Bevaris

Bevacizumab INN

COMPOSITION

Bevaris 100 Concentrated Solution for IV Infusion: Each vial contains Bevacizumab INN 100 mg as 4 ml concentrated solution for IV infusion.

Bevaris 400 Concentrated Solution for IV Infusion: Each vial contains Bevacizumab INN 400 mg as 16 ml concentrated solution for IV infusion.

CLINICAL PHARMACOLOGY

Mechanism of action: Bevacizumab is a vascular endothelial growth factor (VEGF) directed recombinant humanized monoclonal antibody that binds with VEGF and prevents the interaction to its receptors on the surface of endothelial cells. The interaction of VEGF with its receptors leads to endothelial cell proliferation and new blood vessel formation known as angiogenesis. Administration of Bevacizumab causes reduction of microvascular growth and inhibition of metastatic disease progression.

Pharmacokinetics: Based on population pharmacokinetic analysis at a dose of 1 to 20 mg/kg every week/every 2 weeks/ every 3 weeks, Bevacizumab pharmacokinetics are linear and the predicted time to reach more than 90% of steady state concentration is 84 days. The accumulation ratio following a dose of 10 mg/kg once every 2 weeks is 2.8. The mean central volume of distribution is 2.9 (22%) liters and the mean clearance is 0.23 l/day. The estimated half-life is 20 days (11 to 50 days).

INDICATIONS

- Metastatic colorectal cancer, in combination with intravenous 5-fluorouracil-based chemotherapy for first- or second-line treatment.
- Metastatic colorectal cancer, in combination with fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin based chemotherapy for second-line treatment in patients who have progressed on a first-line Bevacizumab-containing regimen.
- Unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer, in combination with carboplatin and paclitaxel for first-line treatment.
- Recurrent glioblastoma in adults.
- Metastatic renal cell carcinoma in combination with interferon alfa.
- Persistent, recurrent, or metastatic cervical cancer, in combination with paclitaxel and cisplatin, or paclitaxel and topotecan.
- Epithelial ovarian, fallopian tube, or primary peritoneal cancer:
  - in combination with carboplatin and paclitaxel, followed by Bevacizumab as a single agent, for stage III or IV disease following initial surgical resection.
  - in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens.
  - in combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by Bevacizumab as a single agent, for platinum sensitive recurrent disease.
- Hepatocellular Carcinoma:
  - in combination with atezolizumab for the treatment of patients with unresectable or metastatic HCC who have not received prior systemic therapy.
- Age-related Macular Degeneration (AMD)

DOSAGE AND ADMINISTRATION

Bevacizumanb is not recommended to be used within 28 days of a major surgery and until surgical wound is fully healed.

Metastatic colorectal cancer
- 5 mg/kg every 2 weeks with bolus-IFL
- 10 mg/kg every 2 weeks with FOLFOX4
- 5 mg/ kg every 2 weeks or 7.5 mg/kg every 3 weeks with fluoropyrimidine-irinotecan or fluoropyrimidine-oxaliplatin-based chemotherapy after progression on a first-line Bevacizumab containing regimen

First-Line Non–squamous non–small cell lung cancer
- 15 mg/kg every 3 weeks with carboplatin and paclitaxel

Recurrent glioblastoma
- 10 mg/kg every 2 weeks

Metastatic renal cell cancer
- 10 mg/kg every 2 weeks with interferon alfa

Persistent, recurrent, or metastatic cervical cancer
- 15 mg/kg every 3 weeks with paclitaxel and cisplatin, or paclitaxel and topotecan

Stage III or IV epithelial ovarian, fallopian tube or primary peritoneal cancer following initial surgical resection
- 15 mg/kg every 3 weeks with carboplatin and paclitaxel for up to 6 cycles, followed by 15 mg/kg every 3 weeks as a single agent, for a total of up to 22 cycles

Platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer
- 10 mg/kg every 2 weeks with paclitaxel, pegylated liposomal doxorubicin, or topotecan given every week
- 15 mg/kg every 3 weeks with topotecan given every 3 weeks

Platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer
- 15 mg/kg every 3 weeks with carboplatin and paclitaxel for 6-8 cycles, followed by 15 mg/kg every 3 weeks as a single agent
- 15 mg/kg every 3 weeks with carboplatin and gemcitabine for 6-10 cycles, followed by 15 mg/kg every 3 weeks as a single agent

Hepatocellular Carcinoma
- 15 mg/kg after administration of 1,200 mg of atezolizumab every 3 weeks.

