

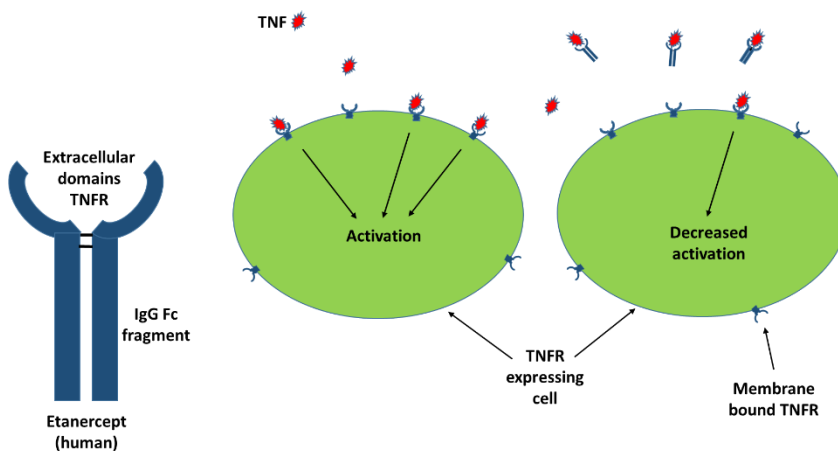
Etanercept – Fact Sheet

Molecule

Etanercept (Enbrel®) is a dimeric human receptor fusion protein consisting of the extracellular ligand-binding domain of human 75 kDa (p75) tumor necrosis factor receptor (TNFR) linked to the Fc-part of human IgG1. The Fc-part of etanercept contains CH2 domain, CH3 domain and the hinge region. The molecular weight is approximately 150 kDa.

Mode of Action

TNF is a cytokine primarily produced by activated macrophages and T cells. One of the naturally occurring receptors is p75 TNFR. Monomers of the extracellular portion of TNFR are physiologically cleaved from cell surface (soluble TNFR, sTNFR) and bind with high affinity to circulating TNF- α . As such, they act as competitive inhibitors to TNF- α preventing it from binding to cell-bound TNFRs. Thus, the fusion protein etanercept competitively inhibits binding of TNF- α to TNFRs, rendering TNF- α biologically inactive. Etanercept also modulates indirectly different biological functions such as expression of adhesion molecule E-selectin, production of interleukin-6 (IL-6) and matrix metalloproteinase 3 (MMP-3), as well as IL-1.



Indication

Etanercept is indicated for the treatment of rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, psoriatic arthritis, ankylosing spondylitis and plaque psoriasis.

Patent Situation

Enbrel® patents expired in 2012 in US and in 2015 in Europe. However, Amgen, the owner of the originator Enbrel® fights to hold off biosimilars from the market in the US until 2029 with new preparation patents.

Market and Competitive Field

Amgen's Enbrel® (co-marketed by Pfizer) has received its first approval by FDA in 1998 and by EMA in 2000. In 2019, Enbrel® had sales of 4.77 billion € (Amgen) and 1.57 billion € (Pfizer). In respect of these blockbuster sales many companies are developing or marketing biosimilars of the drug, e.g. Samsung and Sandoz. In 2019, Benepali® had sales of 442 million €.

		Etanercept
		Enbrel®
		Altebrel™, Benepali®, Brenzys™, Davictrel™, Etacept, Erelzi™, Etanar®, Inifitam, Qiangke®
Clone selection/ comparability		
HPLC	Separation based on size (SE-HPLC)	
	Separation based on hydrophobicity (RP-HPLC)	
	Detection of charge variants (CEX-HPLC)	
Binding	Binding to cell surface expressed target (Flow cytometry)	c.l.d.
	Binding to soluble target (ELISA)	
	Binding to specific antibody or antigen (SPR-BIACORE, ELISA)	n.a.
	Affinity/ kinetic to recombinant target (SPR-BIACORE)	
Effector function	Binding to C1q, ¹CDC surrogate (ELISA)	
	Affinity to recombinant Fc-receptors (SPR-BIACORE)	
	Reporter gene assays, ²ADCC surrogate (Luminescence)	c.l.d.
	¹CDC (Flow cytometry)	c.l.d.
	²ADCC (DELFA, Fluorescence)	c.l.d.
	Additional bioassays (Luminescence, fluorescence)	
Gly	Glyco-pattern with Lectin Microarray (45 different lectins)	
(Pre)clinical application		
Clinics	Pharmacokinetics – PK (ECL, ELISA)	
	Pharmacodynamics – PD (ECL, ELISA, flow cytometry, bioassay)	
	Immunogenicity - ³ADAs (ECL, Biacore, ELISA, neutr. assay)	

¹CDC = Complement Dependent Cytotoxicity
²ADCC = Antibody Dependent Cellular Cytotoxicity
³ADA = Anti-Drug Antibody

	VelaLabs portfolio
	VelaLabs planned
	c.l.d. = cell line dependent
	n.a. = not applicable
	In development