Report JYSELECA® filgotinib

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: filgotinib **Brand Name:** Jyseleca **Originator/licensee:** Gilead Sciences Ireland UC **Classification:** NI **ATC code:**L04AA45 **Orphan Status:** **Eu:** No **Us:** - **Mechanism of action:** Filgotinib is an ATP-competitive and reversible inhibitor of the JAK family, which plays an important role in the inflammatory process [1].	**Authorized Indication:** **EMA:** filgotinibis indicated for the treatment of adult pts with moderately to severely active ulcerative colitis who have had an inadequate response with, lost response to, or were intolerant to either conventional therapy or a biologic agent [2]. **Route of administration:**OS **Licensing status** **EU CHMP P.O. date:** 16/09/2021 **FDA M.A. date:** - **EU Speed Approval Pathway:**No **FDA Speed Approval Pathway: -** ----- **ABBREVIATIONS:** **AEs**: Adverse Events **CHMP:** Committee for Medicinal Products for Human Use **IBDs:** Inflammatory Bowel Diseases **JAKs:** Janus kinases **M.A.:** Marketing Authorization **MCS**: Mayo Clinic Score **P.O.:** Positive Opinion **Pts:** patients **QD:** Every Day **SAEs**: Serious Adverse Events **TEAEs**: Treatment-Emergent Adverse Events **TNF:** Tumor Necrosis Factor **vs.**: versus	**Summary of clinical EFFICACY:** **SELECTION study (NCT02914522)** was a phase IIb/III, double blind, multicenter, randomized, placebo-controlled trial including two induction studies and one maintenance study in adults (≥ 18 and ≤ 75 years) with moderately to severely active ulcerative colitis. Eligible pts (*n*=2,040) were enrolled into one of the two induction studies (A and B), based on their experience with TNF antagonists or vedolizumab: ● **Induction study A**(*n*=659): pts with loss of response to or intolerance to corticosteroids or immunosuppressants, naïve to TNF antagonists and vedolizumab (biologic-naïve); ● **Induction study B**(*n*=689): pts with an inadequate clinical response, loss of response to or intolerance to any TNF antagonist or vedolizumab, and had not used any TNF antagonist or vedolizumab within eight weeks before screening (biologic-experienced). Pts in induction studies A/B were randomly assigned (2:2:1) to receive oral filgotinib 200 mg (*n*=245 study A vs. *n*=262 study B), 100 mg (*n*=277 study A vs. *n*=285 study B) or matched placebo (*n*=137 study A vs. *n*=142 study B) QD for 11 weeks. Efficacy was assessed at week 10, and pts who had either clinical remission or MCS-defined* response were re-randomized 2:1 at week 11 to continue their induction filgotinib regimen or to receive placebo to week 58 (**maintenance study**; *n*=664). Placebo responders (*n*=93) continued to receive placebo in the maintenance study. The primary endpoint was the proportion of pts achieving clinical remission based on components of MCS* at weeks 10 and 58. At week 10, a greater proportion of pts given filgotinib 200 mg had clinical remission than those given placebo (**induction study A** 26.1% vs. 15.3%, difference 10.8%; 95% CI 2.1-19.5, *p*= 0.0157; **induction study B** 11.5% vs. 4.2%, 7.2%; 1.6-12.8, *p*=0.0103). Clinical remission was not significantly different between filgotinib 100 mg and placebo in either induction study. At week 58, 37.2% of pts given filgotinib 200 mg had clinical remission vs. 11.2% in the respective placebo group (difference 26.0%, 95% CI 16.0 – 35.9; *p*<0.0001).23.8% of pts given filgotinib 100 mg had clinical remission vs. 13.5% of pts in placebo arm (difference 10.4%; 0.0-20.7, *p*=0.0420) [3]. **MCS assesses the stage of ulcerative colitis on the basis of four components: frequency of defecation, rectal bleeding, endoscopic assessment and overall judgment. For each component, the score ranges from zero (normal or inactive disease) to three (severe disease).* **Summary of clinical SAFETY:** ● **Induction studies:** the proportion of pts who had TEAEs was similar in the placebo (157/279 [56%]), filgotinib 100 mg (283/562 [50%]), and filgotinib 200 mg (272/507 [54%]) groups. SAEs occurred in 28 (5%) pts given filgotinib 100 mg, 22 (4%) pts given filgotinib 200 mg, and 13 (5%) pts given placebo. AEs of interest were infections (filgotinib 200 mg arm=18%; filgotinib 100 mg arm=15%;placebo arm=14%) and serious infections (1% of pts in all study arms). No deaths were reported. ● **Maintenance study:** TEAEs occurred in 135/202 (67%) pts in the filgotinib 200 mg arm vs. 59/99 (60%) in the placebo arm; 108/179 (60.3%) pts in the filgotinib 100 mg arm vs. 60/91 (66%) in the placebo arm; 57/93 (61%) in the placebo maintenance group. SAEs occurred in nine (4%) pts in the filgotinib 200 mg arm vs. none in the placebo arm; eight (4%) pts in the filgotinib 100 mg arm vs. seven (8%) in the placebo arm; four (4%) pts in the placebo maintenance group. Two pts died (one left ventricular failure, one asthma), neither death was deemed related to the study treatment [3]. **Ongoing studies:** ● ***For the same indication:***Yes. ● ***For other indications:***Yes. **Discontinued studies (for the same indication):**No. **References:** 1.https://www.ema.europa.eu/en/medicines/human/EPAR/jyseleca 2.https://www.ema.europa.eu/en/medicines/human/summaries-opinion/jyseleca-0 3. https://pubmed.ncbi.nlm.nih.gov/34090625/ 4. https://www.gazzettaufficiale.it/ 5. https://pubmed.ncbi.nlm.nih.gov/33784448/ 6. https://www.io.nihr.ac.uk/wp-content/uploads/2019/12/12986-TSID_10169-Filgotinib-for-Ulcerative-Colitis-V1.0-NOV2019-NON-CONF.pdf 7. https://clinicaltrials.gov/ct2/home	**Cost of therapy:** The price forone-month treatment with30 tablets of filgotinib200 mg is 1,179.40 €* [4]. **Retail price including VAT.* **Epidemiology:** In Italy, the available incidence estimates are generallybased on relatively small populations. A review based on 16 studies reported for the early 2010s incidence rates ofulcerative colitis as 10-15 cases per 100,000 inhabitants per year [5]. ----- **POSSIBLE PLACE IN THERAPY** According to NICE, specialist drug treatment for ulcerative colitis is generally given for induction and maintenance of remission. The main classes of drugs used include: •Aminosalicylates (melsalazine, balsalazide, olsalazine, sulfasalazine); •Corticosteroids (hydrocortisone, methylprednisolone, prednisolone, beclometasonedipropionate) •Calcineurininhibitors (ciclosporin, tacrolimus) •Immunosuppressive therapy (azathioprine, ciclosporin, mercaptopurine, tacrolimus) •Biologic therapy (adalimumab, golimumab, infliximab, vedolizumab, tofacitinib) [6]. **OTHER INDICATIONS IN DEVELOPMENT:** Yes (Perianal Fistulizing Crohn's Disease) [7]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: -** **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** Yes (PRV-300, ABX464, Ontamalimab). *Service reorganization: No *Possible off label use: No

Issued on: October 2021