DRUG–DRUG INTERACTIONS FOR ETANERCEPT—A FUSION PROTEIN

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The treatment of immune-mediated inflammatory diseases, such as rheumatoid arthritis, psoriasis, and psoriatic arthritis has been changed with the introduction of biological agents in the 1990s. Previously available biological agents, such as insulin, were replacements for endogenous proteins that were missing in patients with diabetes, while newer agents such as etanercept were constructs not found in nature. In this case study of drug–drug interaction assessments for etanercept, a fusion protein targeting tumor necrosis factor α (TNF-α) used in the treatment of several immune-mediated inflammatory diseases, background information about etanercept will be discussed, followed by a general assessment on the likelihood of drug interactions with fusion proteins such as etanercept and finally the results of specific etanercept–drug interaction investigations will be discussed.

12.1 ETANERCEPT BACKGROUND

Etanercept is a human tumor necrosis factor receptor (TNFR) p75 Fc fusion protein produced by recombinant DNA technology in a Chinese hamster ovary (CHO) mammalian cell expression system. It is a dimer of a chimeric protein genetically engineered by fusing the extracellular ligand binding domain of human tumor necrosis factor receptor 2 (TNFR2/p75) to the Fc domain of human immunoglobulin G1 (IgG1). The Fc component of etanercept contains the hinge, CH2 and CH3 regions, but not the CH1 region of IgG1. Etanercept has a molecular weight of approximately 150 kDa. It causes immune suppression by binding tumor necrosis factor, which is increased in patients with inflammatory diseases.[1]

Initially approved for the treatment of rheumatoid arthritis (RA), etanercept has subsequently received approval for the treatment of juvenile rheumatoid arthritis

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