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AVASTIN® bevacizumab
100 MG/4 ML INJECTION FOR IV USE

NOW APPROVED FOR STAGE III OR IV OVARIAN CANCER AFTER PRIMARY SURGERY.

Avastin, in combination with carboplatin and paclitaxel, followed by Avastin 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.[1]

Avastin continues to be a leader in oncology, with 14 years of market experience in solid tumors since its first FDA approval for metastatic colorectal cancer (mCRC) in 2004.[1] See the following page for a complete list of approved indications for Avastin.

Avastin plus chemotherapy followed by single-agent Avastin demonstrated a superior median progression-free survival (PFS) benefit of >6 months compared with chemotherapy alone in stage III or IV ovarian cancer patients after primary surgery.[1]

- In the GOG-0218 study, median PFS with Avastin plus chemotherapy, followed by single-agent Avastin, was 18.2 months vs 12.0 months with chemotherapy alone (HR=0.62 [95% CI, 0.52-0.75], $P<0.0001$)[1]
- GOG-0218 was a Phase III, multicenter, randomized, double-blind, placebo-controlled, three-arm study that included 1873 patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection[1]
- The recommended dose is Avastin 15 mg/kg (starting at cycle 2) intravenously every 3 weeks in combination with carboplatin and paclitaxel for up to 6 cycles, followed by Avastin 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[1]

Select Codes for Your Reference[1,2] Note: The following Avastin codes have not changed since previously approved indications.

NDC	**10-digit** **50242-060-01** — 100-mg/4-mL single-use vial **50242-061-01** — 400-mg/16-mL single-use vial	**11-digit** **50242-0060-01** — 100-mg/4-mL single-use vial **50242-0061-01** — 400-mg/16-mL single-use vial
ICD-10-CM codes	**C48.1** — Malignant neoplasm of specified parts of peritoneum **C48.2** — Malignant neoplasm of unspecified parts of peritoneum **C48.8** — Malignant neoplasm of overlapping sites of retroperitoneum and peritoneum **C56.1** — Malignant neoplasm of right ovary	**C56.2** — Malignant neoplasm of left ovary **C56.9** — Malignant neoplasm of unspecified ovary **C57.00** — Malignant neoplasm of unspecified fallopian tube **C57.01** — Malignant neoplasm of right fallopian tube **C57.02** — Malignant neoplasm of left fallopian tube

ICD-10-CM, International Classification of Diseases, Tenth Revision, Clinical Modification; NDC, National Drug Code.

These codes are not all-inclusive; appropriate codes can vary by patient, setting of care, and payer. Correct coding is the responsibility of the provider submitting the claim for the item or service. Please check with the payer to verify codes and special billing requirements. Genentech does not make any representation or guarantee concerning reimbursement or coverage for any service or item.

For more information, please visit www.avastin-hcp.com, contact your Account Manager or Field Reimbursement Manager, or submit your inquiry at https://www.gene.com/contact-us.

Pricing[3]

Wholesale Acquisition Cost (WAC)*	$777.50 per 100-mg vial, or $7.78 per milligram
	$3,110.00 per 400-mg vial, or $7.78 per milligram

WAC is the list price for wholesalers, distributors, or other direct accounts before any rebates, discounts, stocking or distribution allowances, chargebacks, and/or other price concessions or fees that may be offered by Genentech.

*Price current as of April 1, 2018.

IMPORTANT SAFETY INFORMATION

Boxed WARNINGS

- **Gastrointestinal (GI) perforation**
  - —Serious and sometimes fatal GI perforation occurs at a higher incidence in Avastin-treated patients compared to patients treated with chemotherapy
  - —The incidence of GI perforation ranged from 0.3% to 3% across clinical studies
  - —Discontinue Avastin in patients with GI perforation
- **Surgery and wound healing complications**
  - —The incidence of wound healing and surgical complications, including serious and fatal complications, is increased in Avastin-treated patients
  - —Withhold Avastin for at least 28 days prior to elective surgery. Do not administer Avastin for at least 28 days after surgery and until the wound is fully healed
  - —Discontinue in patients with wound healing complications requiring medical intervention
- **Hemorrhage**
  - —Severe or fatal hemorrhage, including hemoptysis, GI bleeding, hematemesis, central nervous system hemorrhage, epistaxis, and vaginal bleeding, occurred up to 5-fold more frequently in patients receiving Avastin. In clinical studies, the incidence of grade ≥3 hemorrhagic events among patients receiving Avastin ranged from 0.4% to 7%
  - —Do not administer Avastin to patients with serious hemorrhage or a recent history of hemoptysis (≥1/2 tsp of red blood)
  - —Discontinue Avastin in patients who develop grade 3-4 hemorrhage

Please see the following page and accompanying Prescribing Information for additional important safety information.

