Mass General Brigham
Health Plan

Multiple Myeloma Agents
Blenrep (belantamab mafodotin-blmf)
Darzalex (daratumumab)
Darzalex Faspro (daratumumab-hyaluronidase-fihi)
Empliciti (elotuzumab)
Kyprolis (carfilzomib)
Sarclisa (isatuximab
Effective 06/01/2025

<table>
<tr><td>Plan</td><td>☒ MassHealth UPPL
☐Commercial/Exchange</td><td rowspan="2">Program Type</td><td rowspan="2">☒ Prior Authorization
☐ Quantity Limit
☐ Step Therapy</td></tr>
<tr><td>Benefit</td><td>☐ Pharmacy Benefit
☒ Medical Benefit</td></tr>
<tr><td>Specialty Limitations</td><td colspan="3">N/A</td></tr>
<tr><td rowspan="2">Contact Information</td><td colspan="3">Medical and Specialty Medications
All Plans | Phone: 877-519-1908 | Fax: 855-540-3693</td></tr>
<tr><td colspan="3">Non-Specialty Medications
All Plans | Phone: 800-711-4555 | Fax: 844-403-1029</td></tr>
<tr><td>Notes</td><td colspan="3">Blenrep is also available on the pharmacy benefit. Please see the MassHealth Drug List for coverage and criteria.

Additional agents from this class are available through the pharmacy benefit. Please see the MassHealth Drug List for coverage and criteria.</td></tr>
</table>

Overview

Blenrep is a B-cell maturation antigen (BCMA)-directed antibody and microtubule inhibitor conjugate indicated for the treatment of adult patients with relapsed or refractory multiple myeloma who have received at least 4 prior therapies including an anti-CD38 monoclonal antibody, a proteasome inhibitor, and an immunomodulatory agent.

Darzalex is indicated for is a CD38-directed cytolytic antibody indicated for the treatment of adult patients with multiple myeloma.

Darzalex Faspro is a combination of daratumumab, a CD38-directed cytolytic antibody, and hyaluronidase, an endoglycosidase, indicated for the treatment of adult patients with multiple myeloma.

Empliciti is a SLAMF7-directed immunostimulatory antibody indicated in combination with lenalidomide and dexamethasone for the treatment of patients with multiple myeloma who have received one to three prior therapies.

Kyprolis is indicated in combination with dexamethasone or with lenalidomide plus dexamethasone for the treatment of patients with relapsed or refractory multiple myeloma

Sarclisa is a CD38-directed cytolytic antibody indicated, in combination with pomalidomide and dexamethasone, for the treatment of adult patients with multiple myeloma who have received at least two prior therapies including lenalidomide and a proteasome inhibitor.

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:

Blenrep (belantamab mafodotin-blmf)

1. Diagnosis of multiple myeloma
2. Prescriber is an oncologist or hematologist
3. Appropriate dosing
4. Member has received at least **FOUR** prior chemotherapy regimens **OR** contraindication to the use of recommended chemotherapy regimens
5. Inadequate response or adverse reaction to **ONE** or contraindication to **ALL** of the following proteasome inhibitors: bortezomib, Kyprolis (carfilzomib), Ninlaro (ixazomib), and Velcade (bortezomib)
6. Inadequate response or adverse reaction to **ONE** or contraindication to **ALL** of the following immunomodulatory agents: Pomalyst (pomalidomide), Revlimid (lenalidomide), and Thalomid (thalidomide)
7. Inadequate response or adverse reaction to **ONE** or contraindication to **ALL** of the following anti-CD38 monoclonal antibodies: Darzalex (daratumumab), Darzalex Faspro (daratumumab-hyaluronidase-fihj), and Sarclisa (isatuximab-irfc)

Documentation of prior treatments with listed agents above (criteria 5-7) is sufficient to meet approval criteria, regardless of clinical response.

