Report ENTYVIO® vedolizumab

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: vedolizumab **Brand Name:** Entyvio® **Originator/licensee:** Takeda Pharma A/S **Classification:** NI **ATC code:** L04AA **Orphan Status:** **Eu:** No **Us:** - **Mechanism of action:** vedolizumab is a humanized IgG1 monoclonal antibody directed against the human integrin α4β7 which is preferentially expressed on T helper lymphocytes. Vedolizumab selectively inhibits the binding of α4β7 integrin with the adhesion molecule cellular (MAdCAM-1) overexpressed in blood vessels and lymph nodes of the GI tract inflamed. By inhibiting this bond, vedolizumab prevents the passage of lymphocytes from the blood circulation to the gut lamina propria and GALT [1].	**Authorized Indication:** **EMA:** vedolizumab is indicated for the treatment of adults with moderately to severely active CP, who have undergone proctocolectomy and IPAA for UC and have had an inadequate response with or lost response to antibiotic therapy. [2] **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:** 16/12/2021 **FDA M.A. date:** - **EU Speed Approval Pathway:** - **-----** **ABBREVIATIONS:** **AEs**: Adverse Events **CDP:** Crohn's disease of the pouch **CHMP:** Committee for Medicinal Products for Human Use **CP:** chronic pouchitis **GI:** gastrointestinal **GALT:** gut associated lymphoid tissue **IgG1**: Immunoglobulin G1 **IPAA:** ileal pouch anal anastomosis **M.A.:** Marketing Authorization **mPDAI:** modified Pouchitis Disease Activity Index **P.O.:** Positive Opinion **Pts:** patients **SAEs:** Serious Adverse Events **UC:** ulcerative colitis	**Summary of clinical EFFICACY** **EARNEST (NCT02790138):** multicentric**,** randomized, double-blind, placebo-controlled, phase IV study. Eligible pts (n=102) were adults with UC who had undergone a proctocolectomy and IPAA, and had developed active chronic pouchitis, defined as pts who had inadequate response or lost response to antibiotics therapy. Pts were randomly assigned (1:1) to receive vedolizumab IV 300 mg (n=51) or placebo IV (n=51) once at day 1, weeks 2, 6, 14, 22, and 30 along with ciprofloxacin 500 mg, tablet, orally twice daily up to week 4. The primary endpoint was the percentage of pts with chronic or recurrent pouchitis achieving clinically relevant remission after 14 weeks of treatment. Measured using the mPDAI, clinical remission rates were 31.4% (95% CI: 19.1% – 45.9%) in pts in the vedolizumab IV arm, compared with 9.8% (95% CI: 3.3% – 21.4%) in the placebo arm [3,4]. **Summary of clinical SAFETY:** no new safety signals were identified in the trial. AEs were reported in 92.2% and 86.3% of pts treated with vedolizumab and placebo, respectively. Treatment-related AEs were reported in 23.5% and 21.6% of pts treated with vedolizumab and placebo, respectively. SAEs were reported in three (5.9%) and four (7.8%) pts treated with vedolizumab and placebo, respectively [3,4]. **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/assessment-report/entyvio-epar-public-assessment-report_en.pdf 2. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/entyvio-0 3. https://adisinsight.springer.com/trials/700272522 4. https://www.takeda.com/newsroom/newsreleases/2021/takeda-receives-positive-chmp-opinion-for-vedolizumab-iv-for-the-treatment-of-active-chronic-pouchitis/ 5. https://gallery.farmadati.it/Home.aspx 6. https://pubmed.ncbi.nlm.nih.gov/33784448/ 7. https://intestino.iannetti.it/MALATTIA-INTESTINO/MALATTIE_CRONICHE_INTESTINALI/ 8. https://www.dldjournalonline.com/article/S1590-8658(21)00143-2/fulltext#seccesectitle0016 9. https://www.msdmanuals.com/it-it/professionale/disturbi-gastrointestinali/malattia-infiammatoria-cronica-intestinale/colite-ulcerosa	**Cost of therapy:** the cost of one administration (300mg, IV) is € 2.036,04*; the cost of therapy cycle is 12.216,04 [5]. *ex-factory price. **Epidemiology:** In Italy, the available incidence estimates are generally based on relatively small populations. A review based on 16 studies reported for the early 2010s incidence rates of UC as 10-15 cases per 100,000 inhabitants per year [6]. 15% of pts with UC undergo surgery. After surgery, some pts develop CP or CDP but the proportion is highly variable; about 15-20% of pts with pouchitis can have a chronic, continuous or intermittent course [7]. A study conducted in France, in the Paris area, found that two and five years after surgery, 7.6% (95% CI: 3.8–11.3) and 19.5% (95%CI: 12.2–26.2) of patients had a CP, respectively [8]. ----- **POSSIBLE PLACE IN THERAPY** In pts with moderately to severely active CP, the use of antibiotics (es: quinolones) is recommended. The use of probiotics can prevent the appearance of CP. 5-10% of pts are refractory to all medical therapies and require conversion to a conventional ileostomy according to Brooke [9]. **OTHER INDICATIONS IN DEVELOPMENT:** HIV-infection (phase II, NCT03147859), Hematopoietic Stem Cells (phase III, NCT03657160). **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT: -** **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** tofacitinib, fecal microbiota transplantation, ustekinumab, AMT-101. *Service reorganization: Yes *Possible off label use: Yes

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