadati.it/ 4. https://www.ema.europa.eu/en/documents/variation-report/rinvoq-h-c-004760-ii-0005-epar-assessment-report-variation_en.pdf 5. https://onlinelibrary.wiley.com/doi/epdf/10.1002/art.41042 6. https://adisinsight.springer.com/drugs/800037410 7. https://www.clinicaltrials.gov/ct2/results?cond=Non-radiographic+axial+spondyloarthritis&recrs=b&recrs=a&recrs=f&recrs=d&age_v=&gndr=&type=&rslt=&phase=2&Search=Apply	**Cost of therapy:** 28 sustained release tablets of UPA 15 mg cost € 722 (ex-factory price) [3]. **Epidemiology:** The prevalence of AS differs between regions and has been estimated to be up to 0,5% with similar estimated prevalence rates for nr-axSpA, resulting in an overall prevalence for axial SpA in the United States of approximately up to 1% or even higher in the overall population [4]. --- **POSSIBLE PLACE IN THERAPY** NSAIDs are recommended as first-line treatment of adults with active nr-axSpA. In patients with persistently high disease activity despite treatment with NSAIDs, treatment with TNFi is strongly recommended. Other treatment options include JAKi and IL-17i [5]. **OTHER INDICATIONS IN DEVELOPMENT** Crohn's disease, Giant cell arteritis, vasculitis [6]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** No **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Secukinumab, bimekizumab [7]. *Service reorganization: No *Possible off label use: Yes

*ASAS40 response (Assessment of Spondyloarthritis international Society 40 response): at least 40% improvement and an absolute improvement of at least 2 units on a numerical rating scale of 0– 10 from baseline in at least three of the following four domains, with no worsening in the remaining domain: Patient's Global Assessment of Disease Activity, Patient's Assessment of Total Back Pain, Bath Ankylosing Spondylitis Functional Index (BASFI), and inflammation defined as the mean of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions on severity and duration of morning stiffness.

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