Mass General Brigham
Health Plan

Angiogenesis Inhibitors
Alymsys (bevacizumab-maly)
Avastin (bevacizumab)
Jobevne (bevacizumab-nwgd)
Cyramza (ramucirumab)
Zaltrap (ziv-aflibercept)
Effective 01/04/2027

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 Benefit** **Pharmacy Benefit**	Phone: 833-895-2611 Phone: 800-711-4555	Fax: 888-656-6671 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), **Jobevne** (bevacizumab-nwgd), **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. Jobevne (bevacizumab-nwgd), 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.

Coverage Guidelines
If member is new to the plan (as evidenced by coverage effective date of less than or equal to 90 days), submission of medical records documenting that the member is currently receiving treatment with the requested drug, 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:

Alymsys (bevacizumab-maly)
Avastin (bevacizumab)
Jobevne (bevacizumab-nwgd)

Cervical Cancer

1. Diagnosis of persistent, recurrent, or metastatic cervical cancer
2. Prescriber is an oncologist
3. Appropriate dosing (weight required)
4. ONE of the following:
    a. Requested agent will be used in combination with **ONE** of the following:
        i. Paclitaxel and carboplatin (if PD-L1-positive tumors, pembrolizumab or atezolizumab can be added)
        ii. paclitaxel and cisplatin (if PD-L1-positive tumors, pembrolizumab or atezolizumab can be added)
        iii. paclitaxel and topotecan
    b. Requested agent will be used as monotherapy
    c. Clinical rationale for the requested agent used in combination with an NCCN-supported category 1 or 2A recommended regimen
5. BOTH of the following:
    a. Inadequate response, adverse reaction, or contraindication to **ALL** of the following:
        i. Mvasi (bevacizumab-awwb)
        ii. Vegzelma (bevacizumab-adcd
        iii. Zirabev (bevacizumab-bvzr)
    b. Clinical rationale why the requested non-preferred agent is expected to provide a different clinical outcome than the preferred agents

Recurrent Glioblastoma, Ovarian Cancer, Fallopian Cancer, Primary Peritoneal Cancer

1. Diagnosis of **ONE** of the following:
    a. Recurrent glioblastoma
    b. Ovarian cancer
    c. Fallopian cancer
    d. Primary peritoneal cancer
2. Prescriber is an oncologist
3. Appropriate dosing (weight required)
4. BOTH of the following:
    a. Inadequate response, adverse reaction, or contraindication to **ALL** of the following:

i. Mvasi (bevacizumab-awwb)
ii. Vegzelma (bevacizumab-adcd
iii. Zirabev (bevacizumab-bvzr)

b. Clinical rationale why the requested non-preferred agent is expected to provide a different clinical outcome than the preferred agents

Metastatic Colorectal Cancer (mCRC)

1. Diagnosis of metastatic colorectal cancer (mCRC)
2. Prescriber is an oncologist
3. Appropriate dosing (weight required)
4. ONE of the following:
    a. Requested agent will be used in combination with **ONE** of the following:
        i. fluoropyrimidine-containing therapy
        ii. capecitabine- containing therapy
        iii. oxaliplatin- containing therapy
        iv. irinotecan-containing therapy
        v. Lonsurf (trifluridine/tipiracil)
    b. Clinical rationale for the requested agent used in combination with an NCCN-supported category 1 or 2A recommended regimen
5. BOTH of the following:
    a. Inadequate response, adverse reaction, or contraindication to **ALL** of the following:
        i. Mvasi (bevacizumab-awwb)
        ii. Vegzelma (bevacizumab-adcd
        iii. Zirabev (bevacizumab-bvzr)
    b. Clinical rationale why the requested non-preferred agent is expected to provide a different clinical outcome than the preferred agents

Metastatic Renal Cell Carcinoma (mRCC)

1. Diagnosis of metastatic renal cell carcinoma (mRCC)
2. Prescriber is an oncologist
3. Appropriate dosing (weight required)
4. BOTH of the following:
    a. Inadequate response, adverse reaction, or contraindication to **ALL** of the following:
        i. Mvasi (bevacizumab-awwb)
        ii. Vegzelma (bevacizumab-adcd
        iii. Zirabev (bevacizumab-bvzr)
    b. Clinical rationale why the requested non-preferred agent is expected to provide a different clinical outcome than the preferred agents

Metastatic Non-Small Cell Lung Cancer (NSCLC)

1. Diagnosis of unresectable, locally advanced, recurrent or metastatic nonsquamous NSCLC
2. Prescriber is an oncologist
3. Appropriate dosing (weight required)
4. Requested agent will be used in combination with **BOTH** of the following: (see Appendix)
    a. carboplatin
    b. paclitaxel
5. BOTH of the following:

a. Inadequate response, adverse reaction, or contraindication to **ALL** of the following:
    i. Mvasi (bevacizumab-awwb)
    ii. Vegzelma (bevacizumab-adcd
    iii. Zirabev (bevacizumab-bvzr)
b. Clinical rationale why the requested non-preferred agent is expected to provide a different clinical outcome than the preferred agents

