

Drug Therapy Guidelines

Bevacizumab (Avastin® [bevacizumab], Mvasi® [bevacizumab-awwb], Zirabev™ [bevacizumab-bvzr])

*Applicable**

Medical Benefit	x	Effective: 5/28/2021
Pharmacy- Formulary 1		Next Review: 3/22
Pharmacy- Formulary 2		Date of Origin: 10/06
Pharmacy- Formulary 3/Exclusive		Review Dates: 10/15/06, 11/5/07, 12/15/08, 12/09, 12/10, 12/11,
Pharmacy- Formulary 4/AON		12/12, 12/13, 12/14, 3/15, 3/16, 3/17, 3/18, 3/19, 9/19, 3/20, 3/21

I. Medication Description

Bevacizumab binds to vascular endothelial growth factor (VEGF) and prevents the interaction of VEGF to its receptors (Flt-1 and KDR) on the surface of endothelial cells. The interaction of VEGF with its receptors leads to endothelial cell proliferation and new blood vessel formation in in-vitro models of angiogenesis. Administration of bevacizumab to xenotransplant models of colon cancer in nude (athymic) mice caused a reduction of microvascular growth and inhibition of metastatic disease progression. Vascular targeting therapies are aimed at inhibiting tumor neovascularization and are not directly cytotoxic. Therefore, vascular targeting therapies used in cancer therapy usually need to be given in combination with traditional cytotoxic treatment modalities, except in maintenance regimens.

Mvasi® (bevacizumab-awwb) is biosimilar** to Avastin®(bevacizumab).
Zirabev™ (bevacizumab-bvzr) is biosimilar** to Avastin®(bevacizumab).

II. Position Statement

- Requests for use with certain diagnostic codes do not require prior authorization and supporting clinical documentation. See Addendum.
- Coverage is determined through a prior authorization process with supporting clinical documentation for all other requests.

III. Policy

Avastin: See Sections A, B, and C

Mvasi, Zirabev: See Sections A and B

A. Coverage of Avastin, Mvasi, or Zirabev is available for ophthalmic indications:

- Neovascular (wet) Age-related macular degeneration (AMD)
- Diabetic Macular Edema (DME)

B. Coverage of Avastin, Mvasi, or Zirabev is available for oncology indications as follows:

- Member is at least 18 years of age **AND**
- The medication is prescribed by a hematologist/oncologist **AND**
- The requested use is supported by the National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines (NCCN Guidelines®) and/or NCCN Drugs & Biologics Compendium (NCCN Compendium®) with a recommendation of category level 1 or 2A **AND**

- When requesting coverage of a brand medication for which a plan-preferred A/B rated generic is available, there is sufficient evidence that the use of the A/B rated generic equivalent has resulted in inadequate results **AND**
- C. Mvasi and Zirabev are plan-preferred medications in cases where:
 - a) Avastin is requested as a newly started therapy **AND**
 - b) Avastin is requested for an indication for which the biosimilar (Mvasi or Zirabev) has been FDA-approved OR is supported by NCCN Guidelines® or NCCN Compendium® with a recommendation of category level 1 or 2A **AND**
 - c) If criteria under both a. and b. apply:
 - Coverage of Avastin will be available if the member has experienced a therapeutic failure or intolerance with the plan-preferred medication (Mvasi or Zirabev) first OR at least ONE of the following criteria are met:
 - The plan-preferred medications are contraindicated or will likely cause an adverse reaction by or physical or mental harm to the member.
 - The plan-preferred medications are expected to be ineffective based on the known clinical history and conditions of the member and the member's prescription drug regimen.
 - The member has tried the plan-preferred medications or another prescription drug in the same pharmacologic class or with the same mechanism of action and such prescription drug was discontinued due to lack of efficacy or effectiveness, diminished effect, or an adverse event.
 - The member is stable on the medication selected by their healthcare professional for the medical condition under consideration (where "stable" is defined as receiving the medication for an adequate period of time, have achieved optimal response, and continued favorable outcomes are expected UNLESS the medication was initially selected due to the availability of a drug sample or a coupon card and the member does not otherwise meet the definition of "stable").
 - The plan-preferred medication is not in the best interest of the member because it will likely cause a significant barrier to the member's adherence or to compliance with the member's plan of care, will likely worsen a comorbid condition of the member, or will likely decrease the member's ability to achieve or maintain reasonable functional ability in performing daily activities.

IV. Quantity Limits

- For oncology indications:
 - No more than 170 billable units (1700mg) in a single administration AND
 - No more than 170 billable units (1700mg) in a 21-day cycle
- For ophthalmic indications:
 - 1 billable unit per eye

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V. Coverage Duration

Coverage is available for 6 months and may be renewed.

