UTILIZATION MANAGEMENT MEDICAL POLICY

POLICY: Oncology (Injectable) – Bevacizumab Products Utilization Management Medical Policy
- Avastin® (bevacizumab intravenous infusion – Genentech)
- Alymsys® (bevacizumab-maly intravenous infusion – Amneal)
- Jobevne™ (bevacizumab-nwgd intravenous infusion – Biocon)
- Mvasi™ (bevacizumab-awwb intravenous infusion – Amgen)
- Vegzelma™ (bevacizumab-adcd intravenous infusion – Celltrion)
- Zirabev™ (bevacizumab-bvzr intravenous infusion – Pfizer)

REVIEW DATE: 02/26/2025; selected revision 08/20/2025

OVERVIEW

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** in combination with paclitaxel and cisplatin OR paclitaxel and topotecan for persistent, recurrent, or metastatic disease.
- **Colorectal cancer**, 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**, for treatment of recurrent disease in adults.
- **Hepatocellular carcinoma**, in combination with Tecentriq® (atezolizumab intravenous infusion) for the treatment of unresectable or metastatic disease in patients who have not received prior systemic therapy.
- **Non-small cell lung cancer (NSCLC)**, for non-squamous disease, 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), or topotecan, in 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, for stage III or IV disease in patients following initial surgical resection.
- **Renal cell carcinoma**, metastatic, in combination with interferon alfa.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of bevacizumab for uses other than ophthalmic conditions. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing document in this policy will be considered on a case-

by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills required for evaluation and diagnosis of patients treated with bevacizumab as well as the monitoring required for adverse events and long-term efficacy, approval requires bevacizumab to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of bevacizumab is recommended in those who meet one of the following criteria:

FDA-Approved Indications

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1. Central Nervous System Tumors. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
Note: For pediatric patients see Pediatric Central Nervous System Tumors.
A) Patient is ≥ 18 years of age; AND
B) Patient has tried at least one previous therapy; AND
Note: Examples are temozolomide capsules or injection, etoposide, carmustine, radiotherapy.
C) Patient has ONE of the following (i, ii, iii, iv, v, vi, vii, viii, or ix):
i. Anaplastic gliomas; OR
ii. Astrocytoma; OR
iii. Glioblastoma; OR
iv. Intracranial and spinal ependymoma (excluding subependymoma); OR
v. Meningiomas; OR
vi. Oligodendroglioma; OR
vii. Medulloblastoma; OR
viii. Neurofibromatosis type 2 vestibular schwannomas; OR
ix. Symptoms due to ONE of the following (a, b, or c):
a) Radiation necrosis; OR
b) Brain edema; OR
c) Mass effect; AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 10 mg/kg administered intravenously not more frequently than once every 2 weeks.

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2. Cervical Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i or ii):
i. Patient has recurrent or metastatic cervical cancer; OR
ii. Patient has persistent, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 15 mg/kg administered intravenously not more frequently than once every 3 weeks.

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3. Colon, Rectal, or Appendiceal Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

A) Patient is ≥ 18 years of age; AND
B) Patient has recurrent, advanced or metastatic colon, rectal, or appendiceal cancer; AND
C) The medication is used in combination with a chemotherapy regimen; AND
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.
D) The medication is prescribed by or in consultation with an oncologist.

Dosing: Approve ONE of the following dosing regimens (A, B, or C):
A) 5 mg/kg administered intravenously not more frequently than once every 2 weeks; OR
B) 10 mg/kg administered intravenously not more frequently than once every 2 weeks; OR
C) 7.5 mg/kg administered intravenously not more frequently than once every 3 weeks.

