Report BENLYSTA®Belimumab

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Substance: belimumab **Brand Name:** Benlysta® **Originator/licensee:** GlaxoSmithKline (Ireland) Limited **Classification:** NI **ATC code:** L04AA26 **Orphan Status:** **Eu:** No **Us:** No **Mechanism of action:** belimumab is a human monoclonal antibody that binds to soluble BLyS and inhibits the survival of B cells, reducing the differentiation of B cells into immunoglobulin-producing plasma cells [1].	**Authorized Indication:** **EMA:** belimumab is indicated in combination with background immunosuppressive therapies for the treatment of adult pts with ALN [2] **FDA:** belimumab is a BLyS-specific inhibitor indicated for the treatment of adult pts with ALN who are receiving ST [3]. **Route of administration:** IV **Licensing status** **EU CHMP P.O. date:** 25/03/2021 **FDA M.A. date:** 16/12/2020 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** No --- **ABBREVIATIONS:** **AE:** adverse events **ALN:** active lupus nephritis **BLys:** B lymphocyte stimulator **CHMP:** Committee for Medicinal Products for Human Use **CI:** confidence interval **eGFR:** estimated glomerular filtration rate **IV:** intravenous **M.A.:** Marketing Authorization **P.O.:** Positive Opinion **pts:** patients **PERR:** primary efficacy renal response **SLE:** systemic lupus erythematosus **ST:** standard therapy (mycophenolate mofetil for induction and maintenance or cyclophosphamide for induction and azathioprine for maintenance, plus steroids) **vs**: versus	**Summary of clinical EFFICACY:** **Study BEL114054 (NCT01639339):** is a Phase 3, randomized, double-blind, placebo-controlled, 104-week study. Pts (N=448) with biopsy-proven ALN were randomized (1:1) to monthly belimumab 10mg/kg IV or placebo, plus ST. Primary endpoint was PERR (defined as urinary protein: creatinine ratio≤0.7; eGFR within 20% of the pre-flare value or ≥60ml/min/1.73m2). 43% of the pts in the belimumab group vs 32.3% of the pts in the placebo arm achieved PERR at week 104 (Odd Ratio 1.6, 95% CI 1.0 to 2.3; p=0.03) [4]. **Summary of clinical SAFETY:** Overall, 214 (96 %) belimumab and 211 (94 %) placebo pts had ≥1 AE. Upper respiratory tract infection (12 % vs 11%), urinary tract infection (7% vs 6%), herpes zoster (6% vs 4%), bronchitis (5% vs 4%) were the most frequent AE detected. 58 (26%) belimumab and 67 (30%) placebo pts had ≥1 serious AE. Infections and infestations (7% vs 8%), respiratory, thoracic, and mediastinal disorders (2% vs <1%), blood and lymphatic system disorders (1% vs 1%), nervous system disorders (0% vs 1%) were the most frequent serious AE detected. 29 (13%) pts in each group had ≥1 AE resulting in study treatment discontinuation. Four (2%) belimumab and three (1%) placebo pts manifested on-treatment fatal AEs. Three (1%) belimumab and zero (0%) placebo pts developed cancer. [4] **Ongoing studies:** • ***For the same indication:*** No [6] • ***For other indications:*** Yes [7] **Discontinued studies (for the same indication):** No [8] --- **References:** 1. https://www.ema.europa.eu/en/documents/overview/benlysta-epar-medicine-overview_en.pdf 2. https://www.ema.europa.eu/en/medicines/human/summaries-opinion/benlysta-0 3. https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125370s073,761043s013lbl.pdf 4. https://www.nejm.org/doi/pdf/10.1056/NEJMoa2001180?articleTools=true 5. https://adisinsight.springer.com/trials/700220412 6. https://clinicaltrials.gov/ct2/results?type=Intr&cond=Lupus+Nephritis&intr=Belimumab&phase=2 7. https://clinicaltrials.gov/ct2/results?cond=&term=&intr=Belimumab&cntry=&state=&city=&dist=&Search=Search&recrs=a&recrs=b&recrs=d&recrs=f&type=Intr&phase=2 8. https://clinicaltrials.gov/ct2/results?cond=Lupus+Nephritis&term=&type=Intr&rslt=&recrs=b&recrs=a&recrs=f&recrs=d&recrs=g&recrs=h&recrs=e&recrs=i&recrs=m&age_v=&gndr=&intr=Belimumab&titles=&outc=&spons=&lead=&id=&cntry=&state=&city=&dist=&locn=&phase=2&rsub=&strd_s=&strd_e=&prcd_s=&prcd_e=&sfpd_s=&sfpd_e=&rfpd_s=&rfpd_e=&lupd_s=&lupd_e=&sort= 9. https://gallery.farmadati.it/Home.aspx 10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7751166/pdf/keaa381.pdf 11. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6026543/ 12. https://ard.bmj.com/content/annrheumdis/79/6/713.full.pdf 13. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2394708/pdf/bmj-336-7654-cr-01185.pdf 14.https://clinicaltrials.gov/ct2/results?intr=Belimumab&Search=Apply&recrs=b&recrs=a&recrs=f&recrs=d&recrs=e&age_v=&gndr=&type=Intr&rslt=&phase=2. 15.https://clinicaltrials.gov/ct2/results?cond=Lupus+Nephritis&term=&intr=&cntry=&state=&city=&dist=&Search=Search&recrs=a&recrs=b&recrs=d&recrs=e&recrs=f&type=Intr&phase=2	**Economic impact:** The recommended dose in the study is 10 mg/kg on day 0, 14 and 28, and then at 4-week intervals. The Italian *ex-factory* price for belimumab (120 mg, single dose) is € 138.91. A single cycle treatment for adult pts (BW = 70 kg) costs € 2500 [9]. **Epidemiology:** ALN occurs in about 40% of SLE pts, mostly within five years from the diagnosis. The incidence of ALN varies with ethnicity. SLE incidence range from 0.3 to 23.7 per 100,000 people per year [10-11]. --- **POSSIBLE PLACE IN THERAPY** *(Guidelines, recommendations…)* In ALN the initial treatment is mycophenolate mofetil or mycophenolic acid or cyclophosphamide, combined with glucocorticoids (methylprednisolone, prednisone). Mycophenolate and calcineurin inhibitors (tacrolimus) combination and cyclophosphamide are alternatives for pts with nephrotic-range proteinuria (creatinine ratio of >300-350 mg/mmol) and adverse prognostic factors. Subsequent long-term maintenance treatment with mycophenolate mofetil or azathioprine should follow, with or without glucocorticoids [12-13]. **OTHER INDICATIONS IN DEVELOPMENT:** myositis, vasculitis. [14] **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:** No **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION:** No [15] [if it is..] *Service reorganization Y/N: No *Possible off label use Y/N: No