Health Technology Briefing
November 2021

Dupilumab for treating Prurigo Nodularis

Company/Developer	Sanofi

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 28874	NICE ID: 10424	UKPS ID: 656961

Licensing and Market Availability Plans

Currently in phase III clinical trials

Summary

Dupilumab is in clinical development for the treatment of prurigo nodularis (PN) for people who have not responded to or cannot have corticosteroid treatment. PN is a chronic skin disorder in which people have firm, raised bumps on the skin known as nodules. The nodules are very itchy and itching the affected area can worsen the condition. The causes of PN are not fully understood, but it is thought that overreaction of the body's immune system may be responsible for the disease. External reasons for the development of PN are not clear, but it may be caused by insect bites, prolonged stress and other related conditions such as asthma and eczema.

Dupilumab is a human monoclonal antibody, which is a manufactured version of an immune protein created by the body to fight infection. It is given as an injection under the skin. Dupilumab stops the action of two immune response mediators, interleukin-4 (IL-4) and interleukin-13 (IL-13). These proteins are responsible for inflammation in the body and blocking them decreases levels of inflammation. It has been demonstrated that PN patients have higher levels of IL-4 and IL-13, which means that blocking these proteins may be a promising treatment option. There are not any recommended treatment options currently available for PN treatment where corticosteroids cannot be given or have not helped.

Proposed Indication

Treatment of adults aged 18 years and older with PN who are inadequately controlled on or not advised to receive topical prescription therapies.[1]

Technology

Description

Dupilumab (Dupixent) is a recombinant human IgG4 monoclonal antibody that inhibits IL-4 and IL-13 signalling. It inhibits IL-4 signalling via the Type I receptor (IL-4Rα/γc), and both IL-4 and IL-13 signalling through the Type II receptor (IL-4Rα/IL-13Rα). IL-4 and IL-13 are major drivers of human type 2 inflammatory disease. Blocking the IL-4/IL-13 pathway with dupilumab decreases many of the mediators of type 2 inflammation in patients.[2]

Dupilumab is currently in phase III clinical development for the treatment of adults with PN inadequately controlled by or contraindicated to corticosteroids. In a phase III clinical trial (PRIME2, NCT04202679), participants received dupilumab via subcutaneous (SC) injection (alongside moisturisers, corticosteroids and calcineurin inhibitors) at an unspecified dose and schedule.[1]

Key Innovation

There are limited treatments available for PN with many current options providing poor results or severe side effects.[3] The treatment options currently utilised may be used off-label.[4] Although the exact pathogenesis of PN is not well understood, there is evidence to suggest that patients with PN have higher levels of expression of IL-4 and IL-13, the cytokines which are targeted by dupilumab. Small studies utilising off-label usage of dupilumab in PN have demonstrated promising treatment outcomes.[3] In a phase III trial, dupilumab showed promising treatment outcomes in PN.[5]

Regulatory & Development Status

Dupilumab has a Marketing Authorisation in the UK for the following indications:[2]

- Treatment of moderate-to-severe atopic dermatitis in adults and adolescents 12 years and older who are candidates for systemic therapy
- Treatment of severe atopic dermatitis in children 6 to 11 years old who are candidates for systemic therapy
- Add-on maintenance treatment in adults and adolescents 12 years and older with severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised fraction of exhaled nitric oxide (FeNO), who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment

Dupilumab as a monotherapy and in addition to various other medicinal products is being developed for the following indications phase II and III clinical trials:[6]

- Peanut allergy
- Atopic dermatitis
- Grass allergy
- Allergic broncopulmonary aspergillosis
- Asthma
- Eosinophilic esophagitis
- Atopic hand and foot dermatitis
- Bullous pemphigoid

- Chronic rhinosinusitis with nasal polyps
- Allergic fungal rhinosinusitis
- Chronic obstructive pulmonary disease (COPD)
- Cold urticaria
- Prurigo nodularis
- Keloids
- Chronic hepatic pruritus
- Prostate cancer
- Contact dermatitis
- Hand eczema
- Cholinergic urticaria
- Atopic keratoconjunctivitis
- Cow's milk allergy
- Aspirin-exacerbated respiratory disease
- Eosinophilic gastritis