Darzalex (daratumumab)
Darzalex Faspro (daratumumab hyaluronidase-fihj)

Multiple Myeloma - Monotherapy

1. Diagnosis of multiple myeloma
2. Agent will be used as monotherapy
3. Prescriber is an oncologist or hematologist
4. Appropriate dosing (For Darzalex (daratumumab): weight is required)
5. Physician attestation of inadequate response or adverse reaction to **ONE** or contraindication to **ALL** of the following:
    a. bortezomib
    b. Kyprolis (carfilzomib)
    c. Ninlaro (ixazomib)
    d. Velcade (bortezomib)
6. Physician attestation of inadequate response or adverse reaction to **ONE** or contraindication to **ALL** of the following immunomodulatory agents:
    a. Pomalyst (pomalidomide)
    b. Revlimid (lenalidomide)
    c. Thalomid (thalidomide)
7. **ONE** of the following:

a. Paid claims within the past 30 days or physician attestation of inadequate response or adverse reaction to **ONE** proteasome inhibitor and **ONE** immunomodulatory agent noted above
b. History of a total of **THREE** trials with chemotherapy regimens for the requested indication (*refer to NCCN guidelines for recommended regimens)*

Documentation of prior treatments with listed agents above (criteria 5-6) is sufficient to meet approval criteria, regardless of clinical response.

Multiple Myeloma – Combination Therapy

1. Diagnosis of multiple myeloma
2. Agent will be used as part of combination therapy
3. Prescriber is an oncologist or hematologist
4. Appropriate dosing (For Darzalex (daratumumab): weight required)
5. **ONE** of the following:
    a. **ALL** of the following:
        i. Member is newly diagnosed and ineligible for transplant
        ii. **ONE** of the following:
            1. Requested agent will be used in combination with Revlimid (lenalidomide) and dexamethasone
            2. Requested agent will be used in combination with Velcade (bortezomib) or bortezomib and melphalan and prednisone*
        iii. Clinical rationale for use of the requested combination instead of Velcade (bortezomib) or bortezomib and Revlimid (lenalidomide) and dexamethasone
    b. **BOTH** of the following:
        i. Member is newly diagnosed and eligible for transplant
        ii. Requested agent will be used in combination with Velcade (bortezomib) or bortezomib and thalidomide and dexamethasone†
    c. **BOTH** of the following:
        i. Physician attestation of inadequate response or adverse reaction to at least one prior line of systemic therapy
        ii. Requested agent will be used in combination with dexamethasone and at least one other agent for treatment of multiple myeloma (excluding anti-CD38 agents)

The NCCN also recommends the use of Darzalex (daratumumab) or Darzalex Faspro (daratumumab-hyaluronidase-fihj) in combination with Velcade (bortezomib) or bortezomib and cyclophosphamide and dexamethasone for this population; therefore, if a request for this combination meets all other criteria it may be **approved.*

*† The NCCN also recommends the use of Darzalex (daratumumab) or Darzalex Faspro (daratumumab-hyaluronidase-fihj) in combination with Velcade (bortezomib) or bortezomib and cyclophosphamide and dexamethasone or in combination with Velcade (bortezomib) or bortezomib and Revlimid (lenalidomide) and dexamethasone for this population; therefore, if a request combination meets all other criteria it may be **approved**.*

Darzalex Faspro (daratumumab-hyaluronidase-fihj)

1. Diagnosis of light chain amyloidosis
2. Prescriber is an oncologist or hematologist
3. Appropriate dosing
4. Requested agent will be used in combination with Velcade (bortezomib) or bortezomib and cyclophosphamide and dexamethasone

Empliciti (elotuzumab)

1. Diagnosis of multiple myeloma
2. Prescriber is an oncologist or hematologist

3. Appropriate dosing *(*weight required)
4. **ONE** of the following:
    a. **BOTH** of the following:
        i. Paid claims or physician attestation of inadequate response or adverse reaction to at least **ONE** prior regimen for the requested indication (*refer to NCCN guidelines for recommended regimens)*
        ii. Requested medication will be used in combination with Revlimid (lenalidomide) and dexamethasone†
    b. **ALL** of the following:
        i. Paid claims or physician attestation of inadequate response or adverse reaction to at least **TWO** prior regimens for the requested indication (*refer to NCCN guidelines for recommended regimens)*
        ii. Paid claims or physician attestation of inadequate response or adverse reaction to **ONE** or contraindication to **ALL** of the following:
            1. bortezomib
            2. Kyprolis (carfilzomib)
            3. Ninlaro (ixazomib)
            4. Velcade (bortezomib)
        iii. Paid claims or physician attestation of inadequate response, adverse reaction, or contraindication to Revlimid (lenalidomide)
        iv. Requested medication will be used in combination with Pomalyst (pomalidomide) and dexamethasone

