Report Dupixent®- dupilumab

Product & Mechanism of action	Authorized indications Licensing status	Essential therapeutic features	NHS impact
Active principle:dupilumab **Brand Name:** Dupixent® **Originator/ licensee:** Sanofi-Aventis Groupe **Classification:** NI **ATC code:** D11AH05 **Orphan Status:** **Eu:** No **Us:** No **Mechanism of action:** Dupilumab is a mAB that inhibits IL-4 and IL-13 signaling. IL-4 and IL-13 are major drivers of human type 2 inflammatory disease, and blocking the IL-4/IL-13 pathway in pts decreases many of the mediators of type 2 inflammation [1].	**Authorized Indication:** **EMA:** Dupixent is indicated for the treatment of adults with moderate-to-severe PrurigoNodularis who are candidates for systemic therapy. [2] **FDA**: Dupixent is indicated for the treatment of adult patients with PrurigoNodularis. [3] **Route of administration:** SC **Licensing status:** **EU CHMP P.O. date**: 10/11/2022 **FDA M.A. date:** 28/09/2022 **EU Speed Approval Pathway:** No **FDA Speed Approval Pathway:** No --- **ABBREVIATIONS**: **AE**: adverse event **CHMP**: Committee for Medicinal Products for Human Use **IL**: interleukin **M.A.**: marketing authorization **mAB**: monoclonal antibody **PN**: PrurigoNodularis **P.O.**: positive opinion **pts**: patients **sc**: subcutaneous **WI-NRS**: Worst Itch Numeric Rating Scale	**Summary of clinical EFFICACY:** The approval of dupilumab for PN was based on PRIME (NCT04183335) and PRIME 2 (NCT04202679) trials, two 24-week randomized, double-blind, placebo-controlled, multicenter, parallel-group trials in 311 pts aged ≥18 years with pruritus (WI-NRS ≥7) and ≥20 nodular lesions. The WI-NRS measures pruritus on a scale from 0 (no itch) to 10 (worst imaginable itch). In these two trials, pts received either scdubilumab 600 mg (two 300 mg injections) on day 1, followed by 300 mg once every 2 weeks for 24 weeks, or matching placebo. At baseline, the mean WI-NRS was 8.5, 66% had 20 to 100 nodules (moderate), and 34% had greater than 100 nodules (severe) [3]. The primary outcome for the efficacy assessment in PRIME trial was the % of pts with ≥4 points reduction in WI-NRS (i.e. improvement) from baseline to week 24 [4], while the primary outcome in PRIME2 trial was the % of pts with ≥4 points reduction in WI-NRS by from baseline to week 12 [5]. Pts who received rescue treatment earlier or had missing data were considered as non-responders. In PRIME trial, the % of pts with ≥4 points reduction in WI-NRS at week 24 was 60.0% in thedupilumab group (N=75) vs 18.4% in the placebo group (N=76) (difference: 42.7%; 95%CI: 2.8 – 57.7). In the PRIME2 trial, the % of pts with ≥4 points reduction in WI-NRS at week 12 was 37.2% in thedupilumab group (N=78) vs 22.0% in the placebo group (N=82) (difference: 16.8%; 95%CI: 2.3 – 31.2) and, at week 24, efficacy results were similar to those of the PRIME trial: 57.7% in the dupilumab group vs 19.5% in the placebo group (difference: 42.6%; 95%CI: 29.1 – 56.1) [3]. **Summary of clinical SAFETY:**A total of 309 adults with PN were evaluated for safety in PRIME and PRIME2 trials. The safety pool included data from the 24-week treatment and 12-week follow-up periods from both trials. The proportion of pts who discontinued treatment due to AEs was 3% in the placebo group and 0% in the dupilumab group. AEs occurring in ≥2% of the pts. in thedupilumab group in both PRIME and PRIME2 trials and at a higher rate than placebo were nasopharyngitis (5% of pts in thedupilumab group vs 2% in the placebo group), conjunctivitis (4% vs 1%), herpes infection (3% vs 0), dizziness (3% vs 1%), myalgia (3% vs 1%) and diarrhea (3% vs 1%) [3]. **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/dupixent-epar-product-information_en.pdf 2.https://www.ema.europa.eu/en/medicines/human/summaries-opinion/dupixent-5 3.https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761055s044lbl.pdf 4.https://clinicaltrials.gov/ct2/show/NCT04183335 5.https://clinicaltrials.gov/ct2/show/NCT04202679 6. https://gallery.farmadati.it/ 7. https://pubmed.ncbi.nlm.nih.gov/31421126/ 8. https://pubmed.ncbi.nlm.nih.gov/35083742/ 9.https://pubmed.ncbi.nlm.nih.gov/33021323/ 10.https://www.io.nihr.ac.uk/wp-content/uploads/2021/12/28874-Dupilumab-for-Treating-Prurigo-Nodularis-V1.0-NOV2021-NON-CONF.pdf 11. https://clinicaltrials.gov	**Cost of therapy:** The ex-factory price for twopre-filled pens/syringes of Dupixent® 300 mg is 1,216.00€ (corresponding to the cost of 28 days therapy, as well as the cost of the starting dose of 600 mg) [6]. **Epidemiology:** Limited data are available on the epidemiology of PN. Real-world epidemiologic studies conducted in the US, England and Germany using medical claims database found an estimated prevalence between 3-10 per 10,000 people [7-9]. **POSSIBLE PLACE IN THERAPY:** Current treatment options for PN include steroid cream, antihistamines and immunosuppressants such as corticosteroids, ciclosporin, methotrexate or azathioprine. There are no treatment options recommended for PN inadequately controlled or contraindicated to corticosteroids [10]. **OTHER INDICATIONS IN DEVELOPMENT:** bullous pemphigoid, chronic obstructive pulmonary disease, chronic spontaneous urticaria, chronic inducible cold urticaria,allergic bronchopulmonary aspergillosis, allergic fungal rhinosinusitis,Netherton syndrome [11]. **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:**- **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATIOS:** Phase3: nemolizumab, nalbuphine ER; Phase 2: vixarelimab, povorcitinib [11]. *Service reorganization: No *Possible off label use: Yes

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