Non-Squamous NSCLC

1. Diagnosis of non-squamous NSCLC with EGFR mutation positive (e.g., Exon 19 deletion or L858R)
2. Prescriber is an oncologist
3. Requested agent will be used in combination with erlotinib
4. BOTH of the following:
    a. Inadequate response, adverse reaction, or contraindication to **ALL** of the following:
        i. Mvasi (bevacizumab-awwb)
        ii. Vegzelma (bevacizumab-adcd
        iii. Zirabev (bevacizumab-bvzr)
    b. Clinical rationale why the requested non-preferred agent is expected to provide a different clinical outcome than the preferred agents

Advanced or Metastatic Adenocarcinoma, Large Cell, NSCLC NOS with PD-L1 Expression Positive

1. Diagnosis of advanced or metastatic adenocarcinoma, large cell, NSCLC not otherwise specified with PD-L1 expression positive
2. Prescriber is an oncologist
3. Requested agent will be used in combination with **ALL** of the following:
    a. carboplatin
    b. paclitaxel
    a. Tecentriq (atezolizumab) or Tecentriq Hybreza (atezolizumab and hyaluronidase-tqjs)*
2. BOTH of the following:
    a. Inadequate response, adverse reaction, or contraindication to **ALL** of the following:
        i. Mvasi (bevacizumab-awwb)
        ii. Vegzelma (bevacizumab-adcd
        iii. Zirabev (bevacizumab-bvzr)
    b. Clinical rationale why the requested non-preferred agent is expected to provide a different clinical outcome than the preferred agents

Initial Therapy - Advanced or Metastatic Adenocarcinoma, Large Cell, NSCLC NOS (performance status [PS] 0-2)

1. Diagnosis of advanced or metastatic NSCLC
2. Prescriber is an oncologist
3. Member is documented to have a contraindication to PD-1 or PD-L1 inhibitors**
4. Requested agent will be used in combination with **ONE** of the following:
    a. carboplatin and pemetrexed
    b. cisplatin and pemetrexed
5. BOTH of the following:
    a. Inadequate response, adverse reaction, or contraindication to **ALL** of the following:
        i. Mvasi (bevacizumab-awwb)
        ii. Vegzelma (bevacizumab-adcd
        iii. Zirabev (bevacizumab-bvzr)

b. Clinical rationale why the requested non-preferred agent is expected to provide a different clinical outcome than the preferred agents

Maintenance Therapy – Advanced or Metastatic Adenocarcinoma, Large Cell, NSCLC NOS (PS 0-2)

1. Diagnosis of advanced or metastatic NSCLC
2. Prescriber is an oncologist
3. **ONE** of the following:
    a. Requested agent will be used as monotherapy
    b. Requested agent will be used in combination with **ONE** of the following:
        i. Tecentriq (atezolizumab) or Tecentriq Hybreza (atezolizumab and hyaluronidase-tqjs)
        ii. pemetrexed
4. BOTH of the following:
    a. Inadequate response, adverse reaction, or contraindication to **ALL** of the following:
        i. Mvasi (bevacizumab-awwb)
        ii. Vegzelma (bevacizumab-adcd
        iii. Zirabev (bevacizumab-bvzr)
    b. Clinical rationale why the requested non-preferred agent is expected to provide a different clinical outcome than the preferred agents

**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.*

Hepatocellular Carcinoma (HCC)

3. Diagnosis of unresectable or metastatic hepatocellular carcinoma (HCC)
4. Prescriber is an oncologist
5. Appropriate dosing (weight required)
6. Requested agent will be used in combination with **ONE** of the following:
    a. Tecentriq (atezolizumab)
    b. Tecentriq Hybreza (atezolizumab and hyaluronidase-tqjs)
7. BOTH of the following:
    a. Inadequate response, adverse reaction, or contraindication to **ALL** of the following:
        i. Mvasi (bevacizumab-awwb)
        ii. Vegzelma (bevacizumab-adcd
        iii. Zirabev (bevacizumab-bvzr)
    b. Clinical rationale why the requested non-preferred agent is expected to provide a different clinical outcome than the preferred agents

Cyramza (ramucirumab)

Gastric or gastro-esophageal junction (GEJ) Adenocarcinoma

1. Diagnosis of gastric or GEJ adenocarcinoma
2. Prescriber is an oncologist
3. Appropriate dosing (weight required)

4. Inadequate response or adverse reaction to **ONE** or contraindication to **BOTH** of the following:
    a. fluoropyrimidine-containing chemotherapy regimen
    b. platinum-containing chemotherapy regimen

Hepatocellular Carcinoma (HCC)

1. Diagnosis of HCC
2. Prescriber is an oncologist
3. Appropriate dosing (weight required)
4. Alpha fetoprotein (AFP) ≥400 ng/mL
5. Inadequate response or adverse reaction to **ONE** or contraindication to **ALL** of the following:
    a. Imfinzi (durvalumab) with or without Imjudo (tremelimumab)
    b. Lenvima (lenvatinib)
    c. sorafenib
    d. Tecentriq (atezolizumab) or Tecentiq Hybreza (atezolizumab and hyaluronidase-tqjs) in combination with bevacizumab
    e. Tevimbra (tislelizumab-jsgr)
    f. Yervoy (ipilimumab) in combination with Opdivo (nivolumab)