All Avastin Indications Are Supported by Phase III Trials

INDICATIONS

Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Cancer (OC)	Avastin, in combination with carboplatin and paclitaxel, followed by Avastin 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. Avastin, 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. Avastin, in combination with carboplatin and paclitaxel, or with carboplatin and gemcitabine, followed by Avastin as a single agent, is indicated for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer.
Persistent, Recurrent, or Metastatic Cervical Cancer (CC)	Avastin, in combination with paclitaxel and cisplatin or paclitaxel and topotecan, is indicated for the treatment of patients with persistent, recurrent, or metastatic cervical cancer.
Metastatic Renal Cell Carcinoma (mRCC)	Avastin, in combination with interferon alfa, is indicated for the treatment of metastatic renal cell carcinoma.
Glioblastoma (GBM)	Avastin is indicated for the treatment of recurrent glioblastoma in adults.
Non-Squamous Non–Small Cell Lung Cancer (NSCLC)	Avastin, 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.
Metastatic Colorectal Cancer (mCRC)	Avastin, in combination with intravenous 5-fluorouracil-based chemotherapy, is indicated for the first- or second-line treatment of patients with metastatic colorectal cancer. Avastin, in combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy, is indicated for the second-line treatment of patients with metastatic colorectal cancer who have progressed on a first-line Avastin-containing regimen. Limitation of Use: Avastin is not indicated for adjuvant treatment of colon cancer.

IMPORTANT SAFETY INFORMATION *(cont)*

Additional serious adverse events

- Additional serious and sometimes fatal adverse events with increased incidence in the Avastin-treated arm vs chemotherapy arm included:
  - —Non-GI fistulae (<1% to 1.8%, highest in patients with cervical cancer)
  - —Arterial thromboembolic events (grade ≥3, 5%, highest in patients with GBM)
  - —Renal injury and proteinuria
    - Grade 3–4 proteinuria ranged from 0.7% to 7% in clinical studies
    - Nephrotic syndrome (<1%)
- Additional serious adverse events with increased incidence in the Avastin-treated arm vs chemotherapy arm included:
  - —Venous thromboembolism (grade ≥3, 11% seen in GOG-0240)
  - —Hypertension (grade 3–4, 5%–18%)
  - —Posterior reversible encephalopathy syndrome (PRES) (<0.5%)
  - —Congestive heart failure (CHF) (1%)
- Infusion reactions with the first dose of Avastin occurred in <3% of patients, and severe reactions occurred in 0.2% of patients
- Avoid use in patients with ovarian cancer who have evidence of recto-sigmoid involvement by pelvic examination or bowel involvement on CT scan or clinical symptoms of bowel obstruction
- Inform females of reproductive potential of the risk of ovarian failure prior to initiating treatment with Avastin

Pregnancy warning

- Based on the mechanism of action and animal studies, Avastin may cause fetal harm
- Advise female patients that Avastin may cause fetal harm, and to inform their healthcare provider of a known or suspected pregnancy
- Advise females of reproductive potential to use effective contraception during treatment with Avastin and for 6 months after the last dose of Avastin
- Advise nursing women that breastfeeding is not recommended during treatment with Avastin and for 6 months following their last dose of treatment
- Avastin may impair fertility

Most common adverse events

- Across studies, the most common adverse reactions observed in Avastin patients at a rate >10% were:
  - —Epistaxis
  - —Headache
  - —Hypertension
  - —Rhinitis
  - —Proteinuria
  - —Taste alteration
  - —Dry skin
  - —Rectal hemorrhage
  - —Lacrimation disorder
  - —Back pain
  - —Exfoliative dermatitis
- Across all studies, Avastin was discontinued in 8% to 22% of patients because of adverse reactions

Indication-specific adverse events

- In Stage III or IV OC after primary surgery, 608 patients received CP+Avastin→Avastin, 607 patients received CP+Avastin→PBO, and 602 patients received CP+PBO→PBO. Grade 3–4 adverse reactions occurring at a higher incidence (≥2%) in either of the Avastin arms vs the chemotherapy only arm were fatigue (CP+Avastin→Avastin, 9%; CP+Avastin→PBO, 6%; CP+PBO→PBO, 6%), hypertension (CP+Avastin→Avastin, 10%; CP+Avastin→PBO, 6%; CP+PBO→PBO, 2%), platelet count decreased (CP+Avastin→Avastin, 21%; CP+Avastin→PBO, 20%; CP+PBO→PBO, 15%), and white blood cell count decreased (CP+Avastin→Avastin, 51%; CP+Avastin→PBO, 53%; CP+PBO→PBO, 50%)

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

Please see accompanying full Prescribing Information, including **Boxed WARNINGS**, for additional important safety information.

References: 1. Avastin (bevacizumab) Prescribing Information. Genentech, Inc., South San Francisco, CA. June 2018. **2.** *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)*. Centers for Disease Control and Prevention website. ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Publications/ICD10CM/2018/2018-ICD-10-CM-Codes-File.zip. Accessed February 20, 2018. **3.** Red Book® Online. Micromedex Healthcare Series [database online]. Greenwood Village, CO: Truven Health Analytics; 2018. Accessed May 10, 2018.

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