†Empliciti (elotuzumab) in combination with Velcade (bortezomib) or bortezomib and dexamethasone is not an FDA-approved regimen; however, based on available data, the NCCN recommends this regimen as a treatment option for patients with relapsed or refractory multiple myeloma. If a request for this combination meets all other criteria (criteria 1 through 4a) and the prescriber documents clinical rationale for use of the requested combination instead of Empliciti (elotuzumab) plus Revlimid (lenalidomide) and dexamethasone, (e.g., inadequate response or adverse reaction to a Revlimid [lenalidomide] containing regimen or contraindication to Revlimid [lenalidomide]), it may be ***approved****.*

Kyprolis (cafirzomib)

Multiple Myeloma - Monotherapy

1. Diagnosis of multiple myeloma (monotherapy)
2. Agent will be used as monotherapy
3. Prescriber is an oncologist or hematologist
4. Appropriate dosing (height and weight OR BSA required)
5. Paid claims or physician attestation of inadequate response or adverse reaction to at least **ONE** prior chemotherapy regimen for the requested indication (*refer to NCCN guidelines for recommended regimens)*

Multiple Myeloma – Combination Therapy

1. Diagnosis of multiple myeloma
2. Agent will be used as part of combination therapy
3. Prescriber is an oncologist or hematologist
4. Appropriate dosing (height and weight OR BSA required)
5. Paid claims or physician attestation of inadequate response or adverse reaction to at least **ONE** prior chemotherapy regimen for the requested indication‡ (*refer to NCCN guidelines for recommended regimens)*

6. Requested medication will be used in combination with dexamethasone with or without additional agents for the treatment of multiple myeloma (excluding proteasome inhibitors)

‡ If the request is for carfilzomib in combination with lenalidomide and dexamethasone or cyclophosphamide and dexamethasone member may be approved without prior chemotherapy if all other criteria are met AND prescriber documents rationale for use of the requested regimen instead of Velcade (bortezomib) or bortezomib and Revlimid (lenalidomide) and dexamethasone.

Sarclisa (isatuximab-irfc)

1. Diagnosis of multiple myeloma
2. Prescriber is an oncologist or hematologist
3. Appropriate dosing (weight required)
4. **ONE** of the following:
    a. **BOTH** of the following:
        i. Paid claims or physician attestation of inadequate response or adverse reaction to **ONE** chemotherapy regimen for the requested indication (*refer to NCCN guidelines for recommended regimens)*
        ii. Requested agent will be used in combination with Kyprolis (carfilzomib) and dexamethasone
    b. **ALL** of the following:
        i. Paid claims or physician attestation of inadequate response or adverse reaction to **ONE** or contraindication to **ALL** of the following:
            1. bortezomib
            2. Kyprolis (carfilzomib)
            3. Ninlaro (ixazomib)
            4. Velcade (bortezomib)
        ii. Paid claims or physician attestation of inadequate response, adverse reaction, or contraindication to Revlimid (lenalidomide)
        iii. History of a total of at least **TWO** trials with appropriate regimens for the requested indication (*refer to NCCN guidelines for recommended regimens)*
        iv. Requested agent will be used in combination with Pomalyst (pomalidomide) and dexamethasone

<u>Continuation of Therapy</u>

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 12 months.

References

1. Carfilzomib (Kyprolis). Briefing Document for Oncologic Drugs Advisory Committee Meeting: NDA 202714. Rockville (MD): Food and Drug Administration: 2012 Jun 20 [cited 2017 Jan 20]. Available from: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/OncologicDrugsAdvisoryCommittee/UCM308563.pdf
2. Laubach JP. Multiple myeloma: Clinical features, laboratory manifestations, and diagnosis. In: Basow DS (Ed). UpToDate [database on the internet]. Waltham (MA): UpToDate; 2021 [cited 2021 Aug 10]. Available from: http://www.utdol.com/utd/index.do.
3. Darzalex [package insert]. Horsham (PA): Janssen Biotech, Inc.; 2025 Jan.