VI. Coverage Renewal Criteria

- Coverage for oncology indications can be renewed based upon the following criteria:
 - Disease response with stabilization of disease or decrease in size of tumor or tumor spread **AND**
 - Absence of unacceptable toxicity from the drug
- Coverage for ophthalmic indications can be renewed based upon the following criteria:
 - Disease response with stabilization or regression of disease **AND**
 - Absence of unacceptable toxicity from the drug.

VII. Billing/Coding Information

- Avastin
 - Available as 100 mg/4 ml and 400 mg/16 ml vials
 - J9035 – 1 billable unit is 10mg
 - C9257- 1 billable unit is 0.25mg
- Mvasi
 - Available as 100 mg/4 ml and 400 mg/16 ml vials
 - Q5107- 1 billable unit is 10mg
- Zirabev
 - Available as 100 mg/4ml and 400 mg/16ml vials
 - Q5118- 1 billable unit is 10mg
- Pertinent indications:
 - Colon cancer – C17.0-C17.2, C17.8, C17.9, C18.0-C18.9, C78.00-C78.02, C78.6, C78.7, Z85.038, Z85.068
 - Rectal Cancer: C19, C20, C21.8, C78.00-C78.02, C78.7
 - Non-squamous non-small cell lung cancer - C33, C34.00-C34.02, C34.10-C34.12, C34.2, C34.30-C34.32, C34.80-C34.82, C34.90-C34.92, Z85.118
 - Breast cancer – C50.011, C50.012, C50.019, C50.021, C50.022, C50.029, C50.111, C50.112, C50.119, C50.121, C50.122, C50.129, C50.211, C50.212, C50.219, C50.221, C50.222, C50.229, C50.311, C50.312, C50.319, C50.321, C50.322, C50.329, C50.411, C50.412, C50.419, C50.421, C50.422, C50.429, C50.511, C50.512, C50.519, C50.521, C50.522, C50.529, C50.611, C50.612, C50.619, C50.621, C50.622, C50.629, C50.811, C50.812, C50.819, C50.821, C50.822, C50.829, C50.911, C50.912, C50.919, C50.921, C50.922, C50.929, Z85.3
 - CNS cancer - C70.0, C70.1, C70.9, C71.0-C71.9, C72.0, C72.9, C79.31, C79.32, C83.30, C83.31, C83.39, C83.80, C83.81, C83.89, C85.89, D32.0, D32.1, D32.9, D42.0, D42.1, D42.9, D43.0-D43.2, D43.4, I67.89, Z85.841, Z85.848
 - Cervical cancer –C53.0, C53.1, C53.8, C53.9, C79.89, C79.9, Z80.49
 - Uterine neoplasms: C54.0-C54.3, C54.8, C54.9, C55

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- Kidney cancer –C64.1, C64.2, C64.9, C65.1, C65.2, C65.9, Z85.528Endometrial cancer – C54.0-C54.3, C54.8, C54.9, C55, Z80.49
- Ovarian cancer - C48.1, C48.2, C48.8, C56.1, C56.2, C56.9, C57.00-C57.02, C57.10-C57.12, C57.20-C57.22, C57.3, C57.4, C57.7-C57.9, Z85.43
- Soft Tissue Sarcoma - C48.0-C48.2, C49.0, C49.10-C49.12, C49.20-C49.22, C49.3-C49.6, C49.8, C49.9, Z85.831
- Endometrial cancer – C54.0-C54.3, C54.8, C54.9, C55, Z80.49
- Malignant pleural mesothelioma- C38.4, C45.0, C45.1
- AIDS-Related Kaposi Sarcoma - C46.0, C46.1, C46.2, C46.3, C46.4, C46.50, C46.51, C46.52, C46.7, C46.9
- Vulvar Cancer - Squamous Cell Carcinoma: C51.0-C51.2, C51.8, C51.9, C79.82, C79.89
- Ophthalmic diagnoses- E08.351, E08.359, E09.351, E09.359, E10.351, E10.359, E11.351, E11.359, E13.351, E13.359, E08.311, E08.321, E08.331, E08.341, E08.351, E09.311, E09.321, E09.331, E09.341, E09.351, E10.311, E10.321, E10.331, E10.341, E10.351, E11.311, E11.321, E11.331, E11.341, E11.351, E13.311, E13.321, E13.331, E13.341, E13.351, H34.811, H34.812, H34.813, H34.819, H34.831, H34.832, H34.833, H34.839, H35.30, H35.32, H35.351, H35.352, H35.353, H35.359, H35.81