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4. Hepatocellular Carcinoma. Approve for the duration noted if the patient meets ALL of the following (A, B, C, and D):
A) Patient is ≥ 18 years of age; AND
B) Patient meets ONE of the following (i or ii):
i. Approve for 1 year (total) if the patient meets ALL of the following (a, b, and c):
a) Patient has undergone resection or ablation therapy; AND
b) Patient is at high-risk of recurrence; AND
Note: High-risk is defined as size > 5 cm, > 3 tumors, macovascular invasion, microvessel invasion on histology, or grade 3/4 histology.
c) The medication is used as adjuvant therapy; OR
ii. Approve for 1 year if the patient meets BOTH of the following (a and b):
a) The medication is used for first-line therapy; AND
b) According to the prescriber, the patient has ONE of the following [(1) or (2)]:
(1) Liver-confined, unresectable disease and is deemed ineligible for transplant; OR
(2) Extrahepatic/metastatic disease and is deemed ineligible for resection, transplant, or locoregional therapy; AND
C) The medication is used in combination with Tecentriq (atezolizumab intravenous infusion); AND
D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 15 mg/kg administered intravenously not more frequently than once every 3 weeks.

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5. Non-Small Cell Lung Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
A) Patient is ≥ 18 years of age; AND
B) Patient does not have a history of recent hemoptysis; AND
C) Patient has recurrent, advanced, or metastatic non-squamous non-small cell lung cancer (NSCLC) and meets ONE of the following (i, ii, iii, iv, or v):
Note: Non-squamous NSCLC includes adenocarcinoma, large cell, or NSCLC not otherwise specified.
i. The NSCLC tumor is negative or unknown for actionable mutations and the patient meets ONE of the following (a, b, or c):
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, *NRG1*,

and ROS proto-oncogene 1 (*ROS1*) rearrangement positive. The tumor may be *KRAS G12C* mutation positive.

a) The medication is used as initial therapy in combination with other systemic therapies; OR
Note: Examples of systemic therapies are cisplatin, carboplatin, Tecentriq (atezolizumab intravenous infusion), pemetrexed, paclitaxel.

b) The medication is used as continuation maintenance therapy and meets ONE of the following [(1), (2), or (3)]:
(1) The medication is used as a single agent; OR
(2) The medication is used in combination with Tecentriq, if Tecentriq was used in combination with bevacizumab for first-line therapy; OR
(3) The medication is used in combination with pemetrexed, if pemetrexed was used in combination with bevacizumab for first-line therapy; OR

c) The medication is used as subsequent therapy in combination with other systemic therapies; OR
Note: Examples of systemic therapies are cisplatin, carboplatin, pemetrexed, paclitaxel.

ii. The tumor is positive for (*EGFR*) exon 19 deletion or exon 21 *L858R* mutations and the patient meets ONE of the following (a or b):

a) The medication is used as first-line or continuation maintenance therapy in combination with erlotinib; OR

b) The medication is used as subsequent therapy following prior targeted therapy; OR
Note: Examples of targeted therapy include Gilotrif (afatinib tablets), Tagrisso (osimertinib tablets), erlotinib, Iressa (gefitinib tablets), Vizimpro (dacomitinib tablets).

iii. Patient meets ALL of the following (a, b, and c):

a) The medication is used first-line; AND

b) The medication is used in combination with other systemic therapies; AND
Note: Examples of systemic therapies include carboplatin plus paclitaxel or pemetrexed; cisplatin plus pemetrexed; and Tecentriq plus carboplatin and paclitaxel.

c) The tumor is positive for ONE of the following mutations [(1), (2), or (3)]:
(1) *EGFR* exon 20 mutation; OR
(2) *ERBB2* (HER2) mutation; OR
(3) *NRG1* gene fusion; OR

iv. Patient meets ALL of the following (a, b, and c):

a) The medication is used as first-line or subsequent therapy; AND

b) The medication is used in combination with other systemic therapies; AND
Note: Examples of systemic therapies include carboplatin plus paclitaxel or pemetrexed; cisplatin plus pemetrexed; and Tecentriq plus carboplatin and paclitaxel.

