Utilization Review Policy 238A

POLICY: Biosimilars – Avastin, Alymsys and Vegzelma

- Avastin® (bevacizumab for intravenous injection – Genentech, Inc.)
- Alymsys® (bevacizumab-maly – Amneal Pharmaceuticals)
- Vegzelma™ (bevacizumab-adcd intravenous infusion – Celltrion)

EFFECTIVE DATE: 1/1/2021
LAST REVISION DATE: 3/20/2024

COVERAGE CRITERIA FOR: UCare Medicaid and Exchange Plans Only (PMAP, Connect, MSC+, MnCare, all Individual and Family Plans)

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 Avastin, Alymsys or Vegzelma is recommended for requests meeting both the biosimilar step therapy requirements and indication requirements. **Note: Ophthalmic indications do not require a prior authorization.** See ICD-10 codes not requiring authorization below.

Preferred Biosimilar Step Therapy Requirements (New Starts Only)

Criteria. *The patient must meet the following criteria (A or B):*

A) For patients new to Avastin, Alymsys or Vegzelma therapy only, must have a trial of Mvasi or Zirabev prior to approval of Avastin, Alymsys or Vegzelma. New starts to therapy defined as no use of Avastin, Alymsys, or Vegzelma within the past 180 days for Medicaid and Commercial patients.

B) Patient has a contraindication or other clinical reason why a preferred biosimilar cannot be tried before Avastin, Alymsys or Vegzelma.

Note: Preferred biosimilar step only required for indications FDA-Approved for both Avastin, Alymsys or Vegzelma and the preferred biosimilar(s).

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, or vii):

- **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.** Symptoms due to ONE of the following (a, b, or c):
  - **a)** Radiation necrosis; OR
  - **b)** Poorly controlled vasogenic 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.

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 1 year if the patient meets ALL of the following (A, B, C, D, E, and F):
- **A)** Patient is ≥ 18 years of age; AND
- **B)** Patient has Child-Pugh Class A or B disease; AND
- **C)** According to the prescriber, the patient has ONE of the following (i, ii, or iii):
  - **i.** Unresectable disease and is not a transplant candidate; OR
  - **ii.** Liver-confined disease, inoperable by performance status, comorbidity, or with minimal or uncertain extrahepatic disease; OR
  - **iii.** Metastatic disease or extensive liver tumor burden; AND
- **D)** The medication is used in combination with Tecentriq (atezolizumab intravenous infusion); AND
- **E)** Patient has not received prior systemic therapy; AND
- **F)** 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, and ROS proto-oncogene 1 (*ROS1*) rearrangement positive. *KRAS G12C* is not considered an actionable mutation (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 tablet), Tagrisso (osimertinib tablet), erlotinib, Iressa (gefitinib tablet), Vizimpro (dacomitinib tablet).

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) or (2)]:
  - **(1)** *EGFR* exon 20 mutation; OR
  - **(2)** *ERBB2* (HER2) mutation; 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), (3), or (4)]:
  - **1)** *BRAF V600E* mutation; OR
  - **2)** *NTRK1/2/3* gene fusion positive; OR
  - **3)** *MET* exon 14 skipping mutation; OR
  - **4)** *RET* rearrangement positive; 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), or (3)]
- **1)** *EGFR S768I, L861Q*, and/or *G719X* mutation; OR
- **2)** *ALK* rearrangement positive; OR
- **3)** *ROS1* rearrangement positive; AND

d) Patient has previously received targeted drug therapy for the specific mutation; AND
Note: Examples of targeted drug therapy include Gilotrif (afatinib tablet), Tagrisso (osimertinib tablet), erlotinib, Iressa (gefitinib tablet), Vizimpro (dacomitinib tablet), Xalkori (crizotinib capsule), Rozlytrek (entrectinib capsule), or Zykadia (ceritinib tablet).

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.[1]

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.** Bevacizumab will be used in combination with a chemotherapy regimen; OR
    Note: Examples of chemotherapy are pemetrexed, cisplatin, carboplatin.
  - **ii.** Bevacizumab 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.

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.

15. Vulvar 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 advanced, recurrent, or metastatic disease; AND
- **C)** Bevacizumab is used in combination with a chemotherapy regimen; AND
  Note: Examples of chemotherapy regimen are cisplatin and paclitaxel, carboplatin and paclitaxel.
- **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.

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.

