Mass General Brigham
Health Plan

Angiogenesis Inhibitors:
Avastin® (bevacizumab)
Alymsys® (bevacizumab-maly)
Mvasi® (bevacizumab-awwb)
Cyramza® (ramucirumab)
Vegzelma® (bevacizumab-adcd)
Zaltrap® (ziv-aflibercept)
Zirabev® (bevacizumab-bvzr
Effective 06/05/23

Plan	☒ MassHealth UPPL ☐Commercial/Exchange	**Program Type**	☒ Prior Authorization ☐ Quantity Limit ☐ Step Therapy
Benefit	☐ Pharmacy Benefit ☒ Medical Benefit		
Specialty Limitations	N/A		
Contact Information	**Medical and Specialty Medications**		
	All Plans	Phone: 877-519-1908	Fax: 855-540-3693
	Non-Specialty Medications		
	All Plans	Phone: 800-711-4555	Fax: 844-403-1029
Exceptions	N/A		

Overview
Avastin® (bevacizumab) is recombinant, humanized monoclonal antibody (mAb) indicated for the treatment of cervical cancer, metastatic colorectal cancer (mCRC), non-squamous non-small cell lung cancer (NSCLC), glioblastoma, metastatic renal cell carcinoma, ovarian cancer (stage III or IV following initial resection, platinum-resistant, or platinum-sensitive), and hepatocellular carcinoma; often as a part of combination therapy.

Alymsys® (bevacizumab-maly), Mvasi® (bevacizumab-awwb), Vegzelma® (bevacizumab-adcd), and Zirabev® (bevacizumab-bvzr) are biosimilars to the reference product Avastin® (bevacizumab). Alymsys® (bevacizumab-maly) has all of the same FDA-approved indications as Avastin® (bevacizumab) except for several ovarian cancer indications and hepatocellular carcinoma. Mvasi® (bevacizumab-awwb), Vegzelma® (bevacizumab-adcd) and Zirabev® (bevacizumab-bvzr) have all of the same FDA-approved indications as Avastin® (bevacizumab) except for hepatocellular carcinoma.

Cyramza® (ramucirumab) is a fully human immunoglobulin G1 (IgG1) mAb that is indicated for the treatment of patients with advanced or metastatic gastric or gastro-esophageal junction (GEJ) adenocarcinoma with disease progression on or after prior fluoropyrimidine- or platinum-containing chemotherapy; in combination with docetaxel, for the treatment of metastatic NSCLC with disease progression on or after platinum-based chemotherapy; in combination with FOLFIRI (irinotecan plus 5- fluorouracin [5-FU]/leucovorin), for the treatment of patients with metastatic colorectal cancer (mCRC) with disease progression on or after prior therapy with bevacizumab, oxaliplatin and a fluoropyrimidine; and as a single agent, for the treatment of

hepatocellular carcinoma in patients who have an alpha fetoprotein (AFP) of ≥400 ng/mL and have been treated with sorafenib.

Zaltrap® (ziv-aflibercept) is a fully humanized recombinant fusion protein that functions as a decoy VEGF receptor that is indicated for patients with mCRC that is resistant to or has progressed following an oxaliplatin-containing regimen.

No PA	Require PA
Alternatives vary by specific malignancy and may include systemic chemotherapy (e.g., platinum [cisplatin, carboplatin]-containing regimens for non-small cell lung cancer).	Alymsys® (bevacizumab-maly) Avastin® (bevacizumab) Cyramza® (ramucirumab) Mvasi® (bevacizumab-awwb) Vegzelma® (bevacizumab-adcd) Zaltrap® (ziv-aflibercept) Zirabev® (bevacizumab-bvzr)

Coverage Guidelines
Authorization may be reviewed on a case by case basis for members who are new to the plan currently receiving treatment with requested medication excluding when the product is obtained as samples or via manufacturer's patient assistance programs.
OR
Authorization may be granted for members when all the following criteria are met, and documentation is provided:

