Mass General Brigham
Health Plan

Off-Label Non-FDA Approved Indication
Effective 1/1/2026

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	Coverage for GLP-1s indicated for weight management or obesity may vary depending on the member's plan. Refer to the member's plan documents for additional details or exclusions.		

Overview
N/A

Coverage Guidelines
Authorization of a medication for off-label use may be approved when ALL of the following criteria are met:
Anti-cancer chemotherapeutic regimen

1. ONE of the following:
    a. Diagnosis is supported as a use in American Hospital Formulary Service Drug Information (AHFS DI)
    b. Diagnosis is supported as a use in the National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium with a Category of Evidence and Consensus of 1, 2A, or 2B (See NCCN Categories of Evidence and Consensus table in Appendix B)
    c. Diagnosis is supported in the FDA Uses/Non-FDA Uses section in DRUGDEX Evaluation with a Strength of Recommendation rating of Class I, Class IIa, or Class IIb (See DRUGDEX Strength of Recommendation table in Appendix A)
    d. Diagnosis is supported as an indication in Clinical Pharmacology
    e. Off-label use is supported in one of the published, peer-reviewed medical literature listed below:
        i. American Journal of Medicine
        ii. Annals of Internal Medicine
        iii. Annals of Oncology
        iv. Annals of Surgical Oncology
        v. Biology of Blood and Marrow Transplantation
        vi. Blood
        vii. Bone Marrow Transplantation
        viii. British Journal of Cancer
        ix. British Journal of Hematology
        x. British Medical Journal
        xi. Cancer
        xii. Clinical Cancer Research

xiii. Drugs
xiv. European Journal of Cancer (formerly the European Journal of Cancer and Clinical Oncology)
xv. Gynecologic Oncology
xvi. International Journal of Radiation, Oncology, Biology, and Physics
xvii. The Journal of American Medical Association
xviii. Journal of Clinical Oncology
xix. Journal of the National Cancer Institute
xx. Journal of the National Comprehensive Cancer Network (NCCN)
xxi. Journal of Urology
xxii. Lancet
xxiii. Lancet Oncology
xxiv. Leukemia
xxv. The New England Journal of Medicine
xxvi. Radiation Oncology

f. Diagnosis is supported as a use in Wolters Kluwer Lexi-Drugs as "Evidence Level A" with a "Strong" recommendation (See Lexi-Drugs Strength of Recommendation tablet in Appendix C)

All other indications

Member meets ALL of the following:

1. ONE of the following:
    a. Diagnosis is supported as a use in American Hospital Formulary Service Drug Information (AHFS DI)
    b. Diagnosis is supported in the FDA Uses/Non-FDA Uses section in DRUGDEX Evaluation with a Strength of Recommendation of IIb or better (see DRUGDEX Strength of Recommendation tablet in Appendix A)
    c. The use is supported by clinical research in two articles from major peer reviewed medical journals that present data supporting the proposed off-label use or uses as generally safe and effective unless there is clear and convincing contradictory evidence presented in a major peer-reviewed medical journal.
2. Documentation that member has had an inadequate response, adverse reaction or contraindication to ALL other formulary products with an FDA-approved indication for the treated diagnosis.

<u>Continuation of Therapy</u>

Requests for reauthorization will be approved when all of the following criteria are met:

1. Documentation the member requires continuation of therapy
2. Documentation demonstrating the member has had a positive clinical response to therapy

Limitations

1. Initial approvals will be granted for up to 6 months or up to a complete course of therapy if treatment duration is less than 6 months.
2. Reauthorization approvals will be granted for 12 months.
3. GLP-1s indicated for the treatment of type 2 diabetes will not be approved for non-FDA approved indications (e.g., weight management, prediabetes, type 1 diabetes).

Appendix

Appendix A: DRUGDEX Strength of Recommendation

Class	Recommendation	Description
Class I	Recommended	The given test or treatment has been proven useful, and should be performed or administered.
Class IIa	Recommended, In Most Cases	The given test or treatment is generally considered to be useful, and is indicated in most cases.
Class IIb	Recommended, in Some Cases	The given test or treatment may be useful, and is indicated in some, but not most, cases.
Class III	Not Recommended	The given test or treatment is not useful, and should be avoided
Class Indeterminate	Evidence Inconclusive	

Appendix B: NCCN Categories of Evidence and Consensus

Category	Level of Consensus
1	Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
2A	Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.
2B	Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.
3	Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

Appendix C:
Lexi-Drugs: Strength of Recommendation for Inclusion in Lexi-Drugs for Oncology Off-Label Use

Strong (for proposed off-label use)	The evidence persuasively supports the off-label use (ie, Level of Evidence A).
Equivocal (for proposed off-label use)	The evidence to support the off-label use is of uncertain clinical significance (ie, Level of Evidence B, C). Additional studies may be necessary to further define the role of this medication for the off-label use.
Against proposed off-label use	The evidence either advocates against the off-label use or suggests a lack of support for the off-label use (independent of Level of Evidence). Additional studies are necessary to define the role of this medication for the off-label use.

