

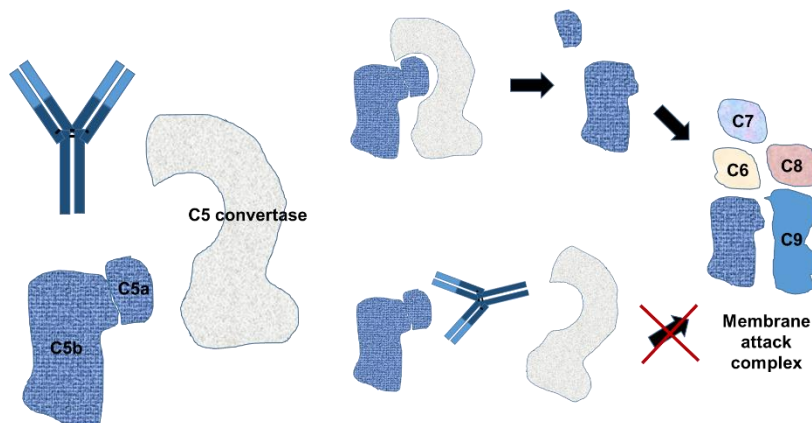
Eculizumab – Fact Sheet

Molecule

Eculizumab (Soliris®) is a humanized monoclonal antibody. This antibody is an immunoglobulin G-kappa type consisting of human constant regions and murine complementarity-determining regions. It has a molecular weight of approximately 148 kDa.

Mode of Action

Eculizumab binds to the complement component 5 (C5), which is a terminal molecule in the complement cascade. C5 normally activates cells by attracting pro-inflammatory immune cells, while also destroying cells by triggering the final pore formation. Eculizumab inhibits the cleavage of C5 by C5 convertase into C5a and C5b and subsequent generation of the terminal complement attack complex C5b-9. Paroxysmal nocturnal hemoglobinuria (PNH) patients are deficient in terminal complement inhibitors. Eculizumab thus inhibits terminal complement mediated intravascular hemolysis and therefore the destruction of erythrocytes.



Indication

Soliris® is indicated for treatment of patients with PNH to reduce hemolysis. It is also indicated for treatment of patients with atypical haemolytic uremic syndrome (aHUS) to inhibit complement mediated thrombotic microangiopathy.

Patent Situation

Patents on Soliris® will expire in US in 2021 and in Europe in 2020. In 2017, in the US new patents directed to the composition of matter and pharmaceutical formulations of eculizumab, and methods of treating PNH were issued. These patents will expire in 2027.

Market and Competitive Field

The originator product, Actelion's (now J&J) Soliris®, was first approved by FDA and EMA in 2007 for the treatment of PNH and then in 2011 for the treatment of aHUS. Both indications are ultra-rare diseases, however, with an annual cost of around 400,000 € per patient (USA, in Canada even higher), Soliris® had 1.94 billion € in global sales in 2018, which increased in 2019 to 2.03 billion €. Soliris® is thus the highest priced monoclonal antibody.

VelaLabs Portfolio

		Eculizumab
		Soliris®
	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)	
	Binding to soluble target (ELISA)	
	Binding to specific antibody or antigen (SPR-BIACORE, ELISA)	
	Affinity/ kinetic to recombinant target (SPR-BIACORE)	
Effector function	Binding to C1q, ¹ CDC surrogate (ELISA)	
	Affinity to recombinant Fc-receptors (SPR-BIACORE)	
	Reporter gene assays, ² ADCC surrogate (Luminescence)	
	¹ CDC (Flow cytometry)	
	² ADCC (DELFI, Fluorescence)	
	Additional bioassays (Luminescence, fluorescence)	Potency assay
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 - ³ ADAs (ECL, Biacore, ELISA, neutr. assay)	

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

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