c) The tumor is positive for ONE of the following mutations [(1), (2), or (3)]:
(1) *BRAF V600E* mutation; OR
(2) *NTRK1/2/3* gene fusion positive; OR
(3) *MET* exon 14 skipping mutation; OR

v. Patient meets ALL of the following (a, b, c, and d):

a) The medication is used as subsequent therapy; AND

b) The medication is used in combination with other systemic therapies; AND
Note: Examples of systemic therapies include carboplatin plus paclitaxel or pemetrexed; cisplatin plus pemetrexed; and Tecentriq plus carboplatin and paclitaxel.

c) The tumor is positive for ONE of the following mutations [(1), (2), (3), or (4)]:
(1) *EGFR S768I, L861Q*, and/or *G719X* mutation; OR
(2) *ALK* rearrangement positive; OR
(3) *ROS1* rearrangement positive; OR
(4) *RET* rearrangement; AND

d) Patient has previously received targeted drug therapy for the specific mutation; AND

Note: Examples of targeted drug therapy include Gilotrif (afatinib tablets), Tagrisso (osimertinib tablets), erlotinib, Iressa (gefitinib tablets), Vizimpro (dacomitinib tablets), Xalkori (crizotinib capsules), Rozlytrek (entrectinib capsules), Zykadia (ceritinib tablets), Gavreto (pralsetinib capsules), Retevmo (selpercatinib capsules and tablets), and Cometriq (cabozantinib capsules and tablets).

D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 15 mg/kg administered intravenously not more frequently than once every 3 weeks.

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6. Ovarian, Fallopian Tube, or Primary Peritoneal Cancer. Approve for 1 year if the patient meets BOTH of the following (A and B):

A) Patient is ≥ 18 years of age; AND

B) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve ONE of the following doses (A or B):

A) Up to 15 mg/kg administered intravenously not more frequently than once every 3 weeks; OR

B) 10 mg/kg administered intravenously not more frequently than once every 2 weeks.

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7. Renal Cell Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

A) Patient is ≥ 18 years of age; AND

B) Patient has relapsed, metastatic, or stage IV renal cell cancer; AND

C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 10 mg/kg administered intravenously not more frequently than once every 2 weeks.

Other Uses with Supportive Evidence

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8. Ampullary Adenocarcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):

A) Patient is ≥ 18 years of age; AND

B) Patient has intestinal type disease; AND

C) The medication is used in combination with chemotherapy; AND
Note: Examples of chemotherapy include FOLFOX (leucovorin, fluorouracil, oxaliplatin), FOLFIRI (leucovorin, fluorouracil, irinotecan), FOLFIRINOX (leucovorin, fluorouracil, oxaliplatin, irinotecan), and CapeOX (capecitabine, oxaliplatin).

D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 7.5 mg/kg administered intravenously not more frequently than once every 3 weeks.

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9. Endometrial Carcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):

A) Patient is ≥ 18 years of age; AND

B) Patient has recurrent, advanced, or metastatic disease; AND

C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 15 mg/kg administered intravenously not more frequently than once every 3 weeks.

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10. Mesothelioma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has ONE of the following (i, ii, iii, or iv):
  - **i.** Pleural mesothelioma; OR
  - **ii.** Peritoneal mesothelioma; OR
  - **iii.** Pericardial mesothelioma; OR
  - **iv.** Tunica vaginalis testis mesothelioma; AND
- **C)** Patient meets ONE of the following (i or ii):
  - **i.** The medication will be used in combination with a chemotherapy regimen; OR
    Note: Examples of chemotherapy are pemetrexed, cisplatin, carboplatin.
  - **ii.** The medication will be used in combination with Tecentriq (atezolizumab intravenous infusion); AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 15 mg/kg administered intravenously not more frequently than once every 3 weeks.

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11. Neovascular or Vascular Ophthalmic Conditions. Approve for 3 years.
Note: Examples of neovascular or vascular ophthalmic conditions include diabetic macular edema (includes patients with diabetic retinopathy and diabetic macular edema), macular edema following retinal vein occlusion, myopic choroidal neovascularization, neovascular (wet) age-related macular degeneration, other neovascular diseases of the eye (e.g., neovascular glaucoma, retinopathy of prematurity, sickle cell neovascularization, choroidal neovascular conditions).

