Bevacizumab Products Clinical Resource

Agents: Alymsys (bevacizumab-maly- Amneal)
Avastin® (bevacizumab intravenous infusion – Genentech)
Mvasi™ (bevacizumab-awwb intravenous infusion – Amgen)
Zirabev™ (bevacizumab-bvzr intravenous infusion – Pfizer)

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OVERVIEW

Bevacizumab biosimilar products do not require prior authorization; however, the use of BRAND Avastin requires an evaluation of medical necessity, prior to approval of use EXCEPT for use in Ophthalmic conditions.

Bevacizumab is a recombinant humanized monoclonal antibody that binds to and inhibits the biologic activity of human vascular endothelial growth factor (VEGF), a key mediator of angiogenesis.[1] Bevacizumab is indicated for the following uses:

- **Cervical cancer** (persistent, recurrent, or metastatic), in combination with paclitaxel and cisplatin OR paclitaxel and topotecan.
- **Colorectal cancer (CRC)**, metastatic:
  - In combination with intravenous fluorouracil-based chemotherapy for first- or second-line treatment.
  - In combination with fluoropyrimidine-irinotecan-based or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment in patients who have progressed on a first-line bevacizumab-containing regimen.

  Limitation of use: Bevacizumab is not indicated for adjuvant treatment of colon cancer.
- **Glioblastoma**, treatment of recurrent disease in adults.
- **Hepatocellular carcinoma (HCC**), in combination with Tecentriq® (atezolizumab intravenous infusion) is indicated for the treatment of patients with unresectable or metastatic HCC who have not received prior systemic therapy.
- **Non-small cell lung cancer (NSCLC)**, non-squamous, in combination with carboplatin and paclitaxel for first-line treatment of unresectable, locally advanced, recurrent, or metastatic disease.
- **Ovarian (epithelial), fallopian tube, or primary peritoneal cancer:**
  - Recurrent disease that is platinum-resistant in combination with paclitaxel, Doxil® (doxorubicin liposome intravenous infusion; i.e., pegylated liposomal doxorubicin), or topotecan for the treatment of patients who received no more than two prior chemotherapy regimens.
  - Recurrent disease that is platinum-sensitive in combination with carboplatin and paclitaxel or in combination with carboplatin and gemcitabine, followed by bevacizumab as a single agent.
  - In combination with carboplatin and paclitaxel, followed by bevacizumab as a single agent, in patients with stage III or IV disease following initial surgical resection.
- **Renal cell carcinoma (RCC)**, metastatic, in combination with interferon alfa.

Bevacizumab is used as intraocular injections for macular degeneration, macular edema, diabetic retinopathy, and retinal vein occlusions. While bevacizumab is not FDA-approved for used as intraocular injections, data support the efficacy in preservation of visual acuity. Use is limited to experts in ophthalmic conditions that warrant VEGF therapy (e.g. Ophthalmologists, etc).

Dosing Information

Dosing varies based upon indication and the National Comprehensive Cancer Network (NCCN) has detailed dosing recommendations for various tumor types.

GUIDELINES

The use of bevacizumab is supported in clinical guidelines in numerous situations and detailed recommendations are available in NCCN. For all indications, prescribing should be in consultation with a specialist in area of expertise (e.g. Oncology, Ophthalmologist, Hematologist, etc.).

FDA-Approved Indications

Central Nervous System Tumors. Consider if the patient meets the following:

- **A)** Patient has tried at least one previous therapy; AND
  Note: Examples are temozolomide capsules or injection, etoposide, carmustine, radiotherapy.
- **B)** Patient has ONE of the following (i, ii, iii, iv, or v):
  - **i.** Anaplastic gliomas; OR
  - **ii.** Glioblastoma; OR
  - **iii.** Intracranial and spinal ependymoma (excluding subependymoma) in patient ≥ 18 years of age; OR
  - **iv.** Meningiomas; OR
  - **v.** Symptoms due to one of the following (a, b, or c):
    - **a)** Radiation necrosis; OR
    - **b)** Poorly controlled vasogenic edema; OR
    - **c)** Mass effect

Dosing. Use bevacizumab dose of 10 mg/kg administered intravenously not more frequently than once every 2 weeks.

Cervical Cancer. Consider if patient has recurrent or metastatic cervical cancer

Dosing. Use bevacizumab dose of 15 mg/kg administered intravenously not more frequently than once every 3 weeks.

Colon or Rectal Cancer Consider if the patient meets the following:

- A. Patient has recurrent, advanced or metastatic colon or rectal cancer [Stage IV]; AND
- B. The medication is used in combination with a chemotherapy regimen
  Note: Examples of chemotherapy are 5-fluorouracil with leucovorin, and may include one or both of oxaliplatin, irinotecan; capecitabine with or without oxaliplatin; irinotecan with or without oxaliplatin.

Dosing: Use one of the following dosing regimens (A, B, or C):

- **A)** Bevacizumab dose of 5 mg/kg administered intravenously not more frequently than once every 2 weeks; OR
- **B)** Bevacizumab dose of 10 mg/kg administered intravenously not more frequently than once every 2 weeks; OR
- **C)** Bevacizumab dose of 7.5 mg/kg administered intravenously not more frequently than once every 3 weeks.

Hepatocellular Carcinoma (HCC). Consider if the patient meets the following:

- **A)** The medication is used in combination with Tecentriq (atezolizumab intravenous infusion); AND
- **B)** Patient has not received prior systemic therapy

Dosing. Use bevacizumab dose of 15 mg/kg administered intravenously not more frequently than once every 3 weeks.

