Clinical Policy Title:	bevacizumab
Policy Number:	RxA.665
Drug(s) Applied:	Avastin®, Zirabev®, Mvasi®, Alymsys®, Vegzelma®
Original Policy Date:	03/19/2021
Last Review Date:	10/19/2023
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

I. Initial Approval Criteria

A. Colorectal cancer (must meet all):

1. Member has a diagnosis of metastatic colorectal cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member must meet one or more of the following (a or b):
   a. Bevacizumab is being used as a first or second line treatment, when added to intravenous 5-fluorouracil based chemotherapy (e.g. IFL, FOLFOX4 etc);
   b. As a second line treatment when added to irinotecan-fluoropyrimidine- or oxaliplatin-fluoropyrimidine-based chemotherapy after disease has progressed on first line therapy containing bevacizumab;
5. Bevacizumab is not being used as adjuvant therapy;
6. For requests other than Zirabev® and Mvasi ®: Member must have tried and failed both Zirabev® and Mvasi ® at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed FDA approved limits or;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

   *Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

B. Non- squamous non-small cell lung cancer (must meet all):

1. Member has a diagnosis of non-squamous non-small cell lung cancer;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Bevacizumab is used as first line treatment in combination with carboplatin and paclitaxel;
5. For requests other than Zirabev® and Mvasi ®: Member must have tried and failed Zirabev® and Mvasi ®, at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b)*:

a. Dose does not exceed FDA approved limits or;
b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

C. Glioblastoma (must meet all):
1. Member has a diagnosis of recurrent glioblastoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member must meet one of the following (a or b):
   a. Bevacizumab is being used as a single agent;
   b. Bevacizumab is used in combination with carmustine, lomustine, or temozolomide if monotherapy with bevacizumab has failed;
5. For requests other than Zirabev® and Mvasi ®: Member must have tried and failed both Zirabev® and Mvasi ®, at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b)*:
   a. Dose does not exceed FDA approved limits or;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

   *Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

D. Metastatic renal cell carcinoma (must meet all):
1. Member has a diagnosis of metastatic renal cell carcinoma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with interferon alfa;
5. For requests other than Zirabev® and Mvasi ®: Member must have tried and failed both Zirabev® and Mvasi ®, at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b):*
   a. Dose does not exceed 10 mg/kg intravenously every 2 weeks;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

   *Prescribed regimen must be FDA-approved or recommended by NCCN

Approval Duration
Commercial: 6 months
Medicaid: 6 months

E. Cervical cancer (must meet all):
1. Member has a diagnosis of persistent, recurrent, or metastatic cervical cancer;
2. Prescribed by or in consultation with an oncologist;

3. Age ≥ 18 years;
4. Prescribed in combination with either paclitaxel and cisplatin or paclitaxel and topotecan;
5. For requests other than Zirabev® and Mvasi ®: Member must have tried and failed both Zirabev® and Mvasi ® at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced;
6. Request meets one of the following (a or b)*:
   a. Dose does not exceed FDA approved limits or;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

F. Epithelial Ovarian, Fallopian Tube or Primary Peritoneal cancer (must meet all):

1. Member has a diagnosis of one of the following (a or b):
   a. Stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial resection; or
   b. Recurrent disease, platinum resistant or platinum sensitive;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Member must meet one of the following (a, b or c):
   a. For Stage III or IV disease, bevacizumab is prescribed initially in combination with carboplatin and paclitaxel, followed by bevacizumab as a single agent;
   b. For recurrent disease-platinum resistant, bevacizumab is prescribed with paclitaxel, pegylated liposomal doxorubicin, or topotecan;
      a. Must not have received no more than 2 prior chemotherapy regimens;
   c. For recurrent disease-platinum sensitive, bevacizumab is prescribed initially in combination with carboplatin and paclitaxel or in combination with carboplatin and gemcitabine, followed by bevacizumab as a single agent;
8. For requests other than Zirabev® and Mvasi ®: Member must have tried and failed both Zirabev® and Mvasi ® at up to maximally indicated doses, unless contraindicated or clinically significant adverse effects are experienced;
9. Request meets one of the following (a or b):*
   a. Dose does not exceed FDA approved limits or;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