VIII. Summary of Policy Changes

- 3/1/11:
 - Coverage duration changed to 6 months for all indications
 - Indications expanded to include ophthalmic uses (no longer a separate policy)
 - Addition of Coverage renewal criteria
 - Addition of Warnings/Precautions
 - Addition of Billing/Coding information
- 6/15/12: Removal of metastatic breast cancer indication as revoked by FDA
- 3/15/13:
 - Breast cancer coverage added back to policy per NCCN recommendations
 - Addition of covered indications under pertinent diagnoses
 - Addition of coverage for soft tissue sarcoma, cervical cancer, uterine cancer
 - Update coverage criteria for NSCLC, RCC, ovarian cancer, and CNS cancers
 - Updated renewal criteria for mCRC
- 6/2013: updated to include statement regarding investigational administration, cited Eylea as related policy
- 3/15/14: metastatic renal cell carcinoma updated to allow first line therapy of Avastin as single agent for non-clear cell histology; coverage of uterine/endometrial cancers no longer supported
- 4/16/14: updated to cervical cancer and endometrial cancer criteria in accordance with NCCN treatment guidelines
- 6/9/14: criteria in ovarian cancer updated to reflect current NCCN guidelines
- 7/21/14: criteria in central nervous system cancers updated to reflect current NCCN guidelines
- 10/2014: addition of topotecan in combination with Avastin as first line therapy in cervical cancer based on FDA approval
- 3/15/15: no policy changes
- 6/15/15: no policy changes

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- 7/1/15: formulary distinctions made
- 10/1/15: ICD9 references omitted
- 6/15/16: included criteria for malignant pleural mesothelioma
- 4/5/17: policy updated to correspond with current NCCN treatment guidelines
- 5/1/18: coverage criteria updated to allow use as supported by current NCCN guidelines; updated ICD-10 codes
- 5/15/19: policy name changed from “Avastin” to “Bevacizumab”; added Mvasi to policy; updated billing/coding information
- 11/15/19: added step therapy to Avastin requests for certain scenarios; added Zirabev to policy; updated billing/coding information
- 1/1/20: policy updated to reflect preferred products Mvasi and Zirabev
- 5/1/20: no policy changes
- 5/28/21: no policy changes

IX. References

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10. National Comprehensive Cancer Network Guidelines [database online]. Fort Washington, PA: National Comprehensive Cancer Network, Inc.; 2021. URL: https://www.nccn.org/professionals/physician_gls/f_guidelines.asp#site .Updated January, 2021.
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14. Zirabev (bevacizumab-bvzr) package insert. New York, NY: Pfizer Inc.; Revised 1/2020.

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- *Addendum:*

ICD10	Description
E08311	Diabetes mellitus due to underlying condition with unspecified diabetic retinopathy with macular edema
E08321, E083211, E083212, E083213, E083219	Diabetes mellitus due to underlying condition with mild nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E08331, E083311, E083312, E083313, E083319	Diabetes mellitus due to underlying condition with moderate nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E08341, E083411, E083412, E083413, E083419	Diabetes mellitus due to underlying condition with severe nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E08351, E083511, E083512, E083513, E083519	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E08359, E083591, E083592, E083593, E083599	Diabetes mellitus due to underlying condition with proliferative diabetic retinopathy without macular edema – right eye, left eye, bilateral, unspecified eye
E09311	Drug or chemical induced diabetes mellitus with unspecified diabetic retinopathy with macular edema
E09321, E093211, E093212, E093213, E093219	Drug or chemical induced diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E09331, E093311, E093312, E093313, E093319	Drug or chemical induced diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E09341, E093411, E093412, E093413, E093419	Drug or chemical induced diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E09351, E093511, E093512, E093513, E093519	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E09359, E093591, E093592, E093593, E093599	Drug or chemical induced diabetes mellitus with proliferative diabetic retinopathy without macular edema – right eye, left eye, bilateral, unspecified eye
E10311	Type 1 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E10321, E103211, E103212, E103213, E103219	Type 1 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E10331, E103311, E103312, E103313, E103319	Type 1 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye

