DISEASE–DRUG–DRUG INTERACTION ASSESSMENTS FOR TOCILIZUMAB—A MONOCLONAL ANTIBODY AGAINST INTERLEUKIN-6 RECEPTOR TO TREAT PATIENTS WITH RHEUMATOID ARTHRITIS

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11.1 INTRODUCTION

Tocilizumab (TCZ, Actemra) is a recombinant humanized monoclonal antibody of the immunoglobulin G (IgG) subclass that selectively binds to human interleukin 6 (IL-6) receptors. TCZ binds to both membrane-bound and soluble forms of IL-6R, blocking signal transduction pathways through competitive inhibition of IL-6 binding.[1] TCZ 8 mg/kg given intravenously (IV) is currently approved for the treatment of rheumatoid arthritis (RA) in over 106 countries, including the United States,[2] Canada,[3] Australia,[4] European countries,[5] and Japan.[6] IL-6 receptor blockade was considered as a mechanism for pharmacologic treatment of RA due to the central role of IL-6 in inflammatory processes. IL-6 is a pleiotropic cytokine with numerous activities, including effects on the immune response and inflammation (e.g., interaction with neutrophils in the synovium), bone metabolism, and hematopoiesis.[7,8] Elevated IL-6 levels have been found in the serum and synovial fluid of RA patients, and inflammatory cell infiltration has been correlated with IL-6 levels in synovial tissues.[9] Furthermore, IL-6 levels correlate with disease activity in RA patients and improvement of the disease after treatment with disease-modifying antirheumatic drugs (DMARDs) is accompanied by a reduction in serum IL-6.[10]

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