G. Hepatocellular carcinoma (must meet all):

1. Request is for Avastin®;
2. Member has a diagnosis of unresectable or metastatic hepatocellular carcinoma;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Member has not received prior systemic therapy;

6. Bevacizumab is being prescribed in combination with atezolizumab;
7. Request meets one of the following (a or b):*
   a. Dose does not exceed FDA approved limits or;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

H. Compendium Recommended Indications (off-label) (must meet all):

1. Diagnosis of one of the following (a-m):
   a. Adult glioma of one of the following types (i, ii, or iii):
      i. Oligodendroglioma that is IDH-mutant, 1p19q codeleted (WHO Grade 2 or 3);
      ii. IDH-mutant astrocytoma;
      iii. Low-grade (WHO Grade I) glioma;
   b. Ampullary adenocarcinoma-intestinal type;
   c. Endometrial carcinoma;
   d. Intracranial and spinal ependymoma;
   e. Malignant peritoneal mesothelioma;
   f. Medulloblastoma;
   g. Meningioma;
   h. Metastatic spine tumors or brain metastases;
   i. Pediatric diffuse high-grade glioma;
   j. Primary central nervous system cancers;
   k. Small bowel adenocarcinoma;
   l. Soft tissue sarcoma-solitary fibrous tumor or angiosarcoma;
   m. Vulvar cancer-squamous cell carcinoma; ;
2. Prescribed by or in consultation with an oncologist;
3. Age 18 years;
4. For requests other than Zirabev® and Mvasi ®: Member must have tried and failed both Zirabev® and Mvasi ® at maximally indicated doses or clinically significant adverse effects are experienced;
5. Request meets one of the following (a or b):*
   a. Dose does not exceed FDA approved limits or;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

I. Pleural mesothelioma (off-label) (must meet all):

1. Member has a diagnosis of malignant pleural mesothelioma;
2. Prescribed by or in consultation with an oncologist;
3. Age ≥ 18 years;
4. Prescribed in combination with pemetrexed and cisplatin or carboplatin if patient is not eligible for cisplatin;
5. For requests other than Zirabev® and Mvasi ®: Member must have tried and failed both Zirabev® and

Mvasi ® at maximally indicated doses or clinically significant adverse effects are experienced;
6. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).
*Prescribed regimen must be FDA-approved or recommended by NCCN.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

J. Age-related macular degeneration (off-label) (must meet all):
1. Member has a diagnosis of macular degeneration;
2. Prescribed by or in consultation with an ophthalmologist;
3. Age ≥ 50 years;
4. For requests other than Zirabev® and Mvasi ®: Member must have tried and failed both Zirabev® and Mvasi ® at maximally indicated doses or clinically significant adverse effects are experienced;
5. Dosing is supported by evidence based-guidelines or peer-reviewed literature for the relevant off-label use.

Approval Duration
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

A. All indications listed in section I (must meet all):
1. Member is currently receiving medication that has been authorized by RxAdvance or the member has met initial approval criteria listed in this policy;
2. Member is positively responding to therapy (e.g. tumour regression, absence of disease progression etc);
3. If request is for dose increase, new dose does not exceed any one of the following (a or b):*
   a. Dose does not exceed FDA approved limits or;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

