Report Xeljanz® tofacitinib

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: tofacitinib **Brand Name:** Xeljanz® **Originator/licensee:** Pfizer Europe MA EEIG **Classification:** NI **ATC code:** L04AA29 **Orphan Status:** **Eu:** No (1) **Us:** No (2) **Mechanism of action:** tofacitinib preferentially inhibits signalling by heterodimeric cytokine receptors that associate with JAK3 and/or JAK1 with functional selectivity over cytokine receptors that signal via pairs of JAK2. Inhibition of JAK1 and JAK3 by tofacitinib attenuates signalling of IL-2, -4, -6, -7, -9, -15, -21 and type I and type II interferons, which will result in modulation of the immune and inflammatory response (1).	**Authorized Indication:** **EMA:** tofacitinib is indicated for the treatment of adult pts with active ankylosing spondylitis who have responded inadequately to conventional therapy (3). **Route of administration:** OS (1) **Licensing status** **EU CHMP P.O. date:** 19/05/2022(3) **EU M.A. date:** - **FDA M.A. date:** 14/12/2021 (2) **EU Speed Approval Pathway:** No (1) **FDA Speed Approval Pathway:** No (2) **-----** **ABBREVIATIONS:** **AE:** adverse event **AS:** ankylosing spondylitis **ASAS:** Assessment of SpondyloArthritis international Society **bDMARDs:** biologic disease-modifying antirheumatic drugs **EULAR:** European Alliance of Associations for Rheumatology **NSAIDs:** non-steroidal anti-inflammatory drugs **OS:** oral administration **pts:** patients	**Summary of clinical EFFICACY: Study NCT03502616:** a phase 3, randomized, double-blind, placebo-controlled, study of the efficacy and safety of tofacitinib in pts with active AS. Adults with AS and with inadequate response/ intolerance to ≥2 non-steroidal anti-inflammatory drugs received tofacitinib 5mg twice daily or placebo for 16 weeks. The primary endpoint was the Assessment of SpondyloArthritis international Society ≥20% improvement (called ASAS20) at week 16. 269 pts were randomised and treated: tofacitinib, n=133; placebo, n=136. At week 16, the ASAS20 response rate was 56.4% (75 of 133) for tofacitinib versus placebo which was 29.4% (40 of 136) (p<0.0001)(4). **Summary of clinical SAFETY:** Up to week 16, with tofacitinib and placebo, respectively, 73 of 133 (54.9%) and 70 of 136 (51.5%) pts had AEs; 2 of 133 (1.5%) and 1 of 136 (0.7%) had serious AEs; 2 of 133 (1.5%) and 0 of 136 (0.0%) had severe AEs. There were no deaths, malignancies, major adverse cardiovascular events, thromboembolic events or opportunistic infections. The most common AEs in the tofacitinib arm were: upper respiratory tract infection [14 cases (10.5%)], nasopharyngitis [9 cases (6.8%)], diarrhoea [6 cases (4.5%)], protein urine present [5 cases (3,8%)], ALT increased [4 cases (3.0%)(4)]. **Ongoing studies:** ● ***For the same indication:*** No (5) ● ***For other indications:*** Yes (6) **Discontinued studies (for the same indication):** No (5)	**Cost of therapy:** the XELJANZ 112 tablets 5 mg cost ex-factory of is € 1441,83 which correspond to € 772,41 for one month treatment (7). **Epidemiology:** the incidence of AS is 0.4–15.0 per 100.000 pt-years, varying by region (8). ----- **POSSIBLE PLACE IN THERAPY** The ASAS-EULAR management recommendations for axial AS reported that: NSAIDs are recommended as first-line treatment, followed by bDMARDs, such as TNFi. Given that bDMARDs are administered parenterally, there is an unmet need for oral therapies with alternative mechanisms of action to treat AS (9). ● **OTHER INDICATIONS IN DEVELOPMENT** Yes (i.e. primary Sjögren's syndrome, interstitial lung disease, glioblastoma, uveitis, scleritis) **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** No (5) **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION Yes** (i.e. secukinumab, thalidomide, bimekizumab, adalimumab) [if it is..] *Service reorganization Y/N No *Possible off label use Y/N No (6) ----- **References:** 1. https://www.ema.europa.eu/en/medicines/human/EPAR/xeljanz#authorisation-details-section 2. https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm?event=overview.process&ApplNo=203214 3. https://www.ema.europa.eu/en/documents/smop/chmp-post-authorisation-summary-opinion-xeljanz_en.pdf 4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8292568/pdf/annrheumdis-2020-219601.pdf 5. https://clinicaltrials.gov/ct2/results?term=tofacitinib&cond=Ankylosing+Spondylitis&age_v=&gndr=&type=&rslt=&phase=1&phase=2&Search=Apply 6. https://clinicaltrials.gov/ct2/results?cond=&term=tofacitinib&cntry=&state=&city=&dist=&Search=Search&phase=1&phase=2 7. https://gallery.farmadati.it/Home.aspx 8. https://pubmed.ncbi.nlm.nih.gov/29148402/

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	TNFi: tumour necrosis factor inhibitors		