Clinical Policy: Zopapogene Imadenovec-drba (Papzimeos)

Reference Number: PA.CP.PHAR.730
Effective Date: 11/2025
Last Review Date: 10/2025

Description

Zopapogene imadenovec-drba (Papzimeos™) is a non-replicating adenoviral vector-based immunotherapy that elicits T-cell immunity specific to human papillomavirus (HPV) types 6 or 11.

FDA Approved Indication(s)

Papzimeos is indicated for the treatment of adults with recurrent respiratory papillomatosis (RRP).

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

All requests reviewed under this policy require **medical director review**.

It is the policy of PA Health & Wellness® that Papzimeos is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Respiratory Papillomatosis (must meet all)**:**

1. Diagnosis of RRP;
2. Diagnosis is confirmed by tissue biopsy;
3. Prescribed by or in consultation with an oncologist, otolaryngologist or pulmonologist;
4. Age ≥ 18 years;
5. Member has required intervention (i.e., surgical resection of papillomas, laser ablation of papillomas) to remove laryngotracheal papillomas prior to treatment with Papzimeos (*see Appendix D*);
6. If age ≤ 45 years, member meets one of the following (a or b):
   a. Has previously completed the HPV vaccination series;
   b. If has not completed the HPV vaccination series, has received at least the first dose of the HPV vaccination series, unless contraindicated or clinically significant adverse effects are experienced;
7. Prior to initiation of Papzimeos treatment, member is scheduled to undergo asurgical debulking procedure to remove laryngotracheal papilloma;
8. Dose does not exceed four total doses of 5×10^{11} particle units (PU).

Approval duration: 6 months

B. Other diagnoses/indications

1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Respiratory Papillomatosis:

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met all initial approval criteria or the Continuity of Care policy (PA.PHARM.01) applies.

Approval duration: Single treatment course (four doses per lifetime) only

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
HPV: human papillomavirus
PU: particle units
RRP: recurrent respiratory papillomatosis

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

None reported

Appendix D: General Information

- Voice and airway symptoms associated with RRP include hoarseness, voice change, chronic cough, difficulty breathing, choking episodes, foreign body sensation in the throat, wheezing, shortness of breath

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
RRP	5×10^{11} PU SC at day 0, 15, 43, and 85 Prior to the initial administration of Papzimeos, perform a surgical debulking of visible papilloma to establish minimal residual disease. To maintain minimal residual disease during treatment with Papzimeos, remove visible papilloma, if present, prior to the third and fourth administration of Papzimeos.	Four doses lifetime

VI. Product Availability
Single-dose vial: 5 x 10^{11} PU/mL

VII. References
1. Papzimeos Prescribing Information. Germantown, MD: Precigen, Inc.; August 2025. Available at: https://precigen.com/papzimeos-prescribing-information.pdf. Accessed August 21, 2025.
2. 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 Jan 21:S2213-2600(24)00368-0.
3. ClinicalTrials.gov. Adjuvant PRGN-2012 in adult patients with recurrent respiratory papillomatosis. Available at: https://clinicaltrials.gov/study/NCT04724980. Accessed March 18, 2025.
4. Lawlor C, Balakrishnan K, Bottero S, et al. International Pediatric Otolaryngology Group (IPOG): Juvenile-onset recurrent respiratory papillomatosis consensus recommendations. Int J Pediatr Otorhinolaryngol. 2020 Jan;128:109697.
5. Sporeni S, Rifaldi F, Lanzetta I, et al. Recurrent respiratory papillomatosis: role of bevacizumab and HPV vaccination. A literature review with case presentations. Radiol Oncol. 2025 Feb 27;59(1):23-30.
6. Balai E, Dronkers EA, Yaghchi CA, et al. Adjuvant treatments for recurrent respiratory papillomatosis: a descriptive review and proposed management guideline in adults. J Laryngol Otol. 2024 Dec;138(12):1133-1143.
7. American Academy of Otolaryngology-Head and Neck Surgery. Position Statement: Recurrent respiratory papillomatosis and Gardasil vaccination. April 5, 2021. Available at: https://www.entnet.org/resource/position-statement-recurrent-respiratory-papillomatosis-and-gardasil-vaccination/. Accessed April 8, 2025.
8. Kohli N, Pai SI, Buckingham J, et al. A clinical consensus statement on pulmonary recurrent respiratory papillomatosis. Laryngoscope. 2025 Aug 1.
9. Rosenberg T, Philipsen BB, Mehlum CS, et al. Therapeutic use of the human papillomavirus vaccine on recurrent respiratory papillomatosis: A systematic review and meta-analysis. J Infect Dis. 2019 Mar 15;219(7):1016-1025.
10. Smahelova J, Hamsikova E, Ludvikova V, et al. Outcomes after human papillomavirus vaccination in patients with recurrent respiratory papillomatosis: A nonrandomized clinical trial. JAMA Otolaryngol Head Neck Surg. 2022 Jul 1;148(7):654-661.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3590	Unclassified biologics
C9399	Unclassified drugs or biologicals

Reviews, Revisions, and Approvals	Date
Policy created	10/2025