Pharmacy Management Drug Policy

SUBJECT: Avastin (bevacizumab), Mvasi (bevacizumab-awwb), Zirabev (bevacizumab-bvzr)
POLICY NUMBER: PHARMACY-05
EFFECTIVE DATE: 9/2007
LAST REVIEW DATE: 01/06/2020

*** This applies to outpatient as well as office-based administration ***

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. Medical or drug policies apply to commercial and Health Care Reform products only when a contract benefit for the specific service exists.

DESCRIPTION:

Bevacizumab, Bevacizumab-awwb, and Bevacizumab-bvzr are a recombinant humanized monoclonal IgG1 antibody that binds to and inhibits the biologic activity of human vascular endothelial growth factor (VEGF). It prevents VEGF from stimulating blood vessel growth to the tumor.

Bevacizumab, Bevacizumab-awwb, and Bevacizumab-bvzr binds 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, bevacizumab-awwb, and bevacizumab-bvzr results in reduction of microvascular growth and inhibition of metastatic disease progression.

Mvasi (bevacizumab-awwb) and Zirabev (bevacizumab-bvzr) are biosimilars to Avastin (bevacizumab). For a biological product to be labeled as a biosimilar, it must be shown that it is highly similar and has no differences from an existing FDA approved reference product (i.e. Avastin) by extensively analyzing the structure, purity, chemical identity, and bioactivity. It has been concluded that there are no clinically meaningful differences demonstrated through human pharmacokinetic/exposure and pharmacodynamic/responses, and assessment of immunogenicity. Biosimilars may be approved for all or a subset of the same indications as the reference product, depending on patent exclusivity. Biosimilars differ from generics in complexity, manufacturing processes, and in the data needed to demonstrate similarity for approval.

POLICY:

Avastin

Based upon our assessment and review of the peer-reviewed literature, Avastin has been medically proven to be effective and, therefore, **medically appropriate** for all FDA-approved indications and those indications which satisfy the Off-Label Use of FDA Approved Drugs policy. Due to the large range of acceptable uses for Avastin and because of the complex and fluid nature of the drug regimen recommendations employed in various clinical circumstances, a list of acceptable indications is not contained in this policy. Requests for Avastin use inconsistent with FDA labeling will be reviewed based on the Off-Label Use of FDA Approved Drugs policy.

Mvasi

Based upon our assessment and review of the peer-reviewed literature, Mvasi has been medically proven to be effective and, therefore, **medically appropriate** for all FDA-approved indications and those indications which satisfy the Off-Label Use of FDA Approved Drugs policy. Due to the large range of acceptable uses for Mvasi and because of the complex and fluid nature of the drug regimen recommendations employed in various clinical circumstances, a list of acceptable indications is not contained in this policy. Requests for Mvasi use inconsistent with FDA labeling will be reviewed based on the Off-Label Use of FDA Approved Drugs policy.

In addition, Mvasi will be covered for any FDA-approved indication and any indication which satisfies the Off-Label Use of FDA Approved Drugs policy for Bevacizumab (Avastin).

Zirabev
Based upon our assessment and review of the peer-reviewed literature, Zirabev has been medically proven to be effective and, therefore, medically appropriate for all FDA-approved indications and those indications which satisfy the Off-Label Use of FDA Approved Drugs policy. Due to the large range of acceptable uses for Zirabev and because of the complex and fluid nature of the drug regimen recommendations employed in various clinical circumstances, a list of acceptable indications is not contained in this policy. Requests for Zirabev use inconsistent with FDA labeling will be reviewed based on the Off-Label Use of FDA Approved Drugs policy.

In addition, Zirabev will be covered for any FDA-approved indication and any indication which satisfies the Off-Label Use of FDA Approved Drugs policy for Bevacizumab (Avastin).

I. Policy Guidelines:

A. Avastin, Mvasi, and Zirabev are administered by a healthcare professional and are covered under the medical benefit.
B. Continuation of Avastin/Mvasi/Zirabev will not be authorized when disease progression has occurred on Avastin/Mvasi/Zirabev therapy and guidelines indicate therapy should be ceased.
    1. This does not apply to individuals with a diagnosis of colorectal cancer and evidence of progression while on a first-line Avastin/Mvasi/Zirabev-containing regimen. In these cases, continuation of Avastin/Mvasi/Zirabev will be allowed when used in combination with a different chemotherapy regimen.
    2. For cases of recurrent glioblastoma, please refer to National Comprehensive Cancer Network (NCCN) guidelines. In a case where a patient with good performance status (PS) who has received Avastin/Mvasi/Zirabev monotherapy shows signs of radiographic progression, continuation of Avastin/Mvasi/Zirabev therapy may prevent rapid neurologic deterioration, whereby approval may be medically appropriate.
C. Avastin/Mvasi/Zirabev therapy should not be initiated until at least 28 days following surgery and once wound healing has occurred. Discontinue Avastin/Mvasi/Zirabev at least 28 days prior to elective surgery.
D. **Dose** should not exceed 15 mg/kg IV every 3 weeks or 10 mg/kg IV every 2 weeks.
E. The safety and effectiveness of Avastin/Mvasi/Zirabev in **pediatric** patients have not been established. Requests for Avastin/Mvasi/Zirabev use in pediatric patients will be reviewed based on the Off-Label Use of FDA Approved Drugs policy.
F. No prior authorization is required for Avastin, Mvasi or Zirabev when used to treat the eye.
G. Unless otherwise stated above within the individual drug criteria, **approval time periods** are listed in the table below.
    - Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the

requested product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary. Recertification reviews may result in the requirement to try more cost-effective treatment alternatives as they become available (i.e.; generics, biosimilars, or other guideline-supported treatment options). Requested dosing must continue to be consistent with FDA-approved or off-label/guideline-supported dosing recommendations.

Line of Business	Initial approval	Continued approval
Medicaid Managed Care (MMC) / Child Health Plus (CHP)	6 months	12 months
Commercial / Exchange	Outpatient Hospital – 6 months	Outpatient Hospital – 6 months
	Home Care or Office Based – 2 years	Home Care or Office Based – 2 years
Medicare	Outpatient Hospital – 2 years	Outpatient Hospital – 2 years
	Home Care or Office Based – 2 years	Home Care or Office Based – 2 years

II. **Bevacizumab (Avastin), Mvasi (bevacizumab-awwb) and Zirabev (bevacizumab-bvzr) are considered experimental and investigational for any of the following** indications because effectiveness for these indications has not been established (not an all-inclusive list) and thus will not be covered: (please refer to Off-Label Use of FDA Approved Drugs policy)

1. Von Hippel Lindau disease
2. Sub-foveal neovascularization due to ocular histoplasmosis
3. Esophageal cancer
4. Pancreatic cancer
5. Prostate cancer
6. Cholangiocarcinoma
7. Melanoma
8. Multiple myeloma
9. Hepatocellular carcinoma
10. Hereditary Hemorrhagic Telangiectasia

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.

CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.

Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).

HCPCS:

J9035 Avastin

Q5107 Mvasi
Q5118 Zirabev

UPDATES:

Date	Revision
01/2020	Revised
01/2020	Revised
10/2019	Revised
10/2019	Revised
10/2019	Revised
09/2019	Revised
5/2019	P&T Approval
5/2019	Reviewed
9/2018	Revised
10/2016	Revised
4/2016	Revised
11/2015	Revised
11/2014	Revised
2/2014	Revised
12/2013	Revised
10/2012	Revised
12/2011	Revised
2/2011	Revised
12/2010	Revised
3/2010	Revised
9/2009	Revised

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