CHAPTER 11

CERTOLIZUMAB PEGOL

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Certolizumab pegol is fragment crystallizable (Fc)-free, polyethlene glycolyated (PGEylated), antigen-binding fragment of a humanized monoclonal antibody.[1,2]

Pharmacodynamic and pharmacokinetic properties

Certolizumab pegol binds and neutralizes both membrane-bound and soluble TNF-α and inhibits signaling through both the p55 and p75 TNF-receptors in vitro.[1,2] cümlesi 'Certolizumab pegol binds and neutralizes both membrane-bound and soluble tumor necrosis factor (TNF)-α and inhibits signaling through both the p55 and p75 TNF-receptors in vitro.[1,2] It was found more potent at neutralising soluble TNF- α mediated signalling than adalimumab and infliximab, and had a similar or lesser potency than etanercept. The abilities of certolizumab pegol, adalimumab, and infliximab to neutralize membrane TNF-α mediated signaling were similar, while etanercept appeared to be about twofold less potent.[4]

Certulizumab pegol inhibits cytokine production slightly more than adalimumab and infliximab, while etanercept only causes patial inhibition.[(3,4)] Certolizumab pegol also directly induced nonapoptotic cell death in transmembrane TNF-α expressing cells. The inhibiting effect on cytokine production and direct cytotoxic effect of certulizumab pegol may explain its efficacy in the treatment of Crohn's disease (CD).[3,5]

Certolizumab pegol inhibits non-immune-stimulated degranulation of mast cells by polyethlene glycol fragment which may explain the low incidence of injection-site pain, given that such pain may be related to the inflammatory mediators relased when mast cells degranulate.[1]

It was shown that certolizumab pegol, adalimumab and infliximab distrubuted more effectively into inflamed tissue rather than noninflamed tissue. Certolizumab pegol also penetred arthritic paws more better than adalimumab and infliximab. These features may be explained by PEGlyation and smaller molecular weight.[6]

Important benefits of PEGylation are reduced immunogenicity, reduced aggregation, increased half-life and increased solubility.[3] The risk of cytotoxicity reduces, because of the lack of an Fc region.[7]

Reaching maximum plasma concentrations of certolizumab pegol takes only about 2-7 days. The elimination half-life is about 14 days.[3]

Recommendations for administration and monitoring

Certolizumab pegol was approved for the treatment of moderate to severe rheumatoid arthritis (RA), CD, psoriatic arthritis (PsA) and axial spondyloarthritis in adults patients.[8] The recommended dosing regimen is a 400 mg loading dose administered subcutaneously at weeks 0, 2 and 4, followed by 200 mg every 2 weeks or 400 mg every 4 weeks.[8,9]

Dermatological uses of Certolizumab Pegol

The usage of certolizumab pegol in dermatology is limited. There have been limited published studies in psoriasis. In a randomized, double-blind, phase 2, placebo-controlled trial in moderate to severe plaque psoriasis, patients received subcutaneous certolizumab pegol 200, 400 mg or placebo every 2 weeks until week 10. Significantly more patients receiving certolizumab pegol 200 or 400 mg achieved PASI 75 compared to the placebo group at week 12 (75 and 83 versus 7 %). A re-treatment extension study was conducted in 71 certolizumab pegol PASI 75 responders who relapsed during a 12- to 24-week observation period without treatment.[10] The efficacy observed during the re-treatment period was similar to that observed during the first treatment period. In RAPID-PsA study, rapid improvements in the signs and symptoms of PsA, including joints, skin, enthesitis, dactylitis and nail disease were observed with certolizumab pegol.[11] A case of disseminated pyoderma gangrenosum associated with RA, which was refractory to several immunosuppressive and immunomodulatory therapies, responded successfully to certolizumab pegol.[12]

Contraindications

Hypersensitivity to the active substance or to any of the excipients of the product.[9]

pegol administration. There is insufficient information on the excretion of certolizumab pegol in human or animal breast milk.[9]

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