



Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

Effective Date: 02/08/2024

Bevacizumab Policy

Almysys[®] (bevacizumab-maly)

Avastin[®] (bevacizumab)

Avzivi[®] (bevacizumab-trjn)

Mvasi[™] (bevacizumab-awwb)

Vegzelma[®] (bevacizumab-adcd)

Zirabev[™] (bevacizumab-bvzr)

HCPCS: Multiple

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

Coverage of the requested drug is provided for FDA approved indications or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1 or 2A recommendation OR when all of the criteria are met. Coverage requests must be supported by submission of chart notes and patient specific documentation.

A. Criteria

- a. Prescribed by, or in consultation with a hematologist/oncologist
- b. A diagnosis of persistent, recurrent, or metastatic cervical cancer, when given in combination with paclitaxel and cisplatin or paclitaxel and topotecan
- c. A diagnosis of epithelial ovarian, fallopian tube, or primary peritoneal cancer
 - i. Platinum-resistant recurrent disease in combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan
OR
 - ii. Platinum-sensitive recurrent disease in combination with carboplatin and paclitaxel or in combination with carboplatin and gemcitabine, followed by bevacizumab or a bevacizumab biosimilar as a single agent
OR
 - iii. Stage III or IV disease following initial surgical resection in combination with carboplatin and paclitaxel, followed by bevacizumab or a bevacizumab biosimilar as a single agent
- d. A diagnosis of metastatic colorectal cancer (adenocarcinoma)
- e. Recurrent glioblastoma
- f. A diagnosis of unresectable, locally advanced, recurrent, or metastatic non-squamous non-small cell lung cancer
 - i. Patient has had no prior chemotherapy

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

- ii. Bevacizumab or a bevacizumab biosimilar is administered in combination with carboplatin and paclitaxel
- g. A diagnosis of metastatic renal cell carcinoma
 - i. Bevacizumab or a bevacizumab biosimilar is administered in combination with interferon-alfa
- h. A diagnosis of unresectable or metastatic hepatocellular carcinoma
 - i. Patient has had no prior chemotherapy
 - ii. Bevacizumab or a bevacizumab biosimilar is administered in combination with atezolizumab
- i. Coverage will be provided for biosimilar products for FDA labeled indications of the innovator product when criteria are met
- j. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list

B. Quantity Limitations, Authorization Period and Renewal Criteria

- a. Quantity Limits: Align with FDA recommended dosing.
- b. Authorization Period: Aligns with FDA recommended or guideline supported treatment duration and provided for at least 60 days and up to 6 months at a time
- c. Renewal Criteria: Continuation of therapy until disease progression or unacceptable toxicity

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Bevacizumab and its biosimilars are monoclonal antibodies that bind to and inhibit the activity of vascular endothelial growth factor (VEGF). Bevacizumab is approved for the following indications:
 - In combination with intravenous fluorouracil-based chemotherapy for first- or second-line treatment of patients with metastatic colorectal cancer (mCRC)
 - In combination with fluoropyrimidine-irinotecan- or fluoropyrimidine-oxaliplatin-based chemotherapy for second-line treatment of patients with mCRC who have progressed on a first-line bevacizumab-containing regimen
 - In combination with carboplatin and paclitaxel for first-line treatment of patients with unresectable, locally advanced, recurrent or metastatic non-squamous non-small cell lung cancer (NSCLC)
 - The treatment of recurrent glioblastoma (GBM) in adults
 - In combination with interferon alfa for the treatment of metastatic renal cell carcinoma (mRCC)
 - In combination with paclitaxel and cisplatin or paclitaxel and topotecan for the treatment of patients with persistent, recurrent, or metastatic cervical cancer
 - In combination with carboplatin and paclitaxel followed by bevacizumab as a single agent for the treatment of patients with stage III or IV epithelial ovarian, fallopian tube, or primary peritoneal cancer following initial surgical resection