ICD-10 CODES NOT REQUIRING AUTHORIZATION

Avastin will require an authorization for any submitted ICD-10 code except for the following.

ICD-10 CODE	DESCRIPTION
E08.311	Diabetes mellitus due to underlying condition with unspecified diabetic retinopathy with macular edema
E08.3211	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema, right eye

ICD-10 CODE	DESCRIPTION
E08.3212	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema, left eye
E08.3213	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema, bilateral
E08.3311	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema, right eye
E08.3312	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema, left eye
E08.3313	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema, bilateral
E08.3411	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema, right eye
E08.3412	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema, left eye
E08.3413	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema, bilateral
E08.3511	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema, right eye
E08.3512	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema, left eye
E08.3513	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema, bilateral
E08.3521	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye
E08.3522	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye
E08.3523	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral
E08.3531	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye
E08.3532	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye
E08.3533	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral
E08.3541	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye
E08.3542	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye
E08.3543	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral

ICD-10 CODE	DESCRIPTION
E08.3551	Diabetes mellitus due to underlying condition with stable proliferative diabetic retinopathy, right eye
E08.3552	Diabetes mellitus due to underlying condition with stable proliferative diabetic retinopathy, left eye
E08.3553	Diabetes mellitus due to underlying condition with stable proliferative diabetic retinopathy, bilateral
E08.3591	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy without macular edema, right eye
E08.3592	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy without macular edema, left eye
E08.3593	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy without macular edema, bilateral
E09.311	Drug or chemical induced diabetes mellitus with unspecified diabetic retinopathy with macular edema
E09.3211	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye
E09.3212	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye
E09.3213	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral
E09.3311	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye
E09.3312	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye
E09.3313	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral
E09.3411	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye
E09.3412	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye
E09.3413	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral
E09.3511	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye
E09.3512	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye
E09.3513	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral
E09.3521	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye
E09.3522	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye

ICD-10 CODE	DESCRIPTION
E09.3523	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral
E09.3531	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye
E09.3532	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye
E09.3533	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral
E09.3541	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye
E09.3542	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye
E09.3543	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral
E09.3551	Drug or chemical induced diabetes mellitus with stable proliferative diabetic retinopathy, right eye
E09.3552	Drug or chemical induced diabetes mellitus with stable proliferative diabetic retinopathy, left eye
E09.3553	Drug or chemical induced diabetes mellitus with stable proliferative diabetic retinopathy, bilateral
E09.3591	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye
E09.3592	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye
E09.3593	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral
E10.311	Type 1 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E10.3211	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye
E10.3212	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye
E10.3213	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral
E10.3311	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye
E10.3312	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye
E10.3313	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral
E10.3411	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye

ICD-10 CODE	DESCRIPTION
E10.3412	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye
E10.3413	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral
E10.3511	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye
E10.3512	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye
E10.3513	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral
E10.3521	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye
E10.3522	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye
E10.3523	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral
E10.3531	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye
E10.3532	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye
E10.3533	Type 1 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral
E10.3541	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye
E10.3542	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye
E10.3543	Type 1 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral
E10.3551	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, right eye
E10.3552	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, left eye
E10.3553	Type 1 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral
E10.3591	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye
E10.3592	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye
E10.3593	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral
E11.311	Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E11.3211	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye
E11.3212	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye

ICD-10 CODE	DESCRIPTION
E11.3213	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral
E11.3311	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye
E11.3312	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye
E11.3313	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral
E11.3411	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye
E11.3412	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye
E11.3413	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral
E11.3511	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye
E11.3512	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye
E11.3513	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral
E11.3521	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye
E11.3522	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye
E11.3523	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral
E11.3531	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye
E11.3532	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye
E11.3533	Type 2 diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral
E11.3541	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye
E11.3542	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye
E11.3543	Type 2 diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral
E11.3551	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, right eye
E11.3552	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, left eye
E11.3553	Type 2 diabetes mellitus with stable proliferative diabetic retinopathy, bilateral

