NEWS, VIEWS, & REVIEWS

An Updated Therapeutic Strategy for Chronic Idiopathic Urticaria

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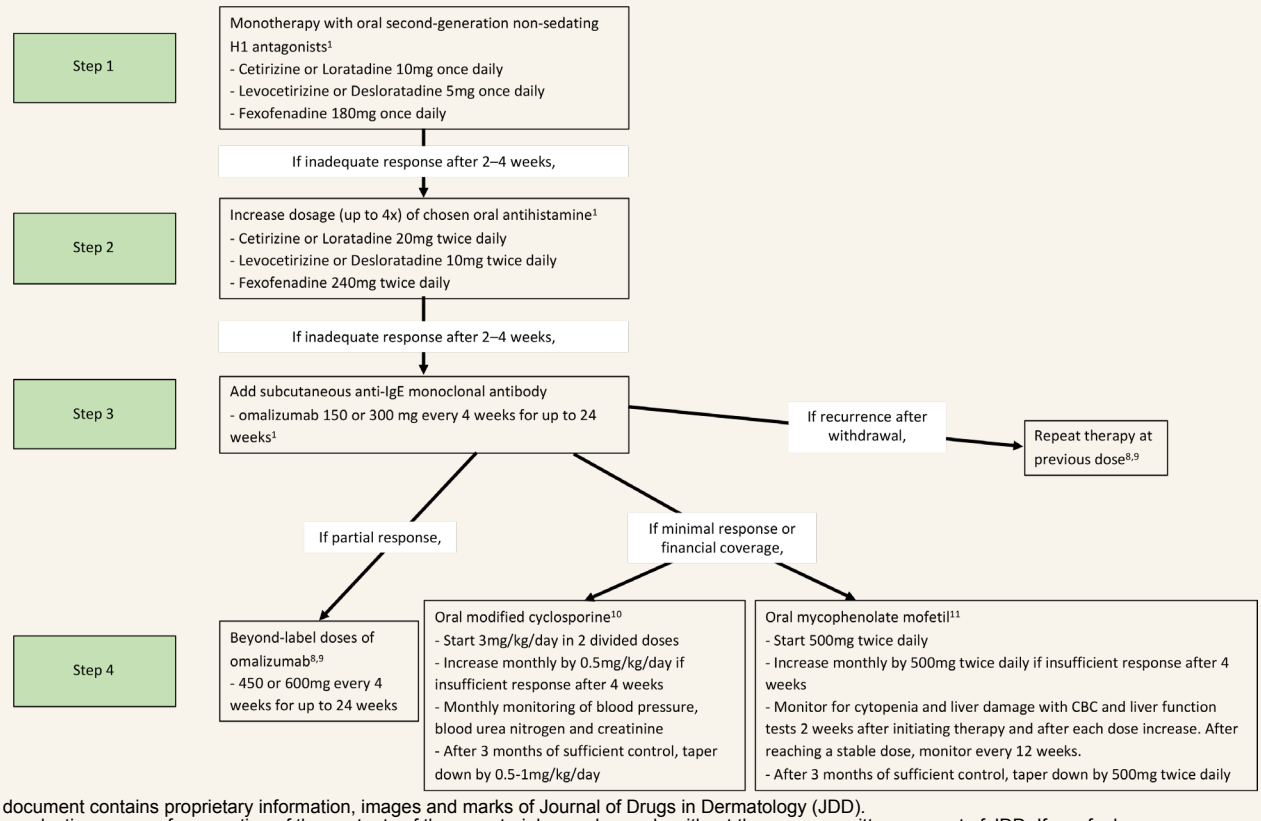
Urticaria, for greater than 6 weeks in the absence of a consistent, identifiable trigger, is termed chronic spontaneous urticaria (CSU).[1] Although the disease course is mostly self-limiting, CSU persists in 20% of patients for more than 5 years, can be debilitating to quality-of-life (QoL), and has been associated with increased anxiety and depression.[2,3] This review provides a step-by-step approach to treatment from recently updated guidelines and summarizes the latest evidence for off-label options.

CSU lesions typically last 4 to 24 hours, and pathology shows a mixed perivascular leukocytic infiltrate.[1,4] Degranulation of skin mast cells and elevated histamine are seen in the wheals and angioedema, but no conclusive pathogenesis or biomarkers predicting treatment response have been established. Although mechanisms for autoimmunity and associations with various autoimmune disorders have been proposed,[5] guidelines advise against a barrage of laboratory tests beyond a complete blood count (CBC) with differential for eosinophilia and instead recommend history and physical to screen for suspected associated conditions.[1]

Treatment should aim for symptom clearance and maintaining remission with long-term medications (Figure 1). A short course of oral corticosteroids should only be used for acute exacerbations or as bridging for long-term options. Due to insufficient evidence, H2 antagonists and leukotriene antagonists are no longer recommended for CSU.[1] Thorough documentation of symptom and QoL progression through standardized, validated clinical measures[3] can be key for insurance coverage of omalizumab.

With 7% of cases failing this algorithm, expanding licensed drugs for stand-alone or adjuvant therapy for CSU is crucial. Due to the implication of eosinophils in CSU pathogenesis, monoclonal antibodies against IL-5 are undergoing clinical trials. Targeting IgE production through IL-4 and IL-13 signaling inhibition with dupilumab (600mg loading dose and 300mg every two weeks) can achieve response for omalizumab-refractory CSU,[6] and dupilumab is under investigation for patients who are intolerant of or incompletely respond to omalizumab (NCT04180488). Reducing proinflammatory mediators from activated mast cells, such as with TNF-α

Figure 1. Stepwise approach to treating chronic spontaneous urticaria.



inhibitors, shows potential for randomized controlled trials.[7] Tranexamic acid (2g daily) has not been effective as stand-alone therapy but may show utility as an adjuvant for levocetirizine (10mg daily) (NCT03789422).

In summary, chronic urticaria can be a relapsing, exhausting condition for patients to manage. Omalizumab has revolutionized outcomes for many, and H2 receptor and leukotriene antagonists have been phased out from the treatment strategy. Expanded-label therapies are rapidly emerging for recalcitrant cases.

Disclosure
The authors declare no conflicts of interest.

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