Health Technology Briefing
March 2024

Dupilumab for treating bullous pemphigoid

Company/Developer	Sanofi

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 29269	NICE ID: 10640	UKPS ID: 666466

Licensing and Market Availability Plans

Currently in phase II/III clinical trials.

Summary

Dupilumab is currently in phase II/III development for adult patients with bullous pemphigoid (BP). BP is the most common form of blistering disorders of the skin. The first symptom of BP is usually redness and itching of the skin. BP primarily affects older people, with an average age around 80 years old. The burden of disease in the older population is considerable. BP is commonly treated with steroids (oral or creams). However, these can have side effects such as high blood pressure, weakened bones and increased infection rates, which is a concern, especially amongst frail, older people with multiple co-morbidities.

Dupilumab, is a type of protein designed to block receptors (targets) for interleukin 4 and interleukin 13 (IL-4 and IL-13). By blocking the receptors, dupilumab prevents IL-4 and IL-13 from working and relieves disease symptoms. Dupilumab is administered under the skin. Dupilumab has been shown to be effective in prior studies with no significant adverse events, including patients in whom previous conventional therapy had failed. If licensed, dupilumab will offer an additional treatment option for patients with BP who currently have few well-tolerated therapies available.

Proposed Indication

Adults aged 18 and older with bullous pemphigoid (BP).[1]

Technology

Description

Dupilumab (Dupixent) is a fully human monoclonal antibody against interleukin (IL)-4 receptor alpha that inhibits IL-4/IL-13 signalling, produced in Chinese Hamster Ovary (CHO) cells by recombinant DNA technology.[2] It is designed to block receptors (targets) for IL-4 and IL-13, which may play a role in BP. By blocking the receptors, dupilumab prevents IL-4 and IL-13 from working and relieves disease symptoms.[3,4]

Dupilumab is currently in clinical development for adult patients with BP. In the phase II/III clinical trial (NCT04206553), patients were administered subcutaneously dupilumab 300mg solution once every two weeks with a loading dose of 600mg.[1,a]

Key Innovation

A Cochrane review on available treatments of BP concluded that oral steroids, which are the standard treatment of BP, and strong steroid creams seem safe and effective. However, the use of steroid creams in extensive disease may be limited by side-effects and the practicality of applying creams to large areas of the skin.[5] The National Health Service (NHS) reports that steroid treatment can also result in high blood pressure, weakened bones and a higher chance of getting infections, which causes concerns in older patient populations with multiple co-morbidities.[6]

A recent literature review comprising 15 studies evaluated the treatment of BP with dupilumab and concluded an overall complete response and partial response rates of 74.6% and 11.1%, respectively, with no significant adverse effects.[4] Dupilumab has also been shown to be effective in similar conditions to BP, such as atopic dermatitis and prurigo nodularis.[3] If licensed, dupilumab will offer an additional treatment option for patients with BP who currently have few well-tolerated therapies available.

Regulatory & Development Status

Dupilumab has Marketing Authorisation in the EU/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 months to 11 years old who are candidates for systemic therapy
- Treatment for adults and adolescents 12 years and older as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised fraction of exhaled nitric oxide, who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment
- Add-on therapy with intranasal corticosteroids for the treatment of adults with severe chronic rhinosinusitis with nasal polyposis for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control
- Treatment of adults with moderate-to-severe prurigo nodularis who are candidates for systemic therapy.

[a] Information provided by Sanofi UK

- Treatment of eosinophilic esophagitis in adults and adolescents 12 years and older, weighing at least 40 kg, who are inadequately controlled by, are intolerant to, or who are not candidates for conventional medicinal therapy

Dupilumab is currently in phase II and III clinical development for several other indications such as:[7]

- Chronic obstructive pulmonary disease
- Chronic spontaneous urticaria
- Ulcerative colitis
- Chronic pruritus of unknown origin

Patient Group

Disease Area and Clinical Need

BP is the most common form of autoimmune subepidermal blistering disease.[8] The first symptom of BP is usually redness and itching of the skin. Within weeks to months, thin-walled, tense blisters with clear fluid centres (bullae) appear on the arms and legs (flexor surfaces), in the armpits (axillae), on the abdomen, and/or in the skinfolds of the groin. Mucous membranes may also be involved but are less commonly seen than skin blisters.[9] The cause of this abnormal immune response is unknown, although it can sometimes be triggered using certain medications.[10]

BP is a rare disorder that primarily affects the older people, with an average age around 80 years old. Rare cases have been reported in infants and adolescents.[9] The incidence of BP from 1998 to 2017 was 7.63 per 100,000 person-years and rose with increasing age, particularly for older men. The annual increase in incidence (during the same years) was 0.9%. The prevalence almost doubled over the observation period (1998-2017), reaching 47.99 per 100 000 people and 141.24 per 100,000 people over the age of 60 years. These data demonstrate that the burden of disease in the older population is considerable.[11] In England, 2022-23, there were 1,668 finished consultant episodes (FCEs) of primary diagnosis of pemphigoid (ICD-10 code: L12.0), which resulted in 883 admissions, 347 day cases and 9,178 FCE bed days.[12]

Recommended Treatment Options

There are no treatment options recommended by NICE for BP. The NHS recommends the following for the treatment for BP:[6]

- Steroid creams such as topical corticosteroids
- Anti-inflammatory medicine such as corticosteroid tablets
- Antibiotics

Clinical Trial Information

Trial	**LIBERTY-BP ADEPT**; NCT04206553 ; 2019-003520-20; A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel Group Study to Evaluate the Efficacy and Safety of Dupilumab in Adult Patients With Bullous Pemphigoid **Phase II/III** – Active, not recruiting **Locations:** Four EU countries, Australia, USA, and other countries **Primary completion date:** October 2024
Trial Design	Randomised, parallel assignment, quadruple masking

Population	N=106; adults aged 18-90 years old; characteristic clinical features of BP (e.g., urticarial or eczematous or erythematous plaques, bullae, pruritus) at the screening and baseline visits or confirmed diagnosis of BP at baseline visit
Intervention(s)	SC dupilumab 300mg solution once every two weeks with a loading dose of 600mg[a] in addition to standard of care (prednisone/prednisolone)
Comparator(s)	Matched placebo
Outcome(s)	Primary outcome measure: • Proportion of patients achieving sustained remission [Time frame: week 36] See trial record for full list of other outcomes
Results (efficacy)	-
Results (safety)	-

Estimated Cost

The cost of a dupilumab 300mg/2ml pre-filled pen/syringe and 200mg/1.14ml pre-filled pen/syringe is £1,264.89.[13]

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

- German Society of Dermatology. S2k guidelines for the treatment of pemphigus vulgaris/foliaceus and bullous pemphigoid. 2020.[14]
- European Academy of Dermatology and Venereology. S2 K guidelines for the management of bullous pemphigoid initiated by the European Academy of Dermatology and Venereology. 2022.[15]
- British Association of Dermatologists. British Association of Dermatologists' guidelines for the management of bullous pemphigoid. 2012.[16]

Additional Information

[a] Information provided by Sanofi UK

References

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