ICD-10 CODE	DESCRIPTION
E11.3591	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye
E11.3592	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye
E11.3593	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral
E13.311	Other specified diabetes mellitus with unspecified diabetic retinopathy with macular edema
E13.3211	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, right eye
E13.3212	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, left eye
E13.3213	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema, bilateral
E13.3311	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, right eye
E13.3312	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, left eye
E13.3313	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema, bilateral
E13.3411	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, right eye
E13.3412	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, left eye
E13.3413	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema, bilateral
E13.3511	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, right eye
E13.3512	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, left eye
E13.3513	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema, bilateral
E13.3521	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, right eye
E13.3522	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, left eye
E13.3523	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment involving the macula, bilateral
E13.3531	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, right eye
E13.3532	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, left eye

ICD-10 CODE	DESCRIPTION
E13.3533	Other specified diabetes mellitus with proliferative diabetic retinopathy with traction retinal detachment not involving the macula, bilateral
E13.3541	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, right eye
E13.3542	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, left eye
E13.3543	Other specified diabetes mellitus with proliferative diabetic retinopathy with combined traction retinal detachment and rhegmatogenous retinal detachment, bilateral
E13.3551	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, right eye
E13.3552	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, left eye
E13.3553	Other specified diabetes mellitus with stable proliferative diabetic retinopathy, bilateral
E13.3591	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, right eye
E13.3592	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, left eye
E13.3593	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema, bilateral
H21.1X1	Other vascular disorders of iris and ciliary body, right eye
H21.1X2	Other vascular disorders of iris and ciliary body, left eye
H21.1X3	Other vascular disorders of iris and ciliary body, bilateral
H21.1X9	Other vascular disorders of iris and ciliary body, unspecified eye
H34.8110	Central retinal vein occlusion, right eye, with macular edema
H34.8111	Central retinal vein occlusion, right eye, with retinal neovascularization
H34.8112	Central retinal vein occlusion, right eye, stable
H34.8120	Central retinal vein occlusion, left eye, with macular edema
H34.8121	Central retinal vein occlusion, left eye, with retinal neovascularization
H34.8122	Central retinal vein occlusion, left eye, stable
H34.8130	Central retinal vein occlusion, bilateral, with macular edema
H34.8131	Central retinal vein occlusion, bilateral, with retinal neovascularization
H34.8132	Central retinal vein occlusion, bilateral, stable
H34.8310	Tributary (branch) retinal vein occlusion, right eye, with macular edema
H34.8311	Tributary (branch) retinal vein occlusion, right eye, with retinal neovascularization

ICD-10 CODE	DESCRIPTION
H34.8312	Tributary (branch) retinal vein occlusion, right eye, stable
H34.8320	Tributary (branch) retinal vein occlusion, left eye, with macular edema
H34.8321	Tributary (branch) retinal vein occlusion, left eye, with retinal neovascularization
H34.8322	Tributary (branch) retinal vein occlusion, left eye, stable
H34.8330	Tributary (branch) retinal vein occlusion, bilateral, with macular edema
H34.8331	Tributary (branch) retinal vein occlusion, bilateral, with retinal neovascularization
H34.8332	Tributary (branch) retinal vein occlusion, bilateral, stable
H35.051	Retinal neovascularization, unspecified, right eye
H35.052	Retinal neovascularization, unspecified, left eye
H35.053	Retinal neovascularization, unspecified, bilateral
H35.059	Retinal neovascularization, unspecified, unspecified eye
H35.3210	Exudative age-related macular degeneration, right eye, stage unspecified
H35.3211	Exudative age-related macular degeneration, right eye, with active choroidal neovascularization
H35.3212	Exudative age-related macular degeneration, right eye, with inactive choroidal neovascularization
H35.3213	Exudative age-related macular degeneration, right eye, with inactive scar
H35.3220	Exudative age-related macular degeneration, left eye, stage unspecified
H35.3221	Exudative age-related macular degeneration, left eye, with active choroidal neovascularization
H35.3222	Exudative age-related macular degeneration, left eye, with inactive choroidal neovascularization
H35.3223	Exudative age-related macular degeneration, left eye, with inactive scar
H35.3230	Exudative age-related macular degeneration, bilateral, stage unspecified
H35.3231	Exudative age-related macular degeneration, bilateral, with active choroidal neovascularization
H35.3232	Exudative age-related macular degeneration, bilateral, with inactive choroidal neovascularization
H35.3233	Exudative age-related macular degeneration, bilateral, with inactive scar
H35.351	Cystoid macular degeneration, right eye
H35.352	Cystoid macular degeneration, left eye
H35.353	Cystoid macular degeneration, bilateral
H35.359	Cystoid macular degeneration, unspecified eye

