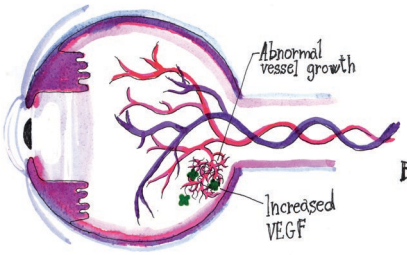
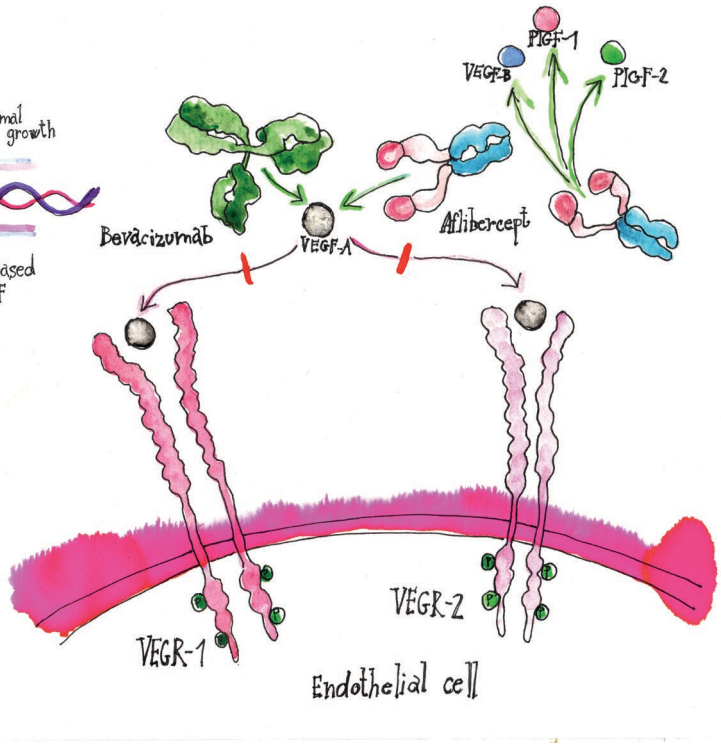
vela
LABORATORIES
A Tentamus Company





FACT SHEET

Bevacizumab

Key words

- Drug class: antibody targeting VEGF; Vascular endothelial growth factor
- Molecule: monoclonal antibody, IgG1
- Binding/inhibiting/MoA: inhibition of VEGF-A
- Originator brand name: Avastin®

Molecule

Bevacizumab (Avastin®) is a typical humanized monoclonal IgG1 / kappa antibody comprised of a tetramer of two heavy and two light chains with one N-glycosylation site per heavy chain.

Mode of Action

Bevacizumab inhibits angiogenesis (formation of new blood vessels) by blocking the interaction of Vascular Endothelial Growth Factor A (VEGF-A) with its receptors, VEGF receptor-1 or VEGF receptor-2. Bevacizumab can, therefore, also slow the growth of new blood vessels in tumors.

Indication

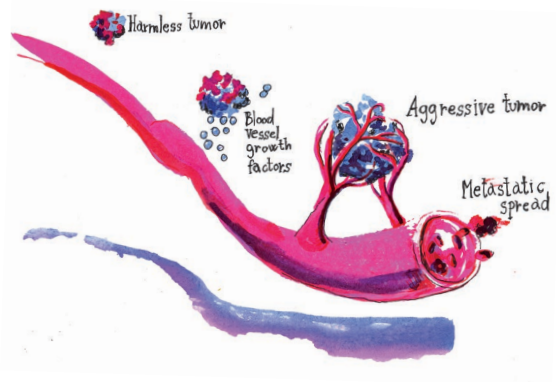
Bevacizumab is indicated for various cancers, including metastatic colorectal cancer, non-squamous non-small cell lung cancer, metastatic renal cell carcinoma, recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer, and also for a few glioblastomas.

Patent Situation

Bevacizumab patents expired in the US (2019) and will expire in the EU (2022). Roche as the owner of the originator, will defend these dates, and all biosimilar developments in the late stage will have to wait for market entry in the EU until the expiration of the patents.

Market and Competitive Field

The originator product, Roche's Avastin®, was approved by FDA in 2004 and by EMA in 2005. Avastin® had sales of 4.58 and 2.96 billion in 2020 and 2021, respectively, obviously decreasing due to biosimilars. Mvasi® from Amgen had in 2021 increased sales of already 1.08 billion € (up from 0.659 million € in 2020). Pfizer also started sales of Zirabev®, and in developing countries, non-originator biologicals are marketed as well.



We offer characterization and quality measurement by GMP, GLP, GCLP certified methods

Contact us

Contact us to discuss a custom-made characterization adapted to your quality needs.
Our experts at VelaLabs will share their experience using state-the-of-the-art equipment.
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● Ready ○ Possible × Not applicable

Bevacizumab: selected GMP, GLP, GCLP methods

Characterization of the molecule & GMP techniques

CBA - CELL BASED ASSAYS

- ○ Cell based assay
- ○ Reporter gene assay
- ● ADCC - Antibody-Dependent Cell-mediated Cytotoxicity
- ○ ADCP - Antibody-Dependent Cell-mediated Phagocytosis
- ● CDC - Complement-Dependent Cytotoxicity
- ● Proliferation assay
- ○ Neutralization assay
- ○ Primary cell assays
- ○ Flow cytometric assay
- ○ Fluorescent microscopy
- ● Bioassay
- ○ Receptor autophosphorylation bioassay
- × Glycogen formation bioassay
- × Glucose transport bioassay

LBA - LIGAND BINDING ASSAYS

- ● Binding ELISA - Enzyme-Linked Immunosorbent Assays
- ○ ELISA general (impurities, e.g. Host Cell Proteins - HCP)
- ● SPR kinetic measurements - surface plasmon resonance (Biacore)
- ● SPR potency assays (Biacore)
- ● SPR FcR affinity assays (Biacore)
- ○ MesoScaleDiscovery method

PCM - PHYSICAL-CHEMICAL METHODS

- ○ Size exclusion HPLC
- ○ Ion exchange HPLC
- ○ Reversed phase HPLC
- ○ SDS-PAGE
- ○ Western blot
- ● PCR (Polymerase Chain Reaction)
- ○ Capillary electrophoresis (in partnership with TPMD)
- ○ IEF (isoelectric focusing)

COMPENDIAL PCM METHODS (EP & USP)

- ○ pH measurement (EP 2.2.3)
- ○ Appearance (EP 2.2.1)
- ○ Turbidity (EP 2.2.1)
- ○ Colour of solution (EP 2.2.2)
- ○ Osmolality (EP 2.2.35)
- ○ Visible particles (2.9.20)
- ○ Subvisible particles (2.9.19)
- ○ Extractable volume (EP 2.9.17)
- ○ Protein concentration by OD280 (EP 2.5.33)

MIBI - MICROBIOLOGY / STERILITY ASSAYS

- ● Sterility (EP 2.6.1)
- ● Endotoxin, gel-clot limit test (EP 2.6.14)
- ● Endotoxin, chromogenic LAL test (EP 2.6.14)
- ● Endotoxin, recombinant Factor C (EP 2.6.32)

CLINICAL ANALYSIS TECHNIQUES with GLP and GCLP certification

- ○ PD - Pharmacodynamics
- ○ PK - Pharmacokinetics
- ○ ADA - Anti-Drug Antibody testing
- ○ Biomarker studies