SK+F

ESKAYEF PHARMACEUTICALS LTD.

Murapara, Rupganj, Narayanganj 1464, Bangladesh.

Packaging Material Code: R/PM2246
Version No.: V02

75 mm

305 mm

Bemab™

Bevacizumab INN IV Injection

DESCRIPTION

Bemab™ is a preparation of Bevacizumab. Bevacizumab is a vascular endothelial growth factor inhibitor. Bevacizumab is a recombinant humanized monoclonal IgG1 antibody that contains human framework regions and murine complementarity-determining regions. Bevacizumab is produced in a mammalian cell (Chinese Hamster Ovary) expression system. 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 in vitro models of angiogenesis. Administration of bevacizumab to xenotransplant models of colon cancer in nude (athymic) mice caused reduction of microvascular growth and inhibition of metastatic disease progression.

INDICATIONS

- Metastatic Colorectal Cancer
- Recurrent or metastatic Non-Squamous Non–Small Cell Lung Cancer
- Recurrent Glioblastoma
- Metastatic Renal Cell Carcinoma
- Persistent, Recurrent, or Metastatic Cervical Cancer
- Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer
- Hepatocellular Carcinoma

DOSAGE AND ADMINISTRATION

Important Administration Information

Withhold for at least 28 days prior to elective surgery. Do not administer **Bemab**™ until at least 28 days following major surgery and until adequate wound healing.

Metastatic Colorectal Cancer

The recommended dosage when **Bemab**™ 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.

Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer

Stage III or IV Disease Following Initial Surgical Resection

The recommended dosage is 15 mg/kg intravenously every 3 weeks in combination with carboplatin and paclitaxel for up to 6 cycles, followed by Bemab 15 mg/kg every 3 weeks as a single agent for a total of up to 22 cycles or until disease progression, whichever occurs earlier.

Recurrent Disease

a) Platinum Resistant: The recommended dosage is 10 mg/kg intravenously every 2 weeks in combination with palitaxel, pegylated liposomal doxorubicin, or topotecan (every week). The recommended dosage is 15 mg/kg intravenously every 3 weeks in combination with topotecan (every 3 weeks).

b) Platinum Sensitive: The recommended dosage is 15 mg/kg intravenously every 3 weeks, in combination with carboplatin and paclitaxel for 6 to 8 cycles, followed by Bevacizumab 15 mg/kg every 3 weeks as a single agent until disease progression. The recommended dosage is 15 mg/kg intravenously every 3 weeks, in combination with carboplatin and gemcitabine for 6 to 10 cycles, followed by Bevacizumab 15 mg/kg every 3 weeks as a single agent until disease progression.

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. Refer to the Prescribing Information for atezolizumab prior to initiation for recommended dosage information.

Preparation

- Use appropriate aseptic technique.
- Use sterile needle and syringe to prepare **Bemab**™
- Visually inspect vial for particulate matter and discoloration prior to preparation for administration. Discard vial if solution is cloudy, discolored or contains particulate matter.
- Withdraw necessary amount of **Bemab**™ and dilute in a total volume of 100 mL of 0.9% Sodium Chloride Injection USP. DO NOT ADMINISTER OR MIX WITH DEXTROSE SOLUTION.
- Discard any unused portion left in a vial, as the product contains no preservatives.
- Diluted **Bemab**™ solution may be stored at 2°C to 8°C (36°F to 46°F) for up to 8 hours, if not used immediately.
- No incompatibilities between Bevacizumab and polyvinylchloride or polyolefin bags have been observed.

Administration

- Administer as an intravenous infusion.
- 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 second infusion over 60 minutes is tolerated.

CONTRAINDICATIONS

None

SIDE 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 AND WARNINGS

- Gastrointestinal Perforations and Fistula: Discontinue for gastrointestinal perforations, tracheoesophageal fistula, grade 4 fistula, or fistula formation involving any organ.
- Surgery and Wound Healing Complications: In patients who experience wound healing complications during Bevacizumab treatment, withhold Bevacizumab until adequate wound healing. Withhold for at least 28 days prior to elective surgery. Do not administer Bevacizumab for at least 28 days following a major surgery, and until adequate wound healing. The safety of resumption of Bevacizumab after resolution of wound healing complication has not been established. Discontinue for wound healing complication of necrotizing fasciitis.
- Hemorrhage: Severe or fatal hemorrhages have occurred. Do not administer for recent hemoptysis. Discontinue for Grade 3-4 hemorrhage.
- Arterial Thromboembolic Events (ATE): Discontinue for severe ATE.
- Venous Thromboembolic Events (VTE): Discontinue for Grade 4 VTE.
- Hypertension: Monitor blood pressure and treat hypertension. Withhold if not medically controlled; resume once controlled. Discontinue for hypertensive crisis or hypertensive encephalopathy.
- Posterior Reversible Encephalopathy Syndrome (PRES): Discontinue.
- Renal Injury and Proteinuria: Monitor urine protein. Discontinue for nephrotic syndrome. Withhold until less than 2 grams of protein in urine.
- Infusion-Related Reactions: Decrease rate for infusion-related reactions. Discontinue for severe infusion-related reactions and administer medical therapy.
- Embryo-Fetal Toxicity: May cause fetal harm. Advise females of potential risk to fetus and need for use of effective contraception.
- Ovarian Failure: Advise females of the potential risk.
- Congestive Heart Failure (CHF): Discontinue Bevacizumab in patients who develop CHF.

USE IN PREGNANCY AND LACTATION

Based on findings from animal studies and its mechanism of action, Bevacizumab may cause fetal harm in pregnant women. 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. Because of the potential for serious adverse reactions in breastfed infants, advise women not to breastfeed during treatment with Bemab and for 6 months after the last 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.

DRUG INTERACTION

No clinically meaningful effect on the pharmacokinetics of irinotecan or its active metabolite SN38, interferon alfa, carboplatin or paclitaxel was observed when Bevacizumab was administered in combination with these drugs; however, 3 of the 8 patients receiving Bevacizumab with paclitaxel and carboplatin had lower paclitaxel exposure after four cycles of treatment (at Day 63) than those at Day 0, while patients receiving paclitaxel and carboplatin alone had a greater paclitaxel exposure at Day 63 than at Day 0.

PHARMACEUTICAL PRECAUTION

Store under refrigeration at 2°C to 8°C (36°F to 46°F) in the original carton until time of use to protect from light. Do not freeze or shake the vial or carton. Keep away from light and wet place. Keep out of reach of children.

PACKAGING

Bemab™ 100 Injection: Each vial contains Bevacizumab INN 100 mg.
Bemab™ 400 Injection: Each vial contains Bevacizumab INN 400 mg.

SK+F BIOLOGICS

Manufactured by
ESKAYEF PHARMACEUTICALS LIMITED
RUPGANJ, NARAYANGANJ, BANGLADESH.
TM TRADEMARK
R/PM2246 V02

PM SPECIFICATION

Creative ID: CSD_02

Job Name: Bemab Insert		**Size:** L - 305 mm, W - 75 mm	**Paper:** 60 gsm Offset Paper
No. of Color: 2 Extra	**Pantone Color Code**	Black C	2347 C

	Creative Service Department	Marketing Department	PD/QC/Contract Customer	Approved By
Comments				
Signature & Date				