Age-related Macular Degeneration (AMD)
- 1.25 mg/0.05 ml intravitreal injection every 4 or 8 weeks.

Bevacizumab is administered as an intravenous infusion. The first infusion is administered over 90 minutes; the second infusion is administered over 60 minutes if first infusion is tolerated. All subsequent infusions are administered over 30 minutes if second infusion over 60 minutes is tolerated.

PREPARATION AND ADMINISTRATION

Necessary amount of Bevacizumab to be withdrawn and diluted in a total volume of 100 mL of 0.9% Sodium Chloride Injection USP. DO NOT ADMINISTER OR MIX WITH DEXTROSE SOLUTION. Any unused portion left in a vial should be discarded, as the product contains no preservatives. Diluted Bevacizumab solution can be stored at 2-8°C for up to 8 hours. There are no known incompatibilities between Bevacizumab and polyvinylchloride or polyolefin bags.

Appropriate aseptic technique should be applied during preparation of the Bevacizumab solution. All parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

CONTRAINDICATIONS

None.

ADVERSE EFFECTS

Most common adverse reactions incidence (incidence > 10%) are epistaxis, headache, hypertension, rhinitis, proteinuria, taste alteration, dry skin, hemorrhage, lacrimation disorder, back pain and exfoliative dermatitis.

PRECAUTIONS

Pregnancy: Bevacizumab may cause fetal harm when administered to a pregnant woman. Female of reproductive potential should be advised to use effective contraception during treatment with Bevacizumab and for 6 months after the last dose of Bevacizumab.

Nursing mothers: Because of the potential for serious adverse reactions in breastfed infants from bevacizumab, women should be advised not to breastfeed during treatment with Bevacizumab and for 6 months following the final dose.

Pediatric use: The safety and effectiveness of Bevacizumab in pediatric patients have not been established. Bevacizumab is not approved for use in patients under the age of 18 years.

Geriatric use: The overall incidence of arterial thromboembolic events increases in patients receiving Bevacizumab with chemotherapy, this incidence is greater in patients ≥ 65 years.

Precaution in other cases:
- Discontinue for tracheoesophageal fistula, grade 4 fistula, or necrotizing fasciitis. Discontinue for severe Arterial Thromboembolic Events.
- Discontinue for Grade 4 Venous Thromboembolic Events.
- Monitor blood pressure and treat hypertension. Withhold if not medically controlled; resume once controlled. Discontinue for hypertensive crisis or hypertensive encephalopathy.
- Discontinue in case of Posterior Reversible Encephalopathy Syndrome.
- Monitor urine protein. Discontinue for nephrotic syndrome. Withhold until less than 2 grams of protein in urine.
- Decrease the infusion rate in case of infusion reactions. Discontinue for severe infusion reactions and administer medical therapy.
- Discontinue Bevacizumab in patients who develop Congestive Heart Failure.

DRUG INTERACTIONS

Based on the results of population pharmacokinetic analyses, no clinically relevant interaction of co-administered chemotherapy on Bevacizumab pharmacokinetics was observed, no clinically relevant interaction of bevacizumab was observed on the pharmacokinetics of co-administered chemotherapy either.

OVERDOSE

The highest dose tested in humans (20 mg/kg, intravenous every 2 weeks) was associated with severe migraine in several patients.

STORAGE

Store at 2-8°C temperature in a dry place. Protect from light. Do not freeze and avoid shaking. Keep out of the reach of children.

PRESENTATION

Bevaris 100 Concentrated Solution for IV Infusion: Each box contains a single-dose glass vial of Bevacizumab 100 mg.

Bevaris 400 Concentrated Solution for IV Infusion: Each box contains a single-dose glass vial of Bevacizumab 400 mg.

Manufactured by:
ARISTOPHARMA LTD.
Shampur-Kadamtali I/A, Dhaka-Bangladesh

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