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E10341, E103411, E103412, E103413, E103419	Type 1 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E10351, E103511, E103512, E103513, E103519	Type 1 diabetes mellitus with proliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E10359, E103591, E103592, E103593, E103599	Type 1 diabetes mellitus with proliferative diabetic retinopathy without macular edema – right eye, left eye, bilateral, unspecified eye
E11311	Type 2 diabetes mellitus with unspecified diabetic retinopathy with macular edema
E11321, E113211, E113212, E113213, E113219	Type 2 diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E11331, E113311, E113312, E113313, E113319	Type 2 diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E11341, E113411, E113412, E113413, E113419	Type 2 diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E11351, E113511, E113512, E113513, E113519	Type 2 diabetes mellitus with proliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E11359, E113591, E113592, E113593, E113599	Type 2 diabetes mellitus with proliferative diabetic retinopathy without macular edema – right eye, left eye, bilateral, unspecified eye
E13311	Other specified diabetes mellitus with unspecified diabetic retinopathy with macular edema
E13321, E133211, E133212, E133213, E133219	Other specified diabetes mellitus with mild nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E13331, E133311, E133312, E133313, E133319	Other specified diabetes mellitus with moderate nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E13341, E133411, E133412, E133413, E133419	Other specified diabetes mellitus with severe nonproliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E13351, E133511, E133512, E133513, E133519	Other specified diabetes mellitus with proliferative diabetic retinopathy with macular edema – right eye, left eye, bilateral, unspecified eye
E13359, E133591, E133592, E133593, E133599	Other specified diabetes mellitus with proliferative diabetic retinopathy without macular edema – right eye, left eye, bilateral, unspecified eye
H34811, H348110, H348111, H348112	Central retinal vein occlusion, right eye – with macular edema, with retinal neovascularization, or stable

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H34812, H348120, H348121, H348122	Central retinal vein occlusion, left eye – with macular edema, with retinal, neovascularization, or stable
H34813, H348130, H348131, H348132	Central retinal vein occlusion, bilateral – with macular edema, with retinal neovascularization, or stable
H34819, H348190, H348191, H348192	Central retinal vein occlusion, unspecified eye – with macular edema, with retinal neovascularization, or stable
H34831, H348310, H348311, H348312	Tributary (branch) retinal vein occlusion, right eye – with macular edema, with retinal neovascularization, or stable
H348320, H348321, H348322	Tributary (branch) retinal vein occlusion, left eye – with macular edema, with retinal neovascularization, or stable
H348330, H348331, H348332	Tributary (branch) retinal vein occlusion, bilateral – with macular edema, with retinal neovascularization, or stable
H34839, H348390, H348391, H348392	Tributary (branch) retinal vein occlusion, unspecified eye – with macular edema, with retinal neovascularization, or stable
H3530	Unspecified macular degeneration
H3532, H353210, H353211, H353212, H353213	Exudative age-related macular degeneration, right eye – stage unspecified, with active choroidal neovascularization, with inactive choroidal neovascularization, or with inactive scar
H3532, H353220, H353221, H353222, H353223	Exudative age-related macular degeneration, left eye – stage unspecified, with active choroidal neovascularization, with inactive choroidal neovascularization, or with inactive scar
H3532, H353230, H353231, H353232, H353233	Exudative age-related macular degeneration, bilateral – stage unspecified, with active choroidal neovascularization, with inactive choroidal neovascularization, or with inactive scar
H3532, H353290, H353291, H353292, H353293	Exudative age-related macular degeneration, unspecified eye – stage unspecified, with active choroidal neovascularization, with inactive choroidal neovascularization, or with inactive scar
H35351	Cystoid macular degeneration, right eye
H35359	Cystoid macular degeneration, unspecified eye
H3581	Retinal edema

**These guidelines are not applicable to benefits covered under Medicare Advantage. Medicare Advantage benefit coverage requests are reviewed in accordance with the guidance set forth in Chapter 15 Section 50 of the Centers for Medicare & Medicaid Services Medicare Benefit Policy Manual.*

*** Biosimilar means that the biological product is approved based on data demonstrating that it is highly similar to an FDA-approved biological product, known as a reference product, and that there are no clinically meaningful differences between the biosimilar product and the reference product. Biosimilarity of MVASI has been demonstrated for the condition(s) of use (e.g. indication(s), dosing regimen(s)), strength(s), dosage form(s), and route(s) of administration described in its Full Prescribing Information. Biosimilarity of ZIRABEV has been demonstrated for the condition(s) of use (e.g. indication(s), dosing regimen(s)), strength(s), dosage form(s), and route(s) of administration described in its Full Prescribing Information.*

The Plan fully expects that only appropriate and medically necessary services will be rendered. The Plan reserves the right to conduct pre-payment and post-payment reviews to assess the medical appropriateness of the above-referenced therapies.

Drug therapy initiated with samples will not be considered as meeting medical necessity for coverage for non-preferred or prior authorized medications.

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The preceding policy is a guideline to allow for coverage of the pertinent medication/product, and is not meant to serve as a clinical practice guideline.