Cost effectiveness of nemolizumab in the treatment of patients with moderate-to-severe prurigo nodularis in Italy

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Background and objective.

Prurigo nodularis (PN) is a chronic neuroimmune skin condition characterized by multiple pruriginous lesions and intense, persistent itching as the main symptom. According to several studies, itch is the most impactful and debilitating symptom [1–5], representing a hallmark of the disease [6]. Itching has a significant impact on the social life and quality of life (including anxiety and depression) of affected patients [6,7] and, as it often occurs at night, is identified as the main cause of sleep disturbances, which are another of the main manifestations of PN [4].

Nemolizumab is a first-in-class monoclonal antibody (mAb) therapy that binds to the IL-31-α receptor (IL-31Rα) to prevent its activation by IL-31 and signal transduction, downregulating the cellular pathways that cause itching and inflammation. Thanks to its novel mechanism of action, which differs from that of the only other licensed therapeutic option recently reimbursed in Italy (dupilumab), nemolizumab responds to the need for new therapeutic options. In fact, IL-31, is a direct pruritogen, directly eliciting itch [8-10], the most frequent, impactful, and debilitating symptom of PN [1–4,11].

Nemolizumab has demonstrated therapeutic efficacy and safety in the extensive OLYMPIA clinical development program [12-14], providing rapid itch relief and improving sleep disturbances as early as 4 weeks after the first dose, resulting in significant improvements in quality of life.

The study objective is to estimate the cost-effectiveness of nemolizumab + BSC (Best Supportive Care), compared to dupilumab + BSC, for the treatment of patients with moderate-to-severe prurigo nodularis from the Italian National Health Service (NHS) perspective.

Methods.

- The model has a hybrid decision-tree/Markov cohort structure (Figure 1). The decision-tree component captures the short-term (16 weeks) effect of treatment, at the end of which non-responding patients undergo treatment switch or treatment with BSC alone. Responding patients, on the other hand, enter the Markov model, which captures treatment efficacy through transitions between three discrete health states: “Maintained response”, “No response” and “Dead”.

Figure 1. Short-term decision tree structure

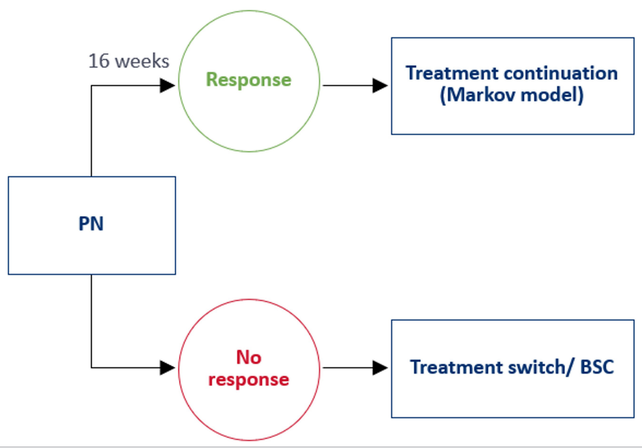
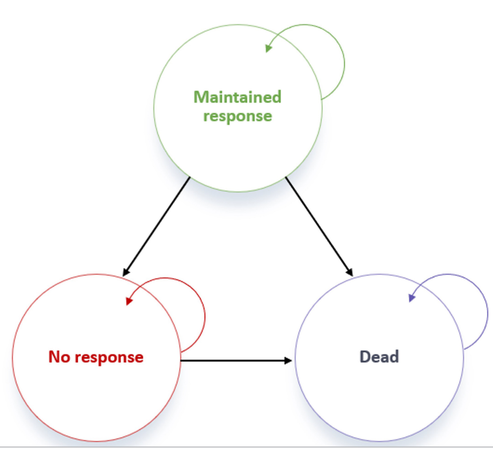