4. Empliciti [package insert]. Princeton (NJ): Bristol-Myers Squibb; 2022 Mar.
5. Kyprolis [package insert]. South San Francisco (CA): Onyx Pharmaceuticals Inc; 2024 Sep.
6. Darzalex Faspro (daratumumab-hyaluronidase-fihj) [package insert]. Horsham (PA): Janssen Biotech, Inc.; 2024 Aug.
7. Sarclisa [package insert]. Bridgewater (NJ): Sanofi-Aventis; 2024 Nov.
8. Blenrep [package insert]. Bridgewater (NJ): Sanofi-Aventis; 2022 Feb.
9. Daratumumab Approved in Multiple Myeloma. The ASCO Post. 2015 Nov 25; Volume 6, Issue 21. Cited 2016 Dec 12. Available from: http://www.ascopost.com/issues/november-25-2015/daratumumab-approved-in-multiple-myeloma/.
10. Lokhorst HM, Plesner T, Laubach JP, Nahi H, Gimsing P, Hansson M, et al. Targeting CD38 with Daratumumab Monotherapy in Multiple Myeloma. N Engl J Med. 2015 Sep 24;373(13):1207-19.
11. Lonial S, Dimopoulos M, Palumbo A. Elotuzumab Therapy for Relapsed or Refractory Multiple Myeloma. N Engl J Med 2015; 373:621-63.
12. FDA approves Empliciti, a new immune-stimulating therapy to treat multiple myeloma [FDA News Release]. Food and Drug Administration. 2015 Nov 30 [cited 2017 Jan 20]. Available from: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm474684.htm.
13. Siegel DS, Martin T, Wang M, Vij R, Jakubowiak AJ, Lonial S, et al. A phase 2 study of single-agent carfilzomib (PX-171-003-A1) in patients with relapsed and refractory multiple myeloma. Blood. 2012 Jul.
14. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Multiple Myeloma Version 7.2021 [guideline on the internet]. Fort Washington, Pennsylvania: National Comprehensive Cancer Network; 2021 Apr 26 [cited 2021 Aug 10]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.
15. Griffin PT, Ho VQ, Fulp W, Nishihori T, Shain KH, Alsina M, Baz RC. A comparison of salvage infusional chemotherapy regimens for recurrent/refractory multiple myeloma. Cancer. 2015 Oct 15;121(20):3622-30.
16. Gentile M, Vigna E, Recchia AG, Morabito L, Mendicino F, Giagnuolo G, Morabito F. Bendamustine in multiple myeloma. Eur J Haematol. 2015 Nov;95(5):377-88.
17. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): Systemic Light Chain Amyloidosis Version 1.2022 [guideline on the internet]. Fort Washington, Pennsylvania: National Comprehensive Cancer Network; 2021 Jun 29 [cited 2021 Aug 10]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.
18. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines): B-Cell Lymphomas Version 4.2021 [guideline on the internet]. Fort Washington, Pennsylvania: National Comprehensive Cancer Network; 2021 May 5 [cited 2021 Aug 10]. Available from: https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf.

Review History

01/26/2022 - Reviewed and created for P&T. Matched MH UPPL criteria to be in compliance with Masshealth unified formulary requirements. Effective 4/1/23.

07/12/2023 – Reviewed and updated for P&T. Darzalex Faspro and Sarclisa added to medical benefit with PA. Formatting for Blenrep and Xpovio updated to make verbiage consistent with other agents in the guideline, and "documentation of prior treatment with listed agents is sufficient to meet approval criteria, regardless of clinical response" footnote was added to agents requiring prior trials with LCAs. Chemotherapy Trials section of appendix was updated to match latest NCCN recommendations. Added appendix for Brand/generic preferred verbiage. Effective 07/31/2023.

05/15/2025 – Reviewed and updated for P&T. Performed annual medical criteria review. Policy has been updated to better reflect agents with prior authorization on medical benefit. Ninlaro, Pomalyst, and Xpovio are

pharmacy benefit only and thus have been removed. Updated formatting & references accordingly. Removed Appendix pertaining to NCCN recommendations as these are accessible online. Effective 6/1/25