Clinical Policy: Zopapogene Imadenovec-drba (Papzimeos)

Reference Number: CP.PHAR.730
Effective Date: 08.14.25
Last Review Date: 11.26
Line of Business: Commercial, HIM/ICHRA, Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

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 Precision Drug Action Committee (PDAC) Utilization Management Review**. Refer to CC.PHAR.21 for process details.

It is the policy of health plans affiliated with Centene Corporation® 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 otolaryngologist or pulmonologist;
4. Age ≥ 18 years;
5. In the previous 12 months, member has had ≥ 3 interventions (surgical resection or laser ablation) aimed at reducing voice and airway symptoms caused by the papilloma (*see Appendix D*);
6. If age ≤ 45 years, member has previously completed 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 an endoscopic surgical 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 (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. Respiratory Papillomatosis
1. Continued therapy will not be authorized as Papzimeos is indicated to be dosed as a single treatment course (four doses lifetime) only.

Approval duration: Not applicable

B. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace/ICHRA, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace/ICHRA) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace/ICHRA, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid.

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 –

CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace/ICHRA, and CP.PMN.53 for Medicaid or evidence of coverage documents.

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 July 9, 2026.
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.

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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
J3404	Injection, zopapogene imadenovec-drba suspension, per therapeutic dose

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created pre-emptively	04.08.25	05.25
RT1: drug is now FDA-approved; added option to be prescribed by or in consultation with a pulmonologist; for HPV vaccination requirement, clarified the vaccination series must be completed; references reviewed and updated.	09.09.25	11.25
Updated language under Policy/Criteria to effectively redirect prior authorization reviews to Precision Drug Action Committee (PDAC) Utilization Management Review.	11.04.25	
HCPCS code added [J3404]; codes removed [J3590, C9399].	02.18.26	
4Q 2026 annual review: added ICHRA line of business; references reviewed and updated.	07.09.26	11.26

Important Reminder
This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted

standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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