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12. Pediatric Central Nervous System Tumors. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient is < 18 years of age; AND
- **B)** Patient has ONE of the following (i or ii):
  - **i.** Pediatric-type diffuse high-grade glioma; OR
    Note: Examples include diffuse hemispheric glioma, diffuse pediatric-type high-grade glioma, infant-type hemispheric glioma, and diffuse midline glioma.
  - **ii.** Pediatric medulloblastoma; AND
- **C)** Patient has recurrent or progressive disease; AND
- **D)** The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 10 mg/kg administered intravenously not more frequently than once every 2 weeks.

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13. Small Bowel Adenocarcinoma. Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has advanced or metastatic disease; AND
- **C)** The medication is used in combination with chemotherapy; AND
  Note: Examples of chemotherapy are fluorouracil, leucovorin, and oxaliplatin (FOLFOX), capecitabine and oxaliplatin (CapeOX), fluorouracil, leucovorin, oxaliplatin, and irinotecan (FOLFIRINOX).

D) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 7.5 mg/kg administered intravenously not more frequently than once every 2 weeks.

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14. Soft Tissue Sarcoma. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Patient has angiosarcoma or solitary fibrous tumor; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve up to 15 mg/kg administered intravenously not more frequently than once every 2 weeks.

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15. Vaginal Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Patient has advanced, recurrent, or metastatic disease; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 15 mg/kg administered intravenously not more frequently than once every 3 weeks.

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16. Vulvar Cancer. Approve for 1 year if the patient meets ALL of the following (A, B, and C):
A) Patient is ≥ 18 years of age; AND
B) Patient has advanced, recurrent, or metastatic disease; AND
C) The medication is prescribed by or in consultation with an oncologist.

Dosing. Approve 15 mg/kg administered intravenously not more frequently than once every 3 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 in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	**Central Nervous System Tumors:** A requirement was added that the patient is ≥ 18 years of age. A Note was added for pediatric patients to refer to the Pediatric Central Nervous System Tumors criteria. Astrocytoma and oligodendroglioma were added as additional options for approval. **Cervical Cancer:** A requirement was added that the patient is ≥ 18 years of age. The option of approval was added that the patient has persistent, recurrent, or metastatic small cell neuroendocrine carcinoma of the cervix. **Colon, Rectal, or Appendiceal Cancer:** Appendiceal was added to the condition of approval. A requirement was added that the patient is ≥ 18 years of age. Appendiceal was added to the requirement that the patient has recurrent, advanced, or metastatic disease. **Hepatocellular Carcinoma:** A requirement was added that the patient is ≥ 18 years of age. A requirement was added that the patient has Child-Pugh Class A disease. Criteria were added that the patient has unresectable or metastatic hepatocellular carcinoma and according to the prescriber, the patient is not a surgical candidate as options for approval. **Non-Small Cell Lung Cancer (NSCLC):** A requirement was added that the patient is ≥ 18 years of age. A requirement was added that the patient does NOT have a history of recent hemoptysis. Adenocarcinoma, large cell or NSCLC not otherwise specified were moved to a Note. For NSCLC that is negative for actionable mutations, continuation maintenance therapy was added as an option of approval. In combination with other systemic therapies was added to the subsequent therapy option for approval. To the epidermal growth factor receptor exon 19 deletion or exon 21 L858R mutations option for approval, exon 21 descriptor was added. As first-line or continuation maintenance therapy was added to the in combination with erlotinib option of approval. The medication is used as subsequent therapy following prior targeted therapy was added as an option of approval. The medication is used for first-line treatment was added as an option of approval. ERBB2 was added as an option of approval for first-line therapy. Requirements for first-line or subsequent therapy (based on genetic markers) were added. Separately, requirements for subsequent therapy (based on genetic markers) were added. **Ovarian, Fallopian Tube, or Primary Peritoneal Cancer:** A requirement was added that the patient is ≥ 18 years of age. The descriptor "up to" was added to the recommended dose. **Renal Cell Carcinoma:** A requirement was added that the patient is ≥ 18 years of age. The descriptor of "advanced" was removed from requirement that the patient has relapsed, metastatic, or stage IV disease. **Ampullary Adenocarcinoma:** This was added as a new condition of approval. **Endometrial Carcinoma:** A requirement was added that the patient is ≥ 18 years of age. The frequency of dosing was changed from once every 2 weeks to once every 3 weeks. **Mesothelioma:** A requirement was added that the patient is ≥ 18 years of age. Bevacizumab was removed if used as a single agent for maintenance therapy as an option of approval. **Pediatric central Nervous System Tumors:** This was added new condition of approval. **Small Bowel Adenocarcinoma:** A requirement was added that the patient is ≥ 18 years of age. A requirement was added that the patient has advanced or metastatic disease. **Soft Tissue Sarcoma:** A requirement was added that the patient is ≥ 18 years of age.	03/22/2023

