Mass General Brigham
Health Plan

Medical Necessity Guidelines
Papzimeos (zopapogene imadenovec-drba)

Policy Number: 111

Contents

Overview

Papzimeos (zopapogene imadenovec-drba) is a non-replicating adenoviral vector-based immunotherapy for adults with recurrent respiratory papillomatosis (RRP). It is designed to generate an immune response directed against HPV 6- and HPV 11-infected cells.

FDA-Approved Indication

- The treatment of RRP in adults.

Medicare Advantage

Prior Authorization Required	Yes ☒ No ☐

Mass General Brigham Health Plan uses guidance from the Centers for Medicare and Medicaid Services (CMS) for medical necessity determinations for its Medicare Advantage plan members. National Coverage Determinations (NCDs), Local Coverage Determinations (LCDs), Local Coverage Articles (LCAs), and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, Mass General Brigham Health Plan's medical policies are used for medical necessity determinations. **As of Mass General Brigham Health Plan's most recent policy review, Medicare had:**

- Medicare Benefit Policy Manual Chapter 15 – Covered Medical and Other Health Services

When CMS documentation references FDA labeling, Mass General Brigham Health Plan develops coverage criteria to clarify medical necessity of the requested services. Mass General Brigham Health Plan coverage criteria align with FDA labeling without contradicting existing determinations and enhance the clarity of medical necessity requirements, documentation requirements, and clinical indications.

Criteria

The member meets all of the following criteria:

1. The member is at least 18 years of age; and

2. The member has a diagnosis of RPP confirmed by biopsy; and
3. The member either has or will undergo debulking prior to administration of Papzimeos; and
4. The medication is prescribed by, or in consultation with, a pulmonologist, oncologist, thoracic surgeon, or otolaryngologist.

Dosage

- Papzimeos is for subcutaneous injection only.
- Recommended dose is 5x1011 particle units per injection administered four times over a 12-week period.
- Perform a surgical debulking of visible papilloma prior to initial administration, and prior to third and fourth administration if still visible.

Mass General Brigham ACO

Prior Authorization Required	Yes ☒ No ☐

Mass General Brigham Health Plan uses the MassHealth Drug List for medical necessity determinations for members of the Mass General Brigham ACO. Criteria for Papzimeos are found in Table 5: Immunological Agents.

One Care and Senior Care Options (SCO)

Prior Authorization Required	Yes ☒ No ☐

Mass General Brigham Health Plan uses guidance from CMS for medical necessity determinations for its One Care and SCO plan members. NCDs, LCDs, LCAs, and documentation included in the Medicare manuals are the basis for medical necessity determinations. When there is no guidance from CMS for the requested service, or the member does not meet all of the medical necessity criteria for the requested service, Mass General Brigham Health Plan uses medical necessity guidelines from MassHealth. **See Medicare Advantage criteria and exclusions above. If Medicare Advantage criteria are not met, then MassHealth criteria are applied.**

Commercial and Qualified Health Plans

Prior Authorization Required	Yes ☒ No ☐

Prior authorization for Papzimeos for Commercial and Qualified Health Plan members is managed by Prime Therapeutics. See the Prime Therapeutics policy for Papzimeos for more information.

Codes

The following codes are included below for informational purposes only; inclusion of a code does not constitute or imply coverage or reimbursement.

Authorized Code	Code Description
J3404	Injection, zopapogene imadenovec-drba suspension, per therapeutic dose

Summary of Evidence

RRP is a chronic, benign but debilitating condition driven by HPV types 6 and 11, marked by the repeated growth of papillomas throughout the airway. Because no curative treatment has historically existed, patients have typically required frequent surgical debridements to preserve airway function and voice quality (Shepherd &

Radchenko, 2026). Adjuvant pharmacologic options such as bevacizumab have been used in refractory cases; however, there remains a significant unmet need for treatments targeting the underlying cause (Symplr, 2025).

In 2025, the FDA approved zopapogene imadenovec-drba (Papzimeos; Precigen, Inc.), the first gene therapy indicated for RRP in adults. Papzimeos uses a replication-incompetent adenoviral vector to deliver HPV-6 and HPV-11 antigen-encoding sequences, stimulating a targeted cytotoxic T-cell immune response against HPV-infected papillomatous tissue rather than simply removing lesions surgically (Papzimeos [package insert], 2025; IPD Analytics, 2025). This immunotherapeutic mechanism represents a meaningful conceptual departure from prior management strategies, which addressed disease burden without modifying the underlying immune response to HPV.

The pivotal phase 1/2 trial by Norberg et al. (2025), published in The Lancet Respiratory Medicine, provided the core evidence base for approval. Among evaluable adult patients with RRP, 51% achieved a complete response with the median duration of complete response yet to be reached (Norberg et al., 2025). Adverse effects were generally mild to moderate and included injection site reactions, fatigue, myalgia, and flu-like symptoms, suggesting a manageable tolerability profile for most patients (Norberg et al., 2025; Papzimeos [package insert], 2025).

From a clinical utility standpoint, Papzimeos holds promise for reducing the cumulative surgical burden in adults with RRP, particularly those with high-frequency debridement needs. However, health technology assessments from both Symplr (2025) and IPD Analytics (2025) note that longer-term durability data are needed, and that real-world integration will depend on payer coverage decisions and the feasibility of administration within otolaryngology practice settings. At present, Papzimeos represents an important first step toward disease-modifying therapy in RRP, though its ultimate place in the treatment algorithm will continue to evolve as post-marketing evidence accumulates.

Effective Dates

May 2026: Effective date.

References

IPD Analytics. New drug review: Papzimeos (zopapogene imadenovec-drba). Sep 3, 2025. Accessed from https://secure.ipdanalytics.com/User/Handler/ViewReport.ashx?type=RP&file=s3%3a%2f%2fipdanalytics%2fReports%2fIPD+Analytics_RxInsights_New+Drug+Review_Papzimeos_09+2025.pdf on 3/17/2026.

Norberg SM, Valdez J, Napier S, et al. PRGN-2012 gene therapy in adults with recurrent respiratory papillomatosis: a pivotal phase 1/2 clinical trial. Lancet Respir Med. 2025 Apr;13(4):318-326. doi: 10.1016/S2213-2600(24)00368-0. Epub 2025 Jan 21. Erratum in: Lancet Respir Med. 2025 Apr;13(4):e22. doi: 10.1016/S2213-2600(25)00078-5. PMID: 39855244; PMCID: PMC11968209.

Papzimeos [package insert]. Germantown, MD: Precigen, Inc.; 2025.

Shepherd W, Radchenko C. Management of non-life-threatening, nonmalignant subglottic and tracheal stenosis in adults. UpToDate. Jan 8, 2026. Accessed from https://www.uptodate.com/contents/management-of-non-life-threatening-nonmalignant-subglottic-and-tracheal-stenosis-in-adults on 3/17/2026.

Symplr. Emerging technology report: zopapogene imadenovec-drba (Papzimeos; Precigen Inc.) for recurrent respiratory papillomatosis. Aug 20, 2025. Accessed from https://evidence.hayesinc.com/report/pg.zopapogene on 3/17/2026.