**Report Spevigo®- spesolimab**

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| **Product &**  **Mechanism of action** | **Authorized indications**  **Licensing status** | **Essential therapeutic features** | **NHS impact** |
| **Substance:** spesolimab  **Brand Name:** Spedigo®  **Originator/licensee:** Boehringer Ingelheim International GmbH  **Classification:**NCE  **ATC code:** L04AC22  **Orphan Status:**  **Eu:**No  **Us:**Yes  **Mechanism of action:** spesolimab is a humanized monoclonal immunoglobulin G1 antibody that inhibits IL-36 signaling by specifically binding to the IL36R. Binding of Spesolimab to IL36R prevents the subsequent activation of IL36R by cognate ligands (IL-36 α, β and γ) and downstream activation of pro-inflammatory and pro-fibrotic pathways. The precise mechanism linking reduced IL36R activity and the treatment of flares of GPP is unclear [1]. | **Authorized Indication:**  **EMA:** Treatment of flares in adult patients with GPP [2].  **FDA:**Spesolimab is an IL36R antagonist indicated for the treatment of GPP flares in adults [1].  **Route of administration:**IV  **Licensing status**  **EU CHMP P.O. date:** 13/10/2022  **FDA M.A. date:** 1/09/2022  **EU Speed Approval Pathway:**Yes [3] **FDA Speed Approval Pathway:** No  **----- ABBREVIATIONS:**  **AE:** Adverse Event  **GPP:** generalized pustular psoriasis  **GPPGA:** Generalized Pustular Psoriasis Physician Global Assessment  **IL-36**: Interleukin-36  **IL36R:** Interleukin-36 receptor  **NPF:** National Psoriasis Foundation  **Pts:** Patients  **SAE:** Serious Adverse Event | **Summary of clinical EFFICACY:**Effisayil 1 **(NCT03782792)** isa phase 2, multicenter, randomized, doubleblind, placebo-controlled trial conducted to investigate the efficacy and safety of Spesolimab. Inclusion criteria included pts aged 18 to 75 years with history of GPP flares, GPPGA total score of ≥3, new or worsening pustules, a GPPGA pustulationsubscore of ≥2, and ≥5% of bodysurface area with erythema and the presence of pustules. Pts in current treatment with methotrexate, cyclosporine, retinoids were excluded from the trial. After the initial screening, pts were randomly assigned in a 2:1 ratio to receive a single IV dose of 900 mg of Spesolimab or placebo.On day 8, pts from both groups were eligible to receive a single, open-label, IV dose of 900 mg of Spesolimab if they had persistent symptoms at the end of week 1, on the basis of: GPPGA total score ≥2;a clinician assessment of GPP severity based on a modified GPPGA;GPPGA pustulationsubscore≥ 2.The primary EP was a GPPGA pustulationsubscore of 0 (no visible pustules) at the end of week 1.  A total of 52 of the 53 enrolled pts completed the first week of the trial: a total of 19 of the 34 pts (54%) who received Spesolimaband 1 of the 18 pts (6%) who received placebo had a GPPGA pustulationsubscore of 0 (difference= 49 percentage points; 95% CI [21 to 67]) [4];  **Summary of clinical SAFETY:**  Safety data refer to all 53 pts enrolled in **NCT03782792** trial. The summery of AEs that occurredthrough the first week of treatment is listed in the table below.   |  |  |  | | --- | --- | --- | |  | **Spesolimab** | **Placebo** | | **Any AE** | 66% | 56% | | **Severe AE: RCTC GRADE 3 or 4** | 6% | 6% | | **Investigator-defined drug-related AE** | 29% | 28% | | **SAE** | 6% | 0 | | **Death** | 0 | 0 | | **AE leading to discontinuation of Spesolimab or Placebo** | 0 | 0 |   Among the AEs recorded, the most common were pyrexia, that was reported by 6% of the pts in the Spesolimab group vs 22% of those in the placebo group. While among the SAEs reported only in the Spesolimab group, the most common were drug reaction with eosinophilia and systemic symptoms, urinary tract infection, drug-induced hepatic injury and arthritis. All these events occurred in 3% of pts in the Spesolimab group. The severity of AEs was graded according to the RCTC and pustular psoriasis was excluded as an AE from this safety analysis [4].  **Ongoing studies:**   * ***For the same indication:****Yes* * ***For other indications:****Yes*   **Discontinued studies (for the same indication):**No  **References:**  [1]<https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761244s000lbl.pdf>  [2]<https://www.ema.europa.eu/en/news/meeting-highlights-committee-medicinal-products-human-use-chmp-10-13-october-2022>  [3]<https://www.ema.europa.eu/en/documents/smop-initial/chmp-summary-positive-opinion-spevigo_en.pdf>  [4]<https://pubmed.ncbi.nlm.nih.gov/34936739/>  [5]<https://www.drugs.com/price-guide/spevigo>  [6]<https://www.orpha.net/consor/cgi-bin/index.php>  [7]https://pubmed.ncbi.nlm.nih.gov/35061230/  [8] <https://clinicaltrials.gov/NCT03482635> | **Cost of therapy:**  The cost for Spesolimab IV solution (450 mg/7.5 mL) is around $53,853 for a supply of 15 milliliters [5].  **Epidemiology:**GPP is a rare diseaseand its estimated prevalence in Europe is 1-9 / 1 000 000 [6].  **POSSIBLE PLACE IN THERAPY**  There are no GPP specific therapies approved in the USA or EU for the treatment of GPP and management of GPP flares. Based on the NPF Medical Board guidelines, the most commonly used treatments for pts with GPP are retinoids, cyclosporine and methotrexate. The evidence that supports the using of these therapies is ill-defined and based on small, single-arm studies. Spesolimab has demonstrated promising efficacy in pts with GPP getting a possible using as a first line treatment in GPP therapy[7].   * **OTHER INDICATIONS IN DEVELOPMENT:** Treatment of ulcerative colitis in males or females aged 18-75 years [8].   **SAME INDICATION IN EARLIER LINE(S) OF TREATMENT:**No  **OTHER DRUGS IN DEVELOPMENT for the SAME INDICATION**  Imsidolimab, Phase 2  \*Service reorganization No  \*Possible off label use Yes |