

BEVACIZUMAB

CLASS: Antineoplastic Agent, Monoclonal Antibody; Vascular Endothelial Growth Factor (VEGF) Inhibitor

INDICATIONS: Treatment of metastatic colorectal cancer (first-or second-line treatment and second-line after progression on a first-line treatment containing bevacizumab); treatment of unresectable, locally advanced, recurrent or metastatic nonsquamous, nonsmall cell lung cancer; treatment of progressive glioblastoma; treatment of metastatic renal cell cancer (not an approved use in Canada)

Note: Not indicated for the adjuvant treatment of colorectal cancer. For the treatment of glioblastoma, effectiveness is based on improvement in objective response rate.

AVAILABLE DOSAGE FROM THE HOSPITAL:

BEVACIZUMAB 1.25MG/0.05ML SYRG.

BEVACIZUMAB 100MG VIAL

BEVACIZUMAB 400MG VIAL

TRADE NAMES:

DOSAGE:

- **Dosing: Adult**

Details concerning dosing in combination regimens should also be consulted.

Colorectal cancer, metastatic, in combination with fluorouracil-based chemotherapy: I.V.: 5 mg/kg every 2 weeks (in combination with bolus-IFL) or 10 mg/kg every 2 weeks (in combination with FOLFOX4)

Canadian labeling: 5 mg/kg every 2 weeks (in combination with fluorouracil-based chemotherapy)

Colorectal cancer, metastatic, following first-line therapy containing bevacizumab: I.V.: 5 mg/kg every 2 weeks or 7.5 mg/kg every 3 weeks (in combination with fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin based regimen)

Glioblastoma: 10 mg/kg every 2 weeks as monotherapy or (unlabeled dosing) 10 mg/kg every 2 weeks (in combination with irinotecan) (Vredenburgh, 2007)

Nonsmall cell lung cancer (nonsquamous cell histology): I.V.: 15 mg/kg every 3 weeks (in combination with carboplatin and paclitaxel) for 4-6 cycles followed by maintenance treatment (unlabeled use) of bevacizumab 15 mg/kg every 3 weeks

as monotherapy until disease progression or unacceptable toxicity (Sandler, 2006)

Renal cell cancer, metastatic: 10 mg/kg every 2 weeks (in combination with interferon alfa) or (unlabeled dosing) 10 mg/kg every 2 weeks as monotherapy (Yang, 2003)

Age-related macular degeneration (unlabeled use/route): Intravitreal: 1.25 mg (0.05 mL) monthly until improvement/resolution, usually ~1-3 injections (Avery, 2006) or 2.5 mg (0.1 mL) every 4 weeks for 3 doses (Bashshur, 2006)

Breast cancer, metastatic (unlabeled use): I.V.: 10 mg/kg every 2 weeks (in combination with paclitaxel) (Miller, 2007)

Ovarian cancer, advanced recurrent, platinum-sensitive (unlabeled use): I.V.: 15 mg/kg every 3 weeks in combination with gemcitabine and carboplatin for 6-10 cycles, followed by 15 mg/kg as monotherapy every 3 weeks until disease progression or unacceptable toxicity (Aghajanian, 2012)

Soft tissue sarcoma, angiosarcoma (unlabeled use): I.V.: 15 mg/kg every 3 weeks until disease progression or unacceptable toxicity (Agulnik, 2013)

- **Dosing: Geriatric**

Refer to adult dosing.

- **Dosing: Renal Impairment**

There are no dosage adjustments provided in manufacturer's labeling

- **Dosing: Hepatic Impairment**

There are no dosage adjustments provided in manufacturer's labeling

- **Dosing: Adjustment for Toxicity**

I.V. administration (systemic): There are no recommended dosage reductions. Temporary suspension is recommended for severe infusion reactions, at least 4 weeks prior to (and after) elective surgery, in moderate-to-severe proteinuria (in most studies, treatment was withheld for ≥ 2 g proteinuria/24 hours), or in patients with severe hypertension which is not controlled with medical management. Permanent discontinuation is recommended (by the manufacturer) in patients who develop wound dehiscence and wound healing complications requiring intervention, necrotizing fasciitis, fistula (gastrointestinal and nongastrointestinal), gastrointestinal perforation, intra-abdominal abscess, hypertensive crisis, hypertensive encephalopathy, serious bleeding/hemorrhage, severe arterial thromboembolic event, nephrotic syndrome, or RPLS.

COMMON SIDE EFFECT:

Percentages reported as monotherapy and as part of combination chemotherapy regimens. Some studies only reported hematologic toxicities grades ≥ 4 and nonhematologic toxicities grades ≥ 3 .

>10%:

Cardiovascular: Hypertension (12% to 34%; grades 3/4: 5% to 18%), thromboembolism ($\leq 21\%$; grades 3/4: 15%; venous thromboembolism: 8%; grades 3/4: 5% to 7%; arterial thrombosis 6%; grades 3/4: 3%), hypotension (7% to 15%)

Central nervous system: Pain (8% to 62%), fatigue ($\leq 45\%$; grades 3/4: 4% to 19%), headache (24% to 37%; grades 3/4: 2% to 4%), dizziness (19% to 26%), taste disorder (14% to 21%), neuropathy (sensory, grades 3/4: 1% to 17%; in combination with paclitaxel: 24%)

Dermatologic: Alopecia (6% to 32%), xeroderma (7% to 20%), exfoliative dermatitis (3% to 19%), skin discoloration (2% to 16%)

Gastrointestinal: Abdominal pain (8% to 61%; grades 3/4: 8%), vomiting (47% to 52%; grades 3/4: $\leq 11\%$), anorexia (35% to 43%), constipation (4% to 40%), diarrhea (grades 3/4: 1% to 34%), stomatitis (30% to 32%), gastrointestinal hemorrhage (19% to 24%), dyspepsia (17% to 24%), weight loss (15% to 20%), flatulence (11% to 19%), nausea (grades 3/4: $\leq 12\%$)

Hematologic & oncologic: Hemorrhage ($\leq 40\%$; grades 3/4: 1% to 5%), leukopenia (grades 3/4: 37%), neutropenia (grade 4: 21% to 27%)

Infection: Increased susceptibility to infection ($\leq 55\%$; serious: 7% to 14%; pneumonia, catheter infection, or wound infection)

Neuromuscular & skeletal: Myalgia (8% to 19%), back pain ($\leq 12\%$)

Renal: Proteinuria (4% to 36%; grades 3/4: $\leq 7\%$; median onset: 5.6 months; median time to resolution: 6.1 months)

Respiratory: Upper respiratory tract infection (40% to 47%), epistaxis (19% to 35%), dyspnea (25% to 26%), rhinitis (3% to $>10\%$)

Miscellaneous: Postoperative wound complication (including dehiscence, 1% to 15%)

PREGNANCY RISK FACTORS: C