Lexi-Drugs: Level of Evidence Scale for Oncology Off-Label Use

A	Consistent evidence from well-performed randomized, controlled trials or overwhelming evidence of some other form (eg, results of the introduction of penicillin treatment) to support off-label use. Further research is unlikely to change confidence in the estimate of benefit.

B	Evidence from randomized, controlled trials with important limitations (eg, inconsistent results, methodologic flaws, indirect, imprecise); or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on confidence in the estimate of benefit and risk and may change the estimate.
C	Evidence from observational studies (eg, retrospective case series/reports providing significant impact on patient care); unsystematic clinical experience; or potentially flawed randomized, controlled trials (eg, when limited options exist for condition). Any estimate of effect is uncertain.
G	Use has been substantiated by inclusion in at least one evidence-based or consensus-based clinical practice guideline.

References

1. Center for Medicaid & Medicare Services. Medicare Prescription Drug Benefit Manual. Chapter 6 – Part D Drugs and Formulary Requirements. Section 10.6. Available at: https://www.cms.gov/Medicare/Prescription-Drug-Coverage/PrescriptionDrugCovContra/Downloads/Part-D-Benefits-Manual-Chapter-6.pdf. Accessed October 27, 2022.
2. Center for Medicaid & Medicare Services. Medicare Benefit Policy Manual. Chapter 15 - Covered Medical and Other Health Services. Section 50.4.5. Available at: https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/downloads/bp102c15.pdf. Accessed October 27, 2022.
3. National Comprehensive Cancer Network Categories of Evidence and Consensus. Available at: https://www.nccn.org/professionals/physician_gls/categories_of_consensus.aspx. Accessed September 9, 2020.
4. Center for Medicaid & Medicare Services. Medicare Benefit Policy Manual. Wolters Kluwer Clinical Drug Information Lexi-Drugs Compendium Revision Request - CAG-00443O. Available at: https://www.cms.gov/medicare-coverage-database/details/medicare-coverage-document-details.aspx?MCDId=31#decision. Accessed October 27, 2022.
5. Wolters Kluwer Clinical Drug Information's Request for CMS evaluation of Lexi-Drugs as a compendium for use in the determination of medically-accepted indications of drugs/biologicals used off-label in anti-cancer chemotherapeutic regimens. Available at: https://www.cms.gov/Medicare/Coverage/CoverageGenInfo/downloads/covdoc31.pdf. Accessed October 27, 2022.
6. Micromedex Healthcare Series. Recommendation, Evidence, and Efficacy Ratings. https://www.micromedexsolutions.com/micromedex2/librarian/ssl/true/CS/6E0ED9/ND_PR/evidencexpert/ND_P/evidencexpert/DUPLICATIONSHIELDSYNC/8B9F5B/ND_PG/evidencexpert/ND_B/evidencexpert/ND_AppProduct/evidencexpert/ND_T/evidencexpert/PFActionId/evidencexpert.IntermediateToDocumentLink?docId=3198&contentSetId=50. Accessed October 27, 2022.

Review History

01/10/2024 – Reviewed for Jan P&T; adopted Optum criteria for Coverage of Off-Label Non-FDA approved Indications. Effective 01/01/2024.
07/09/2025 – Reviewed and updated at July P&T. Administrative update – clarified that criteria apply to off-label use of a medication. Effective 07/09/2025.
08/13/2025 – Reviewed and updated at August P&T. Updated Limitations section to specify that GLP-1s indicated for the treatment of type 2 diabetes will not be approved for any off-label indications. Updated

Exceptions to clarify that coverage of GLP-1s indicated for weight management may vary depending on the member's plan and to review the member's plan documents for more information. Updated initial criteria for all non-anti-cancer chemotherapeutic regimens, requiring inadequate response, adverse reaction, or contraindication to all formulary agents FDA-approved for the requested diagnoses. Added continuation of therapy criteria. Effective 1/1/2026.