Bevacimab®

Bevacizumab INN

Presentation

Bevacimab®-100 concentrated solution for i.v. infusion: 1 vial of 4 ml concentrated solution for i.v. infusion contains Bevacizumab INN 100 mg.

Bevacimab®-400 concentrated solution for i.v. infusion: 1 vial of 16 ml concentrated solution for i.v. infusion contains Bevacizumab INN 400 mg.

Description

Bevacizumab is a recombinant humanized monoclonal IgG1 antibody that binds to and inhibits the biologic activity of human vascular endothelial growth factor (VEGF) in-vitro and in-vivo assay systems. Bevacizumab contains human framework regions and the complementarity-determining regions of a murine antibody that binds to VEGF. Bevacizumab has an approximate molecular weight of 149 kD. Bevacizumab is produced in a mammalian cell (Chinese Hamster Ovary) expression system in a nutrient medium containing the antibiotic gentamicin. Gentamicin is not detectable in the final product. Bevacizumab is a clear to slightly opalescent, colorless to pale brown, sterile, pH 6.2 solution for intravenous infusion.

Indications and usage

Bevacizumab is a vascular endothelial growth factor-specific angiogenesis inhibitor indicated for the treatment of:

• Metastatic colorectal cancer, with intravenous 5-fluorouracil–based chemotherapy for first-or second-line treatment.

• Metastatic colorectal cancer, with fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin based chemotherapy for second-line treatment in patients who have progressed on a first-line Bevacizumab containing regimen.

• Non-squamous non-small cell lung cancer, with carboplatin and paclitaxel for first line treatment of unresectable, locally advanced, recurrent or metastatic disease.

• Glioblastoma, as a single agent for adult patients with progressive disease following prior therapy. Effectiveness of Bevacizumab is based on improvement in objective response rate. No data available demonstrating improvement in disease-related symptoms or survival with Bevacizumab.

• Metastatic renal cell carcinoma with interferon alfa.

• Cervical cancer, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease.

• Recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer that is-

  • Platinum-resistant in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan,
  • Platinum-sensitive in combination with carboplatin and paclitaxel or in combination with carboplatin and gemcitabine, followed by Bevacizumab as a single agent.

Limitation of Use

Bevacizumab is not indicated for adjuvant treatment of colon cancer.

Dosage and administration

• Do not administer as an IV push or bolus.

• Do not initiate Bevacizumab for 28 days following major surgery (until surgical wound is fully healed).

First infusion: Administer infusion over 90 minutes. **Subsequent infusions:** Administer second infusion over 60 minutes if first infusion is tolerated; administer all subsequent infusions over 30 minutes if infusion over 60 minutes is tolerated.

Recommended Doses and Schedules

Patients should continue treatment until disease progression or unacceptable toxicity.

Metastatic Colorectal Cancer (mCRC): The recommended doses are 5 mg/kg or 10 mg/kg every 2 weeks when used in combination with intravenous 5-FU-based chemotherapy.

• Administer 5 mg/kg when used in combination with bolus-IFL.

• Administer 10 mg/kg when used in combination with FOLFOX4.

• Administer 5 mg/kg every 2 weeks or 7.5 mg/kg every 3 weeks when used in combination with a fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin based chemotherapy regimen in patients who have progressed on a first-line Bevacizumab-containing regimen.

Non-Squamous Non-Small Cell Lung Cancer (NSNSCLC): The recommended dose is 15 mg/kg every 3 weeks in combination with carboplatin and paclitaxel.

Glioblastoma:

The recommended dose is 10 mg/kg every 2 weeks.

Metastatic Renal Cell Carcinoma (mRCC):

The recommended dose is 10 mg/kg every 2 weeks in combination with interferon alfa.

Cervical Cancer:

The recommended dose of Bevacizumab is 15 mg/kg every 3 weeks as an intravenous infusion administered in combination with one of the following chemotherapy regimens: paclitaxel and cisplatin, or paclitaxel and topotecan.

Platinum-Resistant Recurrent Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer:

The recommended dose is 10mg/kg every 2 weeks in combination with one of the following intravenous chemotherapy regimens: paclitaxel, pegylated liposomal doxorubicin, or topotecan (weekly); or 15 mg/kg every 3 weeks in combination with topotecan (every 3 weeks).

Platinum-Sensitive Recurrent Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer:

The recommended dose is 15 mg/kg every 3 weeks when administered in combination with carboplatin and paclitaxel for 6 cycles and up to 8 cycles, followed by continued use of Bevacizumab 15 mg/kg every 3 weeks as a single agent until disease progression. Alternatively, 15 mg/kg every 3 weeks when administrated in combination with carboplatin and gemcitabine for 6 cycles and up to 10 cycles, followed by continued use of Bevacizumab 15 mg/kg every 3 weeks as a single agent until disease progression.

Preparation for Administration

Use appropriate aseptic technique. Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. Withdraw necessary amount of Bevacizumab and dilute in a total volume of 100 ml of 0.9% Sodium Chloride injection, USP. Discard any unused portion left in a vial, as the product contains no preservatives.