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

- In combination with paclitaxel, pegylated liposomal doxorubicin, or topotecan for the treatment of patients with platinum-resistant recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer who received no more than 2 prior chemotherapy regimens
- In combination with carboplatin and paclitaxel or with carboplatin and gemcitabine followed by bevacizumab as a single agent for the treatment of patients with platinum-sensitive recurrent epithelial ovarian, fallopian tube, or primary peritoneal cancer
- In combination with atezolizumab for the treatment of patients with unresectable or metastatic hepatocellular carcinoma (HCC) who have not received prior systemic therapy
- While not specifically indicated for ocular conditions, bevacizumab has been used off-label for years to treat multiple eye disorders including macular degeneration, macular edema, and diabetic retinopathy. Bevacizumab has the same mechanism of action as the other therapies for these diseases and its use is guideline supported.
- NCCN guidelines state an FDA approved biosimilar can be substituted for Avastin. The guidelines do not specify what biosimilars are appropriate for a specific tumor type which allows for use of any of the biosimilars to be used for any indication the innovator product is FDA approved for.

References:

1. Avastin [prescribing information]. South San Francisco, CA: Genentech, Inc.; September 2022.
2. © 2014 RegenceRx-Medication Policy Manual, Avastin® (bevacizumab), Policy No:dru215; 2014 April 1.
3. Avastin. Retrieved 1/2/2015 from the American Macular Degeneration Foundation website: [<https://www.macular.org/avastin>] March 2005.
4. Mvasi [prescribing information]. Thousand Oaks, CA: Amgen, Inc.; February 2023.
5. Avzivi [prescribing information]. Guangzhou, Guangdong Province, China: Bio-Thera Solutions, Ltd.; December 2023.
6. Approved Drugs: "FDA approves bevacizumab in combination with chemotherapy for ovarian cancer". U.S. Food & Drug Administration. June 13, 2018. Accessed on: September 5th, 2018. Available from: <https://www.fda.gov/Drugs/InformationOnDrugs/ApprovedDrugs/ucm610664.htm>
7. Pfizer Pipeline: May 1st. 2018. Accessed on September 6th, 2019. Available from: https://www.pfizer.com/sites/default/files/product-pipeline/Pipeline_Update_01MAY2018.pdf
8. Pipeline Summary: Roche. April 26th, 2018. Accessed on September 10th, 2018. Available from: <https://www.roche.com/dam/jcr:4fcd49b1-bcd5-4714-96ed-2589d7413548/en/irp180426-annex.pdf>
9. Avastin (Bevacizumab) Update: Patent Office Holds Hearing In Pfizer's IPR Challenge To Validity Of 2024 Patent. IPD Analytics, January 2019. Accessed on: September 10th, 2018. Available from. IPD Analytics healthcare@ipdanalytics.com.
10. Medical Review: New Formulation – Biosimilar. Antineoplastics: Monoclonal Antibody Mvasi (bevacizumab-awwb) [Amgen], September 2017. Accessed on September 10th, 2018.
11. Gynecologic Oncology Group (GOG)- 0218 (ClinicalTrials.gov identifier NCT00262847)
12. Zirabev [prescribing information]. New York, NY: Pfizer, Inc.; February 2023.
13. National Comprehensive Cancer Network. Hepatocellular carcinoma (Version 2.2023). 2023 Sept 14. Available at: https://www.nccn.org/professionals/physician_gls/pdf/hcc.pdf. Accessed on December 11, 2023.
14. National Comprehensive Cancer Network. Biliary tract cancers (Version 3.2023). 2023 Nov 8. Available at: https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf. Accessed on December 11, 2023.
15. National Comprehensive Cancer Network. Colon cancer (Version 4.2023). 2023 Nov 16. Available from: https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf. Accessed December 11, 2023.
16. National Comprehensive Cancer Network. Non-small cell lung cancer (Version 5.2023). 2023 Nov 8. Available from: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed December 11, 2023.
17. National Comprehensive Cancer Network. Central nervous system cancers (Version 1.2023). 2023 March 24. Available from: https://www.nccn.org/professionals/physician_gls/pdf/cns.pdf. Accessed December 11, 2023.