Patient Group

Disease Area and Clinical Need

PN is a chronic skin condition characterised by severely pruritic, localised or generalised hyperkeratotic papules and nodules on the skin.[4] Nodules usually develop in a symmetrical pattern most often on a person's arms or legs. The causes of PN are not clear but it can be related to insect bites, prolonged periods of stress and those affected often have a comorbidity such as asthma, eczema and other allergic conditions.[7] PN pathophysiology is not well understood, however the underlying disease mechanism may involve cutaneous neurogenic inflammation mediated by neuropeptides, T cells, mast cells and eosinophilic granulocytes. Various common cytokines have also been implicated in PN development.[3]

Studies on the epidemiology of PN are lacking in the current literature.[4] The population likely to be eligible to receive dupilumab could not be estimated from available published sources. In England in 2020-21 there were 184 hospital admissions and 217 finished consultant episodes for PN (ICD-10 L28.1).[8]

Recommended Treatment Options

Currently recommended options for the treatment of PN include:[7]

- Steroid cream
- Antihistamines
- Immunosuppressants such as corticosteroids, ciclosporin, methotrexate or azathioprine

Non-pharmacological treatment options for PN can include the use of paste bandages or cling-film on the affected area, topical emollients, stopping the use of soaps/shower gels/cosmetics and narrowband ultraviolet light treatment.[7]

There are not any treatment options currently recommended for the treatment of PN inadequately controlled or contraindicated to corticosteroids.[7]

Clinical Trial Information

Trial	**PRIME2**, NCT04202679, EudraCT2019-003801-90; A Randomized, Double Blind, Placebo-controlled, Multi-center, Parallel Group Study to Evaluate the

	Efficacy and Safety of Dupilumab in Patients With Prurigo Nodularis Who Are Inadequately on Topical Prescription Therapies or When Those Therapies Are Not Advisable **Phase III:** active, not recruiting **Locations:** EU, UK, USA, Canada and other countries **Primary completion date:** 30 August 2021
Trial Design	Randomised, parallel assignment, quadruple masking
Population	N=160; adults aged 18 to 80 years of age with a clinical diagnosis of PN; WI-history of failing a 2-week course of medium-to-superpotent topical corticosteroids (TCS) or TCS not medically advisable; has applied a stable dose of topical emollient once or twice daily for at least 5 out of the 7 consecutive days before day 1
Intervention(s)	Dupilumab (SC), topical moisturisers, low to medium potent topical corticosteroids, topical calcineurin inhibitors
Comparator(s)	Placebo (SC), topical moisturisers, low to medium potent topical corticosteroids, topical calcineurin inhibitors
Outcome(s)	Primary outcome: Improvement (reduction) in worst-itch numeric rating scale (WI-NRS) by ≥4 [Time frame: baseline to week 12]: Proportion of participants with improvement (reduction) in worst-itch numeric rating scale (WI-NRS) by ≥4 from baseline to week 12 See trial record for full list of other outcomes
Results (efficacy)	Findings showed that 37% of patients treated with dupilumab achieved a clinically meaningful reduction in itch at week 12 compared with 22% of those treated with placebo (*P* =.0216). Moreover, 58% of dupilumab-treated patients had a clinically meaningful reduction in itch at week 24 compared with 20% of placebo-treated patients (*P* <.0001). A greater proportion of patients in the dupilumab arm also achieved clear or almost clear skin at week 24 compared with those in the placebo arm (45% vs 16%; *P* <.0001).[5]
Results (safety)	The most common treatment-emergent adverse events were conjunctivitis and herpes viral infection.[5]

Estimated Cost

Dupilumab is already marketed in the UK for various indications; a 300mg/2ml pre-filled pen/syringe and a 200mg/1.14ml pre-filled pen/syringe cost £1,264.89.[9]

Relevant Guidance

NICE Guidance

No relevant guidance identified

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract For Specialised Dermatology Services (All Ages). A12/S/a.

Other Guidance

- Stander S, Manuel PP, Timothy B, Claudia Z, Augustin MMD et al. IFSI-guideline on chronic prurigo including prurigo nodularis. 2020.[10]
- British Association of Dermatologists. Patient Information Leaflets (PILs): Nodular Prurigo. 2020.[7]

Additional Information

References

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10 Ständer S, Pereira MP, Berger T, Zeidler C, Augustin M, Bobko S, et al. IFSI-guideline on chronic prurigo including prurigo nodularis. *Itch*. 2020;5(4). Available from: https://journals.lww.com/itch/Fulltext/2020/10010/IFSI_guideline_on_chronic_prurigo_including.1.aspx.

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