Dosage forms and strengths

• 100 mg/4 ml, single use vial

• 400 mg/16 ml, single use vial

Contraindications
None

Warnings and precautions
Perforation or Fistula: Discontinue Bevacizumab if perforation or fistula occurs.
Arterial Thromboembolic Events or ATE (e.g., myocardial infarction, cerebral infarction): Discontinue Bevacizumab for severe ATE.
Venous Thromboembolic Events or VTE: Discontinue Bevacizumab for lifethreatening VTE.
Hypertension: Monitor blood pressure and treat hypertension. Temporarily suspend Bevacizumab if not medically controlled. Discontinue Bevacizumab for hypertensive crisis or hypertensive encephalopathy.
Posterior Reversible Encephalopathy Syndrome (PRES): Discontinue Bevacizumab.
Proteinuria: Monitor urine protein. Discontinue Bevacizumab for nephrotic syndrome. Temporarily suspend Bevacizumab for moderate proteinuria.
Infusion Reactions: Stop Bevacizumab for severe infusion reactions.
Embryo-fetal Toxicity: Advise females of potential risk to a fetus and the need for use of effective contraception.
Ovarian Failure: Advise females of the potential risk.

Adverse reactions
Most common adverse reactions (incidence > 10% and at least twice the control arm rate) are epistaxis, headache, hypertension, rhinitis, proteinuria, taste alteration, dry skin, rectal hemorrhage, lacrimation disorder, back pain and exfoliative dermatitis.

Drug interactions
A drug interaction study was performed in which irinotecan was administered as part of the FOLFIRI regimen with or without Bevacizumab. The results demonstrated no significant effect of bevacizumab on the pharmacokinetics of irinotecan or its active metabolite SN38.

Use in specific populations
Pregnancy Risk Summary: Bevacizumab may cause fetal harm based on findings from animal studies and the drug's mechanism of action.

Lactation
No data are available regarding the presence of bevacizumab in human milk, the effects on the breast fed infant, or the effects on milk production. Human IgG is present in human milk, but published data suggest that breast milk antibodies do not enter the neonatal and infant circulation in substantial amounts. Because of the potential for serious adverse reactions in breastfed infants from bevacizumab, advise a nursing woman that breastfeeding is not recommended during treatment with Bevacizumab.

Females and Males of Reproductive Potential Contraception
Females
Bevacizumab may cause fetal harm when administered to a pregnant woman. Advise female patients of reproductive potential to use effective contraception during treatment with Bevacizumab and for 6 months following the last dose of Bevacizumab.

Infertility Females
Bevacizumab increases the risk of ovarian failure and may impair fertility. Inform females of reproductive potential of the risk of ovarian failure prior to starting treatment with Bevacizumab. Long term effects of Bevacizumab exposure on fertility are unknown. In a prospectively designed substudy of 179 premenopausal women randomized to receive chemotherapy with or without Bevacizumab, the incidence of ovarian failure was higher in the Bevacizumab arm (34%) compared to the control arm (2%). After discontinuation of Bevacizumab and chemotherapy, recovery of ovarian function occurred in 22% (7/32) of these Bevacizumab-treated patients.

Pediatric Use
The safety, effectiveness and pharmacokinetic profile of Bevacizumab in pediatric patients have not been established. In published literature reports, cases of non-mandibular osteonecrosis have been observed in patients under the age of 18 years who have received Bevacizumab. Bevacizumab is not approved for use in patients under the age of 18 years. Antitumor activity was not observed among eight children with relapsed glioblastoma treated with bevacizumab and irinotecan. There is insufficient information to determine the safety and efficacy of Bevacizumab in children with glioblastoma.
Animal Data Juvenile cynomolgus monkeys with open growth plates exhibited physeal dysplasia following 4 to 26 weeks exposure at 0.4 to 20 times the recommended human dose (based on mg/kg and exposure). The incidence and severity of physeal dysplasia were dose-related and were partially reversible upon cessation of treatment.

Geriatric Use In Study
Severe adverse events that occurred at a higher incidence (≥2%) in patients aged ≥65 years as compared to younger patients were asthenia, sepsis, deep thrombophlebitis, hypertension, hypotension, myocardial infarction, congestive heart failure, diarrhea, constipation, anorexia, leukopenia, anemia, dehydration, hypokalemia, and hyponatremia. The effect of Bevacizumab on overall survival was similar in elderly patients as compared to younger patients.

Overdosage
The highest dose tested in humans (20 mg/kg IV) was associated with headache in nine out of 16 patients and with severe headache in three out of 16 patients.

Storage
Store Bevacimab® vial in a refrigerator at 2–8°C. Keep vial in the outer carton due to light sensitivity. Do not freeze.

Packaging
Bevacimab®-100: Bevacimab 100 mg is supplied as a sterile, preservative free solution in 6 ml glass vial containing 100 mg of Bevacizumab INN.
Bevacimab®-400: Bevacimab 400 mg is supplied as a sterile, preservative free solution in 20 ml glass vial containing 100 mg of Bevacizumab INN.

Medicine: Keep out of reach of children

For further information, please contact: 01977 158 926
(9.00 am - 5.00 pm)

Healthcare

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HP 52436