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

18. National Comprehensive Cancer Network. Cervical cancer (Version 1.2024). 2023 Sept 20. Available from: https://www.nccn.org/professionals/physician_gls/pdf/cervical.pdf. Accessed December 11, 2023.
19. National Comprehensive Cancer Network. Kidney cancer (Version 1.2024). 2023 June 21. Available from: https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed December 11, 2023.
20. National Comprehensive Cancer Network. Ovarian cancer including fallopian tube cancer and primary peritoneal cancer (Version 2.2023). 2023 June 2. Available at: https://www.nccn.org/professionals/physician_gls/pdf/ovarian.pdf. Accessed on December 11, 2023.
21. Alymsys [prescribing information]. Bridgewater, NJ: Amneal Pharmaceuticals LLC; April 2022.
22. Vegzelma [prescribing information]. Incheon, Republic of Korea: Celltrion, Inc.; February 2023.

Policy History		
#	Date	Change Description
2.8	Effective Date: 02/08/2024	Updated to include Avzivi
2.7	Effective Date: 01/01/2024	UM medical management system update for BCBS and BCN for Avzivi
2.6	Effective Date: 12/14/2023	Annual review of criteria was performed, no changes were made
2.5	Effective Date: 03/09/2023	UM medical management system update to Vegzelma for BCBS and BCN
2.4	Effective Date: 03/01/2023	UM medical management system update to Vegzelma for MAPPO and BCNA
2.3	Effective Date: 12/01/2022	Updated to include Vegzelma and reflect an authorization period of at least 60 days
2.2	Effective Date: 06/09/2022	Updated to include Alymsys and change approval length to allow for FDA recommended dosing or up to 6 months at a time
2.1	Effective Date: 08/12/2021	Updated to remove the ophthalmologist requirement when used for ocular indications and the criteria for initiation of use 28 days after wound healing
2.0	Effective Date: 04/01/2021	UM medical management system update to Avastin for BCBS, BCN, MAPPO, and BCNA
1.9	Effective Date: 08/13/2020	Updated to include the new indication of hepatocellular carcinoma
1.8	Effective Date: 03/16/2020	UM medical management system update to Zirabev for MAPPO and BCNA
1.7	Effective Date: 01/01/2020	UM medical management system update to Mvasi for MAPPO and BCNA
1.6	Effective Date: 12/05/2019	Updated criteria to remove taxane requirement with use in mCRC per guidelines and FDA labeling
1.5	Effective Date: 08/15/2019	Updated criteria to allow use when aligned with NCCN guideline recommendations category 1 and 2A and added Zirabev
1.4	Effective Date: 11/01/2018	New Indication Update
1.3	Effective Date: 05/03/2018	Added Mvasi and changed name of policy to Bevacizumab
1.2	Effective Date: 05/04/2017	New Indication Update
1.1	Effective Date: 11/10/2016	Annual Review of Medical Policy

This policy and any information contained herein is the property of Blue Cross Blue Shield of Michigan and its subsidiaries, is strictly confidential, and its use is intended for the P&T committee, its members and BCBSM employees for the purpose of coverage determinations.

1.0	Effective Date: 05/07/2015	<p data-bbox="451 140 574 170">New Policy</p> <table border="1" data-bbox="537 205 1417 409"> <thead> <tr> <th data-bbox="542 205 1016 268">Line of Business</th> <th data-bbox="1021 205 1412 268">PA Required in Medical Management System (Yes/No)</th> </tr> </thead> <tbody> <tr> <td data-bbox="542 275 1016 302">BCBS</td> <td data-bbox="1021 275 1412 302">No</td> </tr> <tr> <td data-bbox="542 308 1016 336">BCN</td> <td data-bbox="1021 308 1412 336">No</td> </tr> <tr> <td data-bbox="542 342 1016 369">MAPPO</td> <td data-bbox="1021 342 1412 369">No</td> </tr> <tr> <td data-bbox="542 375 1016 403">BCNA</td> <td data-bbox="1021 375 1412 403">No</td> </tr> </tbody> </table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	No	BCN	No	MAPPO	No	BCNA	No
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	No											
BCN	No											
MAPPO	No											
BCNA	No											

* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.