Non-Small Cell Lung Cancer (NSCLC). Consider if the patient meets the following:

- **A)** Patient has recurrent, advanced, or metastatic non-squamous NSCLC (i.e., adenocarcinoma, large cell, or NSCLC not otherwise specified) and meets ONE of the following criteria (i, ii, iii, or iv):
  - **i.** The tumor is positive for epidermal growth factor receptor (*EGFR*) exon 19 deletion or L858R mutations and bevacizumab is used in combination with erlotinib; OR

ii. The tumor is positive for one of the following mutations and bevacizumab is used in combination with other systemic therapies (a, b, c, d, e, or f):

Note: Examples include carboplatin plus paclitaxel or Alimta (pemetrexed intravenous infusion); cisplatin plus Alimta; and Tecentriq (atezolizumab intravenous infusion) plus carboplatin and paclitaxel.

a) Epidermal growth factor receptor (*EGFR*) exon 20 mutation; OR
b) *KRAS G12C* mutation; OR
c) *BRAF V600E*; OR
d) *NTRK1/2/3* gene fusion; OR
e) *MET* exon 14 skipping mutation; OR
f) *RET* rearrangement positive; OR

iii. Patient has previously received targeted drug therapy for an actionable mutation; OR

Note: Examples of actionable mutations include sensitizing epidermal growth factor receptor (*EGFR*) mutation, anaplastic lymphoma kinase (*ALK*) fusions, *RET* rearrangement positive, *MET* exon 14 skipping, *NTRK* gene fusion positive, *BRAF V600E* mutation positive, and ROS proto-oncogene 1 [*ROS1*] rearrangement positive.

iv. The NSCLC tumor is negative or unknown for actionable mutations and the patient meets ONE of the following criteria (a or b):

Note: Examples of actionable mutations include sensitizing epidermal growth factor receptor (*EGFR*) mutation, anaplastic lymphoma kinase (*ALK*) fusions, *RET* rearrangement positive, *MET* exon 14 skipping, *NTRK* gene fusion positive, *BRAF V600E* mutation positive, and ROS proto-oncogene 1 [*ROS1*] rearrangement positive.

a) Bevacizumab is used as initial therapy in combination with other systemic therapies; OR

Note: Examples of systemic therapies are cisplatin, carboplatin, Tecentriq (atezolizumab intravenous infusion), Alimta (pemetrexed intravenous infusion), paclitaxel.

b) Bevacizumab is used as subsequent therapy

Note: Bevacizumab can be used either as a single agent or in combination with other agents.

Dosing. Use bevacizumab dose of 15 mg/kg administered intravenously not more frequently than once every 3 weeks.

Ovarian, Fallopian Tube, or Primary Peritoneal Cancer.

Dosing. Use one of the following doses (A or B):

A) Bevacizumab dose of 15 mg/kg administered intravenously not more frequently than once every 3 weeks; OR
B) Bevacizumab dose of 10 mg/kg administered intravenously not more frequently than once every 2 weeks.

Renal Cell Cancer. Consider if the patient has advanced (e.g., relapsed, metastatic, or Stage IV) renal cell cancer

Dosing. Use bevacizumab dose of 10 mg/kg administered intravenously not more frequently than once every 2 weeks.[1]

Other Uses with Supportive Evidence

Endometrial Carcinoma. Consider if the patient has recurrent, advanced, or metastatic disease

Dosing. Use bevacizumab dose of up to 15 mg/kg administered intravenously not more frequently than once every 2 weeks.

Mesothelioma. Consider if the patient meets the following:

A) Patient has one of the following (i, ii, iii, or iv):
- **i.** Malignant pleural mesothelioma; OR
- **ii.** Malignant peritoneal mesothelioma; OR
- **iii.** Pericardial mesothelioma; OR
- **iv.** Tunica vaginalis testis mesothelioma; AND

B) One of the following applies (i, ii, or iii):
- **i.** Bevacizumab will be used in combination with a chemotherapy regimen; OR

Note: Examples of chemotherapy are Alimta (pemetrexed intravenous infusion), cisplatin, carboplatin.
- **ii.** Bevacizumab will be used in combination with Tecentriq (atezolizumab intravenous infusion); OR
- **iii.** Bevacizumab is being used as a single agent for maintenance therapy after the patient has received combination chemotherapy regimen; AND

Note: Examples of chemotherapy are Alimta (pemetrexed intravenous infusion), cisplatin, carboplatin.

Dosing. Use bevacizumab dose of 15 mg/kg administered intravenously not more frequently than once every 3 weeks.

Small Bowel Adenocarcinoma. Consider if the patient meets the following:

A) The medication is used in combination with chemotherapy

Note: Examples of chemotherapy are fluorouracil, leucovorin, and oxaliplatin (FOLFOX), capecitabine and oxaliplatin (CapeOX), fluorouracil, leucovorin, oxaliplatin, and irinotecan (FOLFOXIRI).

Dosing. Use bevacizumab dose of up to 7.5 mg/kg administered intravenously not more frequently than once every 2 weeks.

Soft Tissue Sarcoma. Consider if the patient has angiosarcoma or solitary fibrous tumor

Dosing. Use bevacizumab dose of up to 15 mg/kg administered intravenously not more frequently than once every 2 weeks.

Vulvar Cancer (Squamous Cell Carcinoma). Consider if the patient meets the following:

A) Bevacizumab is used in combination with a chemotherapy regimen

Note: Examples of chemotherapy regimen are cisplatin and paclitaxel, carboplatin and paclitaxel.

Dosing. Use bevacizumab dose of up to 15 mg/kg administered intravenously not more frequently than once every 2 weeks.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of bevacizumab products is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed as recommendation for use in NCCN Drugs and Biologic Compendium. Clinical Resources will be updated as new published data are available.

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