BlueCross BlueShield
Federal Employee Program

BEVACIZUMAB

Avastin (bevacizumab), Alymsys (bevacizumab-maly), Avzivi* (bevacizumab-tnjn), **Mvasi** (bevacizumab-awwb), Vegzelma (bevacizumab-adcd), **Zirabev** (bevacizumab-bvzr)

Preferred products: Mvasi, Zirabev

*This medication is included in this policy but is not available on the market as of yet

RATIONALE FOR INCLUSION IN PA PROGRAM

Background

Neoplastic tissue originates as host-derived cells that proliferate atypically due to loss of ability to control growth. Vascular endothelial growth factor (VEGF) is an important regulating factor of both normal and abnormal angiogenesis (the formation of new blood cells). VEGF interacts with two different receptor tyrosine kinases, VEGFR-1 and VEGFR-2 to alter angiogenesis. Anti-VEGF pharmacotherapies have been developed with a goal of inhibiting tumor angiogenesis and thereby inhibiting growth and metastasis. Bevacizumab is a VEGF inhibitor that binds to human VEGF preventing the interaction of VEGF with its receptors (Flt-1, KDR) on the surface of endothelial cells (1-14).

Regulatory Status

FDA-approved indications: Bevacizumab is an angiogenesis inhibitor indicated for: (5-11)

1. Metastatic colorectal cancer for the first- or second-line treatment of patients with metastatic carcinoma of the colon or rectum in combination with intravenous 5-fluorouracil–based chemotherapy.
2. 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 product-containing regimen.
3. Non-squamous non-small cell lung cancer (NSCLC), with carboplatin and paclitaxel for first line treatment of unresectable, locally advanced, recurrent, or metastatic disease.
4. Glioblastoma, as a single agent for adult patients with progressive disease following prior therapy.
5. Metastatic renal cell carcinoma in combination with interferon alfa.
6. Metastatic carcinoma of the cervix, in combination with paclitaxel and cisplatin or paclitaxel and topotecan in persistent, recurrent, or metastatic disease
7. Epithelial ovarian, fallopian tube, or primary peritoneal cancer:
    a. In combination with carboplatin and paclitaxel, followed by bevacizumab as a single agent, for stage III or IV disease following initial surgical resection

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b. In combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy regimens
c. In combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by bevacizumab as a single agent, for platinum-sensitive recurrent disease
d. In combination with olaparib for the maintenance treatment of adult patients with advanced cancer who are in complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with homologous recombination deficiency (HRD) positive status defined by either:
    i. a deleterious or suspected deleterious BRCA mutation, and/or
    ii. genomic instability

8. Hepatocellular carcinoma (HCC)
    a. In combination with atezolizumab for the treatment of unresectable or metastatic HCC who have not received prior systemic therapy

Limitations of Use:

Bevacizumab is not indicated for adjuvant treatment of colon cancer (5-11).

Off Label Uses:

- In comparative trials and uncontrolled case series report improvements in visual acuity and decreased retinal thickness by optical coherence tomography following treatment with intravitreal bevacizumab for ocular diseases resulting from intravitreal neovascularization (13-14).
- Bevacizumab is also used off-label in combination with trifluridine and tipiracil after 1st line therapy for the treatment of metastatic colorectal cancer (15).

Bevacizumab carries a warning for GI perforations including wound-healing complications and hemorrhage. The reported incidence of GI perforations was 2% and hemorrhage was 31%. In both

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instances, fatalities occurred. The drug is only approved to be started 28 days after surgery and until the surgical wound is fully healed to prevent wound-healing complications (5-10).

Summary

Bevacizumab is a Vascular Endothelial Growth Factor (VEGF) inhibitor. Bevacizumab binds to human vascular endothelial growth factor (VEGF) and prevents interaction of VEGF with its receptors (Flt-1, KDR) on the surface of endothelial cells. Bevacizumab is medically necessary for the treatment of angiogenesis-dependent neoplasms as approved by the FDA. There is also an evidence base to support the off-label intravitreal use of bevacizumab for the treatment of ocular disease resulting from neovascularization (1-14).

Prior authorization is required to ensure the safe, clinically appropriate, and cost-effective use of bevacizumab while maintaining optimal therapeutic outcomes.

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