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. 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. Avastin (bevacizumab) is a Vascular Endothelial Growth Factor (VEGF) inhibitor. Avastin (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 (1-8).

Regulatory Status
FDA-approved indications: Avastin (bevacizumab) is an angiogenesis inhibitor indicated for: (5)

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 Avastin-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.


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 Avastin as a single agent, for stage III or IV disease following initial surgical resection
   b. In combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for platinum-resistant recurrent disease who received no more than 2 prior chemotherapy.

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c. In combination with carboplatin and paclitaxel or carboplatin and gemcitabine, followed by Avastin as a single agent, for platinum-sensitive recurrent disease

Limitation of Use:
Avastin is not indicated for adjuvant treatment of colon cancer (5).

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 Avastin for ocular diseases resulting from intravitreal neovascularization (7-8).

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

Summary
Avastin (bevacizumab) is medically necessary for the treatment of angiogenesis-dependent neoplasms as approved by the FDA. These indications are first- or second-line metastatic colorectal cancer; first line treatment of unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer; adults patients with progressive glioblastoma; treatment for metastatic renal cell carcinoma or metastatic colorectal cancer; persistent, recurrent, or metastatic cervical cancer; and epithelial ovarian, fallopian tube or primary peritoneal cancer. In addition, there is an evidence base to support the off-label intravitreal use of Avastin (bevacizumab) for the treatment of ocular disease resulting from neovascularization (1-8).

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

References

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