

Avastin™ (bevacizumab)

The following is a brief summary of the uses of this drug. The complete prescribing information should be consulted before use in a specific patient.

Avastin is a monoclonal antibody with activity against vascular endothelial growth factor (VEGF) that was first approved by the FDA in 2004. VEGF stimulates new vessel growth in tumors and is a factor in the survival and permeability of existing tumor vasculature. As a vascular targeting therapy, Avastin is not directly cytotoxic. In cancer therapy it is used in combination with chemotherapy, radiation, or hormonal therapy. Avastin is also being evaluated in other diseases, including colorectal, breast, lung, prostate and renal cancers as well as in diabetic retinopathy and the wet form of age-related macular degeneration.

Pharmacology & Mechanism of Action: Bevacizumab binds to VEGF and prevents it from acting on its receptors on the surface of endothelial cells. VEGF acts specifically on vascular endothelium. It is expressed in tumor cells, macrophages, T-cells, smooth muscle cells, kidney cells, and others. Expression of VEGF is regulated by many factors. In human cancers, the increased expression of VEGF is associated with increased microvascular density, tumor growth, metastasis, and a poor prognosis. The calculated half-life of bevacizumab is about 20 days.

Indications:

- First- and Second-line treatment of metastatic carcinoma of the colon or rectum (in combination with 5-fluorouracil-based chemotherapy)
- (Oct. 2006) First-line treatment of unresectable, locally advanced, recurrent, or metastatic non-squamous, non-small cell lung cancer (NSCLC) in combination with carboplatin and paclitaxel

Contraindications, Warnings, & Precautions: Refer to boxed warning on product literature for details

- Avastin administration can result in development of gastrointestinal perforation, in some instances resulting in fatality. Gastrointestinal perforation, sometimes associated with intra-abdominal abscess, occurred throughout treatment with Avastin (i.e., was not correlated to duration of exposure). Refer to the complete boxed warning in the drug's official product literature for more information. Avastin should be permanently discontinued in patients who develop gastrointestinal perforation.
- Avastin administration can result in the development of wound dehiscence, in some instances resulting in fatality. Avastin should be permanently discontinued in patients with wound dehiscence requiring medical intervention. Because of the potential for impaired wound healing, Avastin should be held for several weeks prior to elective surgery and then after surgery for at least 28 days, or until the surgical incision is fully healed. Refer to the drug's official product literature for more details.
- Fatal pulmonary hemorrhage can occur in patients with NSCLC treated with chemotherapy and Avastin. Patients with recent hemoptysis ($\geq 1/2$ tsp red blood) should not receive Avastin.
- Avastin should be permanently discontinued in patients who develop serious bleeding, a severe thromboembolic event, or hypertensive crisis.
- The safety and efficacy of Avastin in patients with cardiac disease, including coronary artery disease, has not been established. Congestive heart failure and left ventricular dysfunction have been reported during clinical trials for metastatic colorectal cancer. Prior exposure to anthracycline chemotherapy or chest wall radiation therapy may be associated with an increased risk for CHF.
- Use Avastin with caution in patients with renal disease. Nephrotic syndrome has been reported in 0.5% of patients receiving bevacizumab in any clinical trial; one death was reported and one patient required dialysis.
- Patients receiving Avastin in combination with myelosuppressive chemotherapy may be at higher risk for developing infections, including viral infections.
- Discontinue the drug if reversible posterior leukoencephalopathy develops.
- Pregnancy Category C: human data is not available, but bevacizumab is likely to have adverse effects on the fetus. Breast-feeding is a contraindication for Avastin.
- Other side effects may be possible.



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Dosing:

- Avastin is administered by IV infusion. The dose varies according to the diagnosis and chemotherapy regimen. Usual doses for currently approved indications range from 5-15 mg/kg every 2-3 weeks.

Adverse Reactions:

- Infusion reactions are uncommon. The infusion should be stopped if a severe infusion-related reaction occurs (occurred in 0.2% of patients in clinical trials).
- Use with caution in patients with pre-existing hypertension; Avastin may increase blood pressure in both hypertensive and non-hypertensive patients.

Drug Interactions: Bevacizumab may have an effect on the pharmacokinetics of Irinotecan. Patients on both drugs may experience increased incidence of diarrhea and neutropenia. However, no drug interaction studies are available.

Monitoring:

- Check blood pressure every 2-3 weeks during treatment, and more often if hypertension develops.
- Monitor for the development or worsening of proteinuria with serial urinalysis.

Preparation, Stability and Storage: Do not shake the drug vials. Protect the drug from light and from freezing. Do not mix Avastin with dextrose solutions. Dilute each dose in 100 ml of 0.9% sodium chloride injection solution. Discard any unused solution left in the vial. The diluted solution may be stored in the refrigerator for up to 8 hours before use.

Administration: Do not administer as IV push or IV bolus. Administer the initial dose over at least 90 minutes. If the first infusion is well tolerated, the second infusion may be given over 60 minutes. If this is tolerated, all subsequent infusions may be given over 30 minutes.

References:

1. Manufacturer's information and 2. Clinical Pharmacology [database online], Tampa FL: Gold Standard, Inc.; 2006. URL: <http://www.clinicalpharmacology-ip.com/>. Updated 10/12/06.



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Remicade: Good News (Plaque Psoriasis), and Mixed Results (Asthma)

Remicade was approved by the FDA for use in chronic severe plaque psoriasis at the end of September, 2006. The approval was based on data from the phase III EXPRESS trial, in which eight of 10 patients achieved a significant benefit from the drug. Positive results were also obtained in the EXPRESS II trial, which showed a patient benefit for up to a year. The dosing schedule is a 5 mg/kg IV infusion followed by additional doses at 2 and 6 weeks after the first dose, then every 8 weeks.

On the other hand, a small study of Remicade in patients with asthma showed mixed results. The patients treated with Remicade had fewer exacerbations of their asthma, but did not show a statistically significant benefit in their morning measurement of peak expiratory flow—the primary goal of the study. Remicade did have an effect on mean diurnal peak flow variation as compared to placebo. It is likely that further clinical trials will provide a clearer picture of whether or not Remicade has significant clinical benefits in treatment of asthma.

References: www.Remicade.com and medical news sources

Infusion Partners Expands to Bowling Green, Kentucky

On October 1, 2006, Infusion Partners announced the acquisition of a home infusion pharmacy in Bowling Green, Kentucky. Manager Gary Jones, Pharm.D. will continue to lead his team of very experienced home infusion providers at this location. The southwestern Kentucky location will allow Infusion Partners to better serve patients in the Bluegrass State. The Cincinnati office already serves patients in several counties in the northern Kentucky area.

Welcome, Infusion Partners of Bowling Green!