ICD-10 CODE	DESCRIPTION
H35.81	Retinal edema
H40.89	Other specified glaucoma
H44.2A1	Degenerative myopia with choroidal neovascularization, right eye
H44.2A2	Degenerative myopia with choroidal neovascularization, left eye
H44.2A3	Degenerative myopia with choroidal neovascularization, bilateral eye

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Type of Revision	Summary of Changes	Review Date
Annual Revision	**Central Nervous System Tumors:** Moved the subtypes of tumors from indication to criteria. Changed patient has tried "one other therapy" to "one previous therapy". Added carmustine and etoposide to existing examples in Note. For Intracranial and spinal ependymoma subtype, deleted reference to "adults" and instead added "in patients ≥ 18 years of age". **Non-Small Cell Lung Cancer:** Changed "targetable" mutations to "actionable" mutations. For bevacizumab use in combination with erlotinib, deleted criteria requiring "as first-line therapy". Modified criteria requiring use of at least one targeted therapy (if positive for actionable mutation), to state "patient has previously received targeted drug therapy for an actionable mutations". Moved actionable mutations to list as examples in a new Note and added new actionable mutations *RET* rearrangement positive, *MET* exon 14 skipping, *NTRK* gene fusion positive, *BRAF V600E* mutation positive to the list. Deleted criteria referring to NSCLC tumor that is *BRAF V600E* mutation-positive and bevacizumab use as either first-line or subsequent therapy. This is not needed due to the modified criteria regarding targeted drug therapy for actionable mutation. For criteria referring to negative or unknown actionable mutations, moved examples to new Note and updated the list of actionable mutations as above. Previous criteria referring to bevacizumab use specifically in combination with "platinum therapies" was deleted and instead criteria was modified to say "with other systemic therapies". A new Note has been added with examples of systemic therapies. For the other criteria referring to bevacizumab use as subsequent therapy, the criteria referring to "and is used as a single agent or in combination with other agents" was moved to a new Note. **Soft Tissue Sarcoma:** Moved the subtypes angiosarcoma and solitary fibrous tumor from indication to criteria. Deleted reference to hemangiopericytoma since it is no longer in guidelines.	03/17/2021
Annual Revision	**Central Nervous System Tumors:** Added "Symptoms due to radiation necrosis, poorly controlled vasogenic edema, or mass effect" as additional options for approval. **Colon or Rectal Cancer:** Added "recurrent" as additional descriptor in "Patient has recurrent, advanced, or metastatic colon or rectal cancer." Removed requirement that bevacizumab is not used for adjuvant treatment of colon cancer. **Non-Small Cell Lung Cancer (NSCLC):** Added "recurrent" as additional descriptor in "Patient has recurrent, advanced, or metastatic non-squamous cell NSCLC. Added "exon 19 deletion or L858R' as additional descriptor to "NSCLC tumor is positive for epidermal growth factor receptor (EGFR) exon 19 deletion or L858R mutations." Added tumor is positive for one of the following mutations: EGFR exon 20 mutation, KRAS G12C mutation, BRAF V600E, NTRK1/2/3 gene fusion, MET exon 14 skipping mutation, and RET rearrangement; and bevacizumab is used in combination other systemic therapies. Added Note with list of examples of systemic therapies. **Breast Cancer:** Removed breast cancer from Other Uses with Supportive Evidence due to National Comprehensive Cancer Network withdrawing its recommendations for bevacizumab for the treatment of breast cancer.	03/16/2022

	Endometrial Cancer: Removed requirement that the patient has progressed on prior chemotherapy and added requirement that the patient has recurrent, advanced, or metastatic disease. **Mesothelioma:** Removed Malignant Pleural from the condition of approval. Added malignant peritoneal mesothelioma, pericardial mesothelioma, and tunica vaginalis testis mesothelioma as additional options for approval. Added "bevacizumab will be used in combination with Tecentriq" as an additional option for approval.	
UCare Custom revision	Added the new biosimilar bevacizumab product, Alymsys, as a non-preferred biosimilar product requiring step through at least one preferred biosimilar agent for new starts only.	06/03/2022
Selected Revision	**Product:** Added Vegzelma to the list of bevacizumab products.	11/16/2022
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. **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.	03/22/2023

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