Figure 2. Long-term Markov Model structure



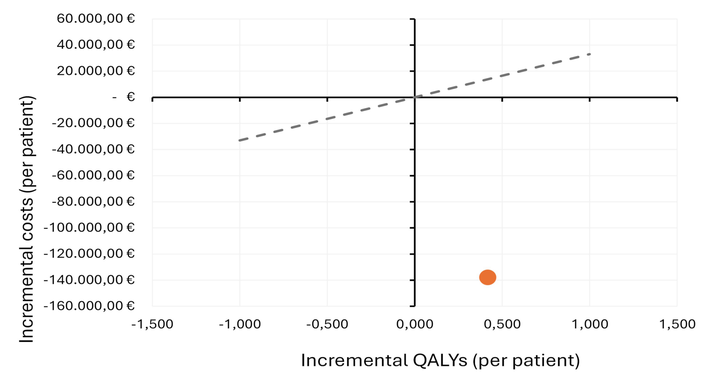
- The analysis was conducted from the Italian NHS perspective assuming a 3% discount rate.
- The model population consists of adult patients with moderate to severe PN (defined as an Investigator’s Global Assessment [IGA] score of three or four, a Peak Pruritus Numerical Rating Scale [PP-NRS] score of at least seven, and at least 20 lesions). The baseline characteristics of the included population are consistent with those of the OLYMPIA 1 and 2 studies [12-13].
- For mortality, Italian data from ISTAT mortality tables were used, to which a hazard ratio of 1.37 was applied [17].
- The BSC drugs used concomitantly (antihistamines, emollients, topical corticosteroids [TCSs], topical calcineurin inhibitors [TCIs], systemic corticosteroids, and immunosuppressants) and their usage rate was determined through a Delphi panel.
- Efficacy and utility values were derived from the phase 3 studies OLYMPIA 1 and OLYMPIA 2 [12-13]. The Long Term Extension (LTE) [14] trial was used to estimate long-term utility values. Comparators efficacy was derived from a Systemic Literature Review (SLR) and Network Meta-Analysis (NMA), in which nemolizumab treatment resulted in better itch relief (based on improvements on the PP NRS scale) and comparable skin clearance and safety.
- Due to the lack of data on long-term efficacy, a decrease over time in the effect of treatment (i.e. treatment waning effect) was hypothesized. This was implemented as an increase in the treatment discontinuation rate in the “Maintained response” health state, based on the findings of the NICE assessment of dupilumab [16].
- The treatment emergent adverse events identified in the literature (allergic conjunctivitis, Injection site reaction, Infectious conjunctivitis, atopic dermatitis, eczema nummular, neurodermatitis) were included in the analysis. Their occurrence rates were obtained from the OLYMPIA 1 trial [12] for nemolizumab and from PRIME and PRIME 2 trials [15] for dupilumab. Adverse events (Aes) costs were derived from the Ministry of Health’s 2024 Tariff Decree and from literature
- The resources used for monitoring and their frequency of use based on response status were taken from the NICE assessment of dupilumab [16]. These values were validated by clinical experts in a Delphi panel and modified to ensure that they represent clinical practice, where necessary.
- Drug acquisition costs were calculated using ex-factory prices inclusive of mandatory discounts (-5% -5%) for nemolizumab (hypothetical price) and for dupilumab.
- The Base Case and sensitivity analysis considered a lifetime horizon, corresponding to 45 years; a scenario analysis was conducted with a time horizon of 10 years.
- The considered Incremental Cost-Effectiveness Ratio (ICER) threshold was € 33.000/Quality-Adjusted Life Year (QALY).

Results.

- In the Base Case analysis, with a lifetime time horizon of 45 years, the results show that nemolizumab + BSC translates into a reduction in total costs of -€137.808, with a gain in terms of QALYs of +0,417 compared to dupilumab + BSC (Figure 3). This corresponds to an ICER of dominance, making nemolizumab a clearly cost-effective therapy for the Italian NHS.

Figure 3. Results for the Base Case analysis

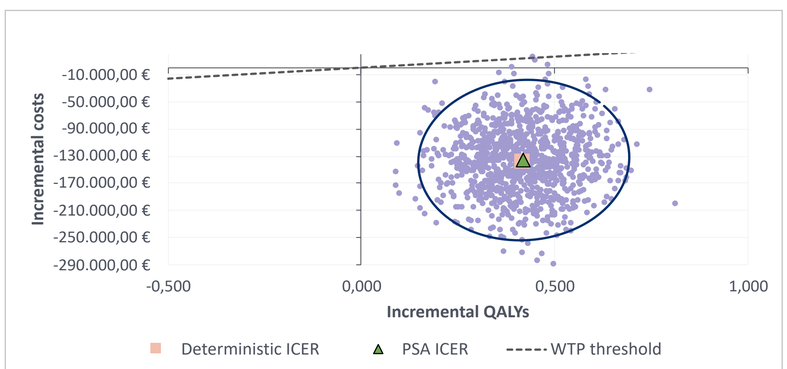
Outcome	Intervention	Comparator	Incremental
Costs	320.412 €	458.220 €	- 137.808 €
QALYs	11,65	11,24	0,417
Life years	17,573	17,573	0,000
ICER (cost/QALY)			**Dominant**
ICER (cost/life year)			**Equivalent life expectancy**



- The scenario analysis conducted over a shorter time horizon, i.e., 10 years, confirms the results observed in the Base Case analysis, demonstrating the results’ robustness. As in the Base Case analysis, the ICER highlights the dominance of the treatment with nemolizumab + BSC vs. dupilumab + BSC.
- The Probabilistic Sensitivity Analysis (PSA) analysis confirms the robustness of the results, with values consistently close to the Base Case ones. The PSA, developed on 1.000 simulations, estimated that in 100% of cases the ICER highlights the dominance of nemolizumab + BSC vs. dupilumab + BSC (Figure 4).

Figure 4. Results for the PSA analysis

Outcome	Nemolizumab + BSC Intervention	Dupilumab + BSC Comparator	Incremental
Costs	319.408,44 €	455.486,19 €	- 136.077,75 €
QALYs	11,626	11,206	0,419
Life years	17,490	17,490	0,000
ICER (cost/QALY)			**Dominant**
Probability of cost-effectiveness	100%		



Conclusion.

- **Nemolizumab is shown to be a cost-effective (dominant) treatment for the Italian NHS.**
- **These results support the decision to introduce nemolizumab in routine clinical practice as a cost-effective treatment for patients with moderate-to-severe prurigo nodularis in Italy.**

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