*Prescribed regimen must be FDA-approved or recommended by NCCN

Approval Duration
Commercial: 12 months
Medicaid: 12 months

References

1. National Comprehensive Cancer Network. Colorectal Cancer Version 2.2023. Available at https://www.nccn.org/professionals/physician_gls/PDF/colon.pdf. Accessed July 03, 2023.
2. National Comprehensive Cancer Network. Non-Small Cell Lung Cancer. Version 3.2023. Available at https://www.nccn.org/professionals/physician_gls/PDF/nscl.pdf. Accessed July 03, 2023.
3. National Comprehensive Cancer Network. Central Nervous System Cancers. Version 1.2023. Available at https://www.nccn.org/professionals/physician_gls/PDF/cns.pdf. Accessed July 03, 2023.
4. National Comprehensive Cancer Network. Kidney Cancer. Version 1.2024. Available at https://www.nccn.org/professionals/physician_gls/PDF/kidney.pdf. Accessed July 03, 2023.
5. National Comprehensive Cancer Network. Hepatobiliary Cancers. Version 5.2022. Available at https://www.nccn.org/professionals/physician_gls/pdf/hepatobiliary_blocks.pdf. Accessed July 03, 2023.
6. National Comprehensive Cancer Network. Cervical cancer. Version 1.2023. Available at: https://www.nccn.org/professionals/physician_gls/PDF/cervical.pdf. Accessed July 03, 2023.

7. National Comprehensive Cancer Network. Soft tissue sarcoma. Version 2.2023. Available at: https://www.nccn.org/professionals/physician_gls/PDF/sarcoma.pdf. Accessed July 03, 2023.
8. National Comprehensive Cancer Network. Uterine Neoplasms. Version 2.2023. Available at https://www.nccn.org/professionals/physician_gls/PDF/uterine.pdf. Accessed July 03, 2023.
9. National Comprehensive Cancer Network. Breast cancer. Version 4.2023. Available at https://www.nccn.org/professionals/physician_gls/PDF/breast.pdf. Accessed July 03, 2023.
10. American Academy of Ophthalmology, Age-related Macular Degeneration PPP 2019. Available at https://www.aao.org/preferred-practice-pattern/age-related-macular-degeneration-ppp. July 03, 2023.
11. American Academy of Ophthalmology. Diabetic Retinopathy PPP 2019. Available at https://www.aao.org/preferred-practice-pattern/diabetic-retinopathy-ppp. Accessed July 03, 2023.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy established.	01/25/2021	03/09/2021
Policy was reviewed: 1. Initial Approval Criteria, I.D: Updated to include approval criteria for indication, Metastatic renal cell carcinoma. 2. Initial Approval Criteria, I.F.1: Updated to remove prior drug request criteria “Request is for Avastin®”. 3. Initial Approval Criteria, I.F.4.b: Updated combination therapy criteria from For recurrent disease-platinum resistant, bevacizumab is being prescribed with paclitaxel, pegylated liposomal doxorubicin, or topotecan to For recurrent disease-platinum resistant, bevacizumab is being prescribed with paclitaxel, pegylated liposomal doxorubicin, or topotecan for members who have received no more than 2 prior chemotherapy regimens. 4. Initial Approval Criteria, I.H: Updated to remove approval criteria for Breast cancer (off-label) changed to CNS cancers. a. Added prescribing requirements, single agent and as combination 5. Initial Approval Criteria, I.K: Updated to remove approval criteria for Diabetic macular edema (off-label). 6. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 7. References were reviewed and updated.	12/09/2021	01/17/2022
Policy was reviewed: 1. References were reviewed and updated.	06/30/2022	07/18/2022
Policy was reviewed:	12/20/2022	01/17/2023

1. Initial Approval Criteria, I.H.1: Rephrased from Central nervous system cancer to Compendium Recommended Indications and added following indications: a. Ampullary adenocarcinoma-intestinal type; b. Endometrial carcinoma; c. Malignant peritoneal mesothelioma; d. Pediatric diffuse high-grade glioma; e. Primary central nervous system cancers; f. Small bowel adenocarcinoma; g. Soft tissue sarcoma-solitary fibrous tumor or angiosarcoma; h. Vulvar cancer-squamous cell carcinoma 2. Initial Approval Criteria, I.H.4: Updated to remove prescribing criteria "Must be prescribed (a or b): a. As a single agent or; b. In combination with carmustine, lomustine, or temozolomide if bevacizumab monotherapy fails and it is desirable to continue the steroid sparing effects of bevacizumab." 3. References were reviewed and updated.		
Policy was reviewed: 1. References were reviewed and updated.	07/03/2023	07/13/2023
Policy was reviewed.	10/19/2023	10/19/2023