

# Biologics for Urticaria

Urticaria, commonly referred to as hives, is a prevalent inflammatory skin condition affecting up to 20% of the global population. It is characterized by transient wheals—raised, pale, or skin-colored swellings that are often surrounded by redness. These lesions typically itch and can vary in size and shape. A wheal may persist for several minutes to 24 hours, while the surrounding erythema may last slightly longer. In some cases, urticaria is accompanied by *angioedema*, a deeper form of swelling that typically affects the skin or mucous membranes and can last for 2-3 days.

## Classification of Urticaria

Urticaria can be classified into two main categories based on the duration of symptoms:

- **Acute Urticaria:** Acute urticaria is defined as symptoms that last less than 6 weeks and typically resolve within hours to days. This form is often triggered by allergic reactions to foods, medications, or infections.
- **Chronic Urticaria:** Chronic urticaria persists for over 6 weeks and is characterized by recurrent or persistent wheals and flares. This form significantly affects quality of life, causing sleep disturbances, anxiety, social withdrawal, and impaired work productivity. It is often categorized into chronic spontaneous urticaria, where the triggers are unknown, and chronic inducible urticaria, where physical factors like pressure or temperature may induce symptoms.

## Pathophysiology and Risk Factors

The pathophysiology of urticaria is driven by the activation of mast cells through the cross-linking of immunoglobulin E (IgE), leading to degranulation and the release of histamine, which causes vasodilation and leakage of fluid from blood vessels, resulting in wheals. Although chronic spontaneous urticaria is not caused by an allergic reaction, it follows a similar biological pathway.

Approximately 30% of chronic urticaria cases involve autoantibodies targeting the IgE receptor on mast cells or IgE itself. This form of urticaria is commonly associated with autoimmune conditions such as thyroid disease, type 1 diabetes, lupus, and rheumatoid arthritis. Moreover, psychiatric comorbidities, including anxiety and depression, are prevalent in 50% of patients with chronic urticaria, further complicating management. In addition, 30% of individuals with chronic urticaria report exacerbations triggered by nonsteroidal anti-inflammatory drugs (NSAIDs) like aspirin.

## Treatment Options

### ***First-line Therapy***

The primary treatment for both acute and chronic urticaria is the use of second-generation H1-antihistamines, such as cetirizine (Zyrtec) or loratadine (Claritin). These agents are preferred due to their minimal sedative effects and effective relief of symptoms. In severe cases, a short course of oral corticosteroids (e.g., prednisone) may be prescribed to manage inflammation and provide rapid symptom relief. However, corticosteroid therapy is not recommended for long-term use due to potential side effects.

### ***Second-line Therapy***

For patients who do not respond adequately to antihistamines, *omalizumab* (Xolair), a monoclonal anti-IgE antibody, is often used. Xolair has been shown to reduce symptoms of chronic urticaria by binding to IgE, preventing its interaction with mast cells and basophils, and reducing histamine release. Xolair is typically administered at a dose of 300 mg every four weeks and is used in conjunction with antihistamines.

Other second-line treatments include cyclosporine, which has been used off-label, though it is not routinely recommended due to its high side effect profile. Emerging therapies, including biologic agents such as ligelizumab and vixarelimab, are currently under investigation for their efficacy in treating chronic urticaria, particularly in refractory cases.

### ***New and Investigational Therapies***

- *Ligelizumab*: A monoclonal anti-IgE antibody similar to omalizumab, ligelizumab has shown potential for higher efficacy in reducing chronic urticaria symptoms.
- *Vixarelimab*: Targets the oncostatin M receptor involved in inflammation and pruritus and may provide benefits for patients with chronic urticaria and associated pruritus.
- *Dupilumab*: An anti-IL-4/IL-13 monoclonal antibody, used primarily for atopic dermatitis, is being explored for chronic urticaria, especially in cases with overlapping atopic conditions.
- *Benralizumab*: An anti-IL-5 receptor monoclonal antibody, which reduces eosinophils and may have a role in the treatment of eosinophilic forms of chronic urticaria.
- *Canakinumab*: An anti-IL-1 $\beta$  monoclonal antibody, under investigation for its potential benefits in patients with urticaria associated with autoinflammatory syndromes.
- *Rituximab*: An anti-CD20 monoclonal antibody being studied for refractory chronic urticaria, particularly in patients with autoimmune components.

### ***Indications and FDA Approval***

Xolair was approved by the U.S. Food and Drug Administration (FDA) for the treatment of chronic spontaneous urticaria in patients aged 12 years and older who have not responded to conventional antihistamine therapy. While Xolair is not FDA-approved for chronic inducible urticaria, it may still be beneficial for certain patients, as emerging studies suggest its efficacy in these cases.

### ***Side Effects of Treatment***

Common side effects associated with Xolair include injection site reactions such as swelling, redness, and pain. Systemic side effects can include headache and, in rare cases, anaphylaxis, although these occurrences are minimal. Patients receiving biologic treatments should be monitored for adverse effects and carefully evaluated by their healthcare provider.

## Conclusion

Urticaria is a common but complex skin disorder with significant implications for affected individuals, particularly those with chronic forms. The pathophysiology involves IgE-mediated mast cell degranulation, and treatment primarily involves antihistamines, corticosteroids, and biologic therapies like Xolair for refractory cases. With ongoing research into novel biologic agents, future therapies may offer more targeted and effective treatments for patients with chronic urticaria, improving their quality of life and clinical outcomes.

## References

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