Alymsys® (bevacizumab-maly), **Avastin®** (bevacizumab), **Mvasi®** (bevacizumab-awwb), **Zirabev®** (bevacizumab-bvzr), and **Vegzelma®** (bevacizumab-adcd)
Prescriber provides documentation of **ONE** of the following:

1. Diagnosis of **cervical cancer**
    a. Prescriber is an oncologist
    b. Appropriate dosing (weight required)
    c. Requested agent will be used in combination with paclitaxel and cisplatin OR paclitaxel and topotecan
2. **ALL** of the following:
    a. Diagnosis of **ONE** of the following:
        i. recurrent glioblastoma
        ii. Ovarian cancer
        iii. Fallopian cancer
        iv. Primary peritoneal cancer
    b. Prescriber is an oncologist
    c. Appropriate dosing (weight required)
3. Diagnosis of **metastatic colorectal cancer (mCRC)**
    a. Prescriber is an oncologist
    b. Appropriate dosing (weight required)
    c. Requested agent will be used in combination with fluoropyrimidine-, capecitabine-, oxaliplatin-, or irinotecan-containing therapy
4. Diagnosis of **metastatic renal cell carcinoma (mRCC)**
    a. Prescriber is an oncologist

b. Appropriate dosing (weight required)
c. If predominant clear cell histology, requested agent will be used in combination with interferon alfa

5. Diagnosis of **metastatic non-small cell lung cancer (NSCLC**) (subtype adenocarcinoma or large cell carcinoma)
    a. Prescriber is an oncologist
    b. Appropriate dosing (weight required)
    c. Requested agent will be used in combination with carboplatin and paclitaxel (See appendix)
6. Diagnosis of **Nonsquamous NSCLC with EGFR mutation positive** (e.g., Exon 19 deletion or L858R) – off label
    a. Prescriber is an oncologist
    b. Requested agent will be used in combination with erlotinib
7. Diagnosis of **adenocarcinoma, large cell, NSCLC not otherwise specified with PD-L1 expression positive** – off label
    a. Prescriber is an oncologist
    b. Requested agent will be used in combination with carboplatin, paclitaxel and atezolizumab *
8. Diagnosis of **advanced or metastatic NSCLC** (initial therapy)
    a. Prescriber is an oncologist
    b. Member is documented to have a contraindication to PD-1 or PD-L1 inhibitors**
    c. **ONE** of the following:
        i. Requested agent will be used in combination with carboplatin and pemetrexed
        ii. Requested agent will be used in combination with cisplatin and pemetrexed
9. Diagnosis of **advanced or metastatic NSCLC** (maintenance therapy)
    a. Prescriber is an oncologist
    b. **ONE** of the following:
        i. Requested agent will be used as monotherapy
        ii. Requested agent will be used in combination with atezolizumab
        iii. Requested agent will be used in combination with pemetrexed

**(If positive response to first-line therapy or member noted to have stable disease, bevacizumab plus atezolizumab can be continued together without carboplatin and paclitaxel)*
***(Contraindications for treatment with PD-1/PD-L1 inhibitors may include active or previously documented autoimmune disease and/or current use of immunosuppressive agents; some oncogenic drivers (i.e., EGFR exon 19 deletion or L858R, ALK rearrangements) have been shown to be associated with less benefit from PD-1/PD-L1 inhibitors.*

Avastin® (bevacizumab)
Prescriber provides documentation of **ONE** of the following:

1. Diagnosis of **unresectable or metastatic hepatocellular carcinoma (HCC)**
    a. Prescriber is an oncologist
    b. Appropriate dosing (weight required)
    c. Requested agent will be used in combination with Tecentriq® (atezolizumab)
    d. Member has Child-Pugh Class A
2. **ALL** of the following:
    a. Diagnosis of one of the following:
        i. Wet age-related macular degeneration (AMD)
        ii. Macular edema following retinal vein occlusion (RVO), diabetic macular edema (DME), diabetic retinopathy (DR) or myopic choroidal neovascularization (mCNV)
    b. Requested dosing is 1.25 mg intravitreally every four or eight weeks or as needed