	Vulvar Cancer: Squamous cell carcinoma was removed from the condition of approval. A requirement was added that the patient is ≥ 18 years of age. A requirement was added that the patient has advanced, recurrent, or metastatic disease. The descriptor "up to" was removed from the recommended dosing regimen. The frequency of dosing was changed from once every 2 weeks to once every 3 weeks.	
Annual Revision	**Hepatocellular Carcinoma:** Remove requirement that the patient has unresectable or metastatic hepatocellular carcinoma or according to the prescriber, the patient is not a surgical candidate. Added "or B" to requirement that the patient has Child-Pugh Class A or B disease. Added requirement that the patient has unresectable disease and is not a transplant candidate; OR has liver-confined disease, inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease; OR has metastatic disease or extensive liver tumor burden. **Non-Small Cell Lung Cancer:** Added *KRAS G12C* is not considered an actionable mutation (the tumor may be *KRAS G12C* mutation positive) to requirement that the patient is negative or unknown for actionable mutations. Removed *KRAS G12C* mutation from requirement that the tumor is positive for one of the following mutations for first-line use. **Mesothelioma:** Removed "malignant" from malignant pleural mesothelioma and malignant peritoneal mesothelioma. **Pediatric Central Nervous System Tumors:** Added pediatric medulloblastoma as an option for approval. Removed requirement that the medication is used for palliation.	03/20/2024
Annual Revision	**Central Nervous System Tumors:** Medulloblastoma and neurofibromatosis type 2 vestibular schwannomas added as new options for approval. Removed poorly control vasogenic from brain edema option for approval. **Hepatocellular Carcinoma:** Changed approval duration from 1 year to duration noted. Patient has Child-Pugh Class A or B disease and patient has not received prior systemic therapy were removed as requirements. Added new option for approval for 1 year (total), if patient has undergone resection or ablation therapy, patient is at high-risk of recurrence, and medication is used as adjuvant therapy. Added option for approval for 1 year if the medication is used for first-line therapy and the patient has liver-confined, unresectable disease and is deemed ineligible for transplant or the patient has extrahepatic/metastatic disease and is deemed ineligible for resection, transplant, or locoregional therapy. Removed liver-confined disease, inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease as an option for approval. **Non-Small Cell Lung Cancer:** Added *NRG1* and removed *KRAS G12C* is not considered an actionable mutation from the Note with examples of actionable mutations. Added *NRG1* as an option of approval for first-line use. Removed *RET* rearrangement as an option for approval for first-line or subsequent therapy. Added *RET* rearrangement as an option for approval for subsequent therapy and added additional targeted drug therapies to the Note. **Vaginal Cancer:** Added new condition of approval. **Vulvar Cancer:** Removed bevacizumab is used in combination with a chemotherapy regimen as a requirement.	02/26/2025
Selected Revision	Jobevne (bevacizumab-nwgd) was added to the policy; the same criteria apply as the other bevacizumab products.	08/20/2025