Purpose of Review: Atopic eczema is a common inflammatory skin disease showing chronically relapsing eczema and high association with elevated serum IgE levels. A subgroup of atopic eczema patients requires systemic immunomodulatory treatment for long time periods. However, beyond cyclosporine A and azathioprine, only limited consent exists on systemic treatment options. Recent Findings: Timely published systemic treatment modalities include studies on efalizumab (anti-CD11a antibody), infliximab, adalimumab, and etanercept (anti-TNF-alpha treatment), omalizumab (an anti-IgE antibody), rituximab (an anti-CD20 antibody), specific immunotherapy, leflunomide, and leukotriene receptor antagonists with varying clinical results and with particular safety profiles. Summary: Although there is not yet a treatment modality reaching clinical efficacy of cyclosporine A as gold standard of systemic therapy, limitation in its application duration as in its side effect profile as well as the search for alternatives has set a focus on the new alternatives of which especially B-cell-directed therapies might be promising candidates.