Cyramza® (ramucirumab)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of **gastric or GEJ adenocarcinoma**
    a. Prescriber is an oncologist
    b. Appropriate dosing (weight required)
    c. Physician documented of an inadequate response or adverse reaction to ONE, or contraindication to BOTH of the following:
        i. fluoropyrimidine-containing chemotherapy regimen
        ii. platinum-containing chemotherapy regimen
3. Diagnosis of **HCC**
    a. Prescriber is an oncologist
    b. Appropriate dosing (weight required)
    c. Alpha fetoprotein (AFP) ≥400 ng/mL
    d. Physician documented of an inadequate response, adverse reaction, or contraindication to Nexavar® (sorafenib)
4. Diagnosis of **mCRC**
    a. Prescriber is an oncologist
    b. Appropriate dosing (weight required)
    c. Requested agent will be used in combination with FOLFIRI (irinotecan, leucovorin and 5-fluorouracil) or irinotecan
    d. Physician documented of an inadequate response, adverse reaction, or contraindication to a 5-fluorouracil/leucovorin or capecitabine-based regimen
5. Diagnosis of **NSCLC**
    a. Prescriber is an oncologist
    b. Appropriate dosing (weight required)
    c. **ONE** of the following:
        i. **ALL** of the following:
            1. Requested agent will be used in combination with docetaxel
            2. Physician documented of an inadequate response, adverse reaction, or contraindication to a platinum-containing chemotherapy regimen
        ii. **ALL** of the following:
            1. Requested agent will be used in combination with erlotinib
        iii. Physician documentation of an EGFR exon 19 deletion or exon 21 L858R mutation
        iv. Physician documented of an inadequate response, adverse reaction, or contraindication to Tagrisso® (osimertinib) and **ONE** of the following:
            1. Gilotrif® (afatinib)
            2. Iressa® (gefitinib)

Zaltrap® (ziv-aflibercept)
Prescriber provides documentation of **ALL** of the following:

1. Diagnosis of **mCRC**
2. Prescriber is an oncologist
3. Appropriate dosing (weight required)
4. Requested agent will be used in combination with either irinotecan or FOLFIRI
5. Physician documented of an inadequate response or adverse reaction to ONE of the following regimens or a contraindication to ALL of the following regimens:
    a. CAPEOX

b. FOLFOX
c. A fluoropyrimidine (capecitabine or 5-FU)
d. oxaliplatin-based therapy

6. Physician documented of an inadequate response, adverse reaction, or a contraindication to a bevacizumab product

Continuation of Therapy

Resubmission by prescriber will infer a positive response to therapy.

Limitations

1. Initial approvals will be granted for 6 months.
2. Reauthorizations will be granted for the following:
    a. Avastin® (bevacizumab) for diagnosis of Wet AMD or macular edema following RVO, DME, DR, or mCNV: 12 months
    b. All other agents: 6 months

Appendix

Chemotherapy Regimens

Platinum-based chemotherapy regimens that may be used to treat NSCLC often include cisplatin and carboplatin.

Platinum-based chemotherapy regimens that may be used to treat gastric cancer often include cisplatin, carboplatin, and oxaliplatin. Fluoropyrimidine include fluorouracil (5-FU) or capecitabine.

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Review History

02/08/2023 - Reviewed and created for Feb P&T; Matched MH UPPL criteria. Added Cyramza and Zaltrep criteria. Renamed criteria to "Angiogenesis Inhibitors." Added Alymsys (bevacizumab-maly). Information for off-label utilization of intravitreal Avastin for wet AMD, macular edema following RVO, DME, or DR added to criteria. Clarified approval durations. Formatting updates. Effective 4/1/23.

05/10/23 – Reviewed and updated for P&T. Added Vegzelma® (bevacizumab-adcd) to policy. Added indication of myopic choroidal neovascularization (mCNV) for Avastin. Effective 6/5/23