

Composition:

Avastex 100 Injection: 1 vial of 4 ml concentrated solution for i.v. infusion contains Bevacizumab INN 100 mg.

Avastex 400 Injection: 1 vial of 16 ml concentrated solution for i.v. infusion contains Bevacizumab INN 400 mg.

Pharmacology:

Bevacizumab binds VEGF and prevents the interaction of VEGF to its receptors (Flt-1 and KDR) on the surface of endothelial cells. The interaction of VEGF with its receptors leads to endothelial cell proliferation and new blood vessel formation in vitro models of angiogenesis.

Indication:

Metastatic Colorectal Cancer: Bevacizumab, in combination with intravenous fluorouracil-based chemotherapy, is indicated for the first-or second-line treatment of patients with metastatic colorectal cancer (mCRC). Bevacizumab, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, is indicated for the second-line treatment of patients with mCRC who have progressed on a first-line bevacizumab product-containing regimen.

First-Line Non-Squamous Non-Small Cell Lung Cancer: Bevacizumab, in combination with carboplatin and paclitaxel, is indicated for the first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer (NSCLC).

Recurrent Glioblastoma: Bevacizumab is indicated for the treatment of recurrent glioblastoma (GBM) in adults.

Metastatic Renal Cell Carcinoma: Bevacizumab, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma (mRCC).

Persistent, Recurrent, or Metastatic Cervical Cancer: Bevacizumab, in combination with paclitaxel and cisplatin or paclitaxel and topotecan, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer.

Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer: Bevacizumab, in combination with carboplatin and paclitaxel, followed by Bevacizumab as a single agent, is indicated for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection. Bevacizumab, in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan, is indicated for the treatment of patients with platinum-resistant recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer who received no more than 2 prior chemotherapy regimens. Bevacizumab, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by Bevacizumab as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.

Hepatocellular Carcinoma: Bevacizumab, in combination with atezolizumab, is indicated for the treatment of patients with unresectable or metastatic hepatocellular carcinoma (HCC) who have not received prior systemic therapy.

Dosage & Administration

Important Administration Information: Withhold for at least 28 days prior to elective surgery. Do not administer Bevacizumab until at least 28 days following major surgery and until adequate wound healing.

Metastatic Colorectal Cancer: The recommended dosage when Bevacizumab is administered in combination with intravenous fluorouracil-based chemotherapy is:

- 5 mg/kg intravenously every 2 weeks in combination with bolus-IFL.
- 10 mg/kg intravenously every 2 weeks in combination with FOLFOX4.
- 5 mg/kg intravenously every 2 weeks or 7.5 mg/kg intravenously every 3 weeks in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy in patients who have progressed on a first-line bevacizumab product-containing regimen.

First-Line Non-Squamous Non-Small Cell Lung Cancer: The recommended dosage is 15 mg/kg intravenously every 3 weeks in combination with carboplatin and paclitaxel.

Recurrent Glioblastoma: The recommended dosage is 10 mg/kg intravenously every 2 weeks.

Metastatic Renal Cell Carcinoma: The recommended dosage is 10 mg/kg intravenously every 2 weeks in combination with interferon alfa.

Persistent, Recurrent, or Metastatic Cervical Cancer: The recommended dosage is 15 mg/kg intravenously every 3 weeks in combination with paclitaxel and cisplatin or in combination with paclitaxel and topotecan.

Hepatocellular Carcinoma: The recommended dosage is 15 mg/kg intravenously after administration of 1,200 mg of atezolizumab intravenously on the same day, every 3 weeks until disease progression or unacceptable toxicity.

Contraindications:

None

Warnings And Precautions:

Gastrointestinal Perforations and Fistulae: Serious, and sometimes fatal, gastrointestinal perforation and fistulae occurred at a higher incidence in patients receiving Bevacizumab compared to patients receiving chemotherapy. Discontinue Bevacizumab in patients who develop gastrointestinal perforation and fistulae.

Surgery and Wound Healing Complications: In patients who experience wound healing complications during Bevacizumab treatment, withhold Bevacizumab until adequate wound healing.

Hemorrhage: Do not administer Bevacizumab to patients with recent history of hemoptysis of 1/2 teaspoon or more of red blood. Discontinue in patients who develop a Grades 3-4 hemorrhage.

Arterial Thromboembolic Events: Discontinue in patients who develop a severe ATE.

Venous Thromboembolic Events: Discontinue Bevacizumab in patients with a Grade 4 VTE, including pulmonary embolism.

Hypertension: Withhold Bevacizumab in patients with severe hypertension that is not controlled with medical management; resume once controlled with medical management. Discontinue in patients who develop hypertensive crisis or hypertensive encephalopathy.

Posterior Reversible Encephalopathy Syndrome: Discontinue Bevacizumab in patients who develop PRES.

Renal Injury and Proteinuria: Discontinue in patients who develop nephrotic syndrome.

Infusion-Related Reactions: Discontinue in patients who develop a severe infusion-related reaction and administer appropriate medical therapy.

Embryo-Fetal Toxicity: Bevacizumab may cause fetal harm when administered to pregnant women.

Ovarian Failure: Long-term effects of Bevacizumab on fertility are unknown. Inform females of reproductive potential of the risk of ovarian failure prior to initiating Bevacizumab

Congestive Heart Failure (CHF): Discontinue Bevacizumab in patients who develop CHF.

Adverse Reactions

The following clinically significant adverse reactions are described in greater details in other section of the insert

Gastrointestinal Perforations and Fistulae
Surgery and Wound Healing Complications
Hemorrhage
Arterial Thromboembolic Events
Venous Thromboembolic Events
Hypertension
Posterior Reversible Encephalopathy Syndrome
Renal Injury and Proteinuria
Infusion-Related Reactions
Embryo-Fetal Toxicity
Ovarian Failure
Congestive Heart Failure (CHF)

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: Bevacizumab may cause fetal harm in pregnant women.

Lactation: No data are available regarding the presence of bevacizumab in human milk

Pediatric Use: The safety and effectiveness of Bevacizumab in pediatric patients have not been established.

Geriatric Use: The overall incidence of ATE was increased in all patients receiving Bevacizumab with chemotherapy as compared to those receiving chemotherapy alone.

Overdose:

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 vials under refrigeration at 2°C- 8°C (36° F- 46°F) in original carton to protect from light. Do not freeze. Do not shake.

Packaging:

Avastex 100 Injection: Each box contains 1 vial of Avastex 100 injection containing Bevacizumab INN 100 mg.

Avastex 400 Injection: Each box contains 1 vial of Avastex 400 injection containing Bevacizumab INN 400 mg.

Manufactured by:



Ziska Pharmaceuticals Ltd.
Kaliakoir, Gazipur, Bangladesh