Metastatic Colorectal Cancer (mCRC)

1. Diagnosis of mCRC
2. Prescriber is an oncologist
3. Appropriate dosing (weight required)
4. Requested agent will be used in combination with **ONE** of the following:
    a. FOLFIRI (irinotecan, leucovorin and 5-fluorouracil)
    b. irinotecan
5. Inadequate response, adverse reaction or contraindication to ALL of the following:
    a. bevacizumab
    b. fluoropyrimidine (i.e. fluorouracil, capecitabine)
    c. oxaliplatin

Non-Small Cell Lung Cancer (NSCLC)

1. Diagnosis of NSCLC
2. Prescriber is an oncologist
3. Appropriate dosing (weight required)
4. **ONE** of the following:
    a. **BOTH** of the following:
        i. Requested agent will be used in combination with docetaxel
        ii. Inadequate response, adverse reaction, or contraindication to a platinum-containing chemotherapy regimen
    b. **ALL** of the following:
        i. Requested agent will be used in combination with erlotinib
        ii. Cancer displays the EGFR exon 19 deletion or exon 21 L858R mutation
    c. Inadequate response or adverse reaction to **ONE** or contraindication to **ALL** of the following:
        i. Tagrisso (osimertinib)
        ii. Gilotrif (afatinib)
        iii. Iressa (gefitinib)
        iv. Vizimpro (dacomitinib)

Zaltrap (ziv-aflibercept)

1. Diagnosis of metastatic colorectal cancer (mCRC)
2. Prescriber is an oncologist
3. Appropriate dosing (weight required)
4. Requested agent will be used in combination with irinotecan or FOLFIRI
5. 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. 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 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
09/11/24 – Reviewed and updated for P&T. Updated criteria for cervical cancer with bevacizumab products to include notation that these can be used in combination with paclitaxel and carboplatin and if PD-L1 positive tumors, pembrolizumab can be added to bevacizumab regimen. NSCLC criteria for Cyramza was updated based on NCCN guideline to include osimertinib or dacomitinib as trial options. Effective 10/1/24
08/13/25 – Reviewed and updated for P&T. Removed criteria point of Child-Pugh class from Avastin HCC per NCCN update. Updated formatting. Cyramza for HCC was updated to include 1st line preferred options per NCCN. Criteria for metastatic RCC updated for bevacizumab products to remove the requirement to use in combination with interferon alfa as no longer listed in NCCN. Tecentriq Hybreza added as an option to use in combination with bevacizumab products for HCC as well as for NSCLC criteria where appropriate. Effective 9/1/25
Reviewed and updated for P&T. Cyramza for HCC was updated to include 1st line preferred options per NCCN. 09/10/25 - Criteria for metastatic RCC updated for bevacizumab products to remove the requirement to use in combination with interferon alfa as no longer listed in NCCN. Tecentriq Hybreza added as an option to use in combination with bevacizumab products for HCC as well as for NSCLC criteria where appropriate. Effective 10/1/25
09/10/26 – Reviewed and updated for P&T. Added Jobevne to policy requiring PA under MB. Updated criteria for cervical cancer with bevacizumab products to include notation that these can be used in combination with paclitaxel and carboplatin and if PD-L1 positive tumors, pembrolizumab or atezolizumab can be added to bevacizumab regimen. Specification of the diagnosis of persistent, recurrent, or metastatic cervical cancer. Added the option of monotherapy or clinical rationale for use of requested agent in combination with an NCCN-supported category 1 or 2A recommended regimen was added to criteria for cervical cancer. Lonsurf (trifluridine/tipiracil) added as an option to use in combination with bevacizumab products for mCRC. Added the option of clinical rationale for use of requested agent in combination with an NCCN-supported category 1 or 2A recommended regimen for mCRC. For Cyramza (ramucirumab) HCC, the addition of first line options of Tevimbra (tislelizumab-jsgr) or Yervoy (ipilimumab) + Opdivo (nivolumab). For Cyramza (ramucirumab) mCRC, the addition of trying ALL first line options of bevacizumab, fluoropyrimidine (i.e. fluorouracil, capecitabine), and oxaliplatin. Effective 10/1/26
11/4/26 – Reviewed and updated for P&T. Removed PA requirement for Mvasi, Vegzelma, and Zirabev. Added these preferred biosimilars as step-through trials for all indications for Alymsys, Avastin, and Jobevne. Removed the criteria for Avastin for the diagnosis of Wet AMD or macular edema following RVO, DME, DR, or mCNV – new management of the ophthalmic VEGF inhibitors is underway. Included Alymsys and Jobevne to the indication of Hepatocellular Carcinoma (HCC). Updated the reauthorization duration to 6 months for all indications. Updated formatting. Effective 1/4/27