Drug Coverage Policy

Effective Date.....4/1/2026
Coverage Policy Number.....IP0765
Policy Title.....Papzimeos

Papillomatosis –Papzimeos

- Papzimeos™ (zopapogene imadenovec-drba subcutaneous injection – Precigen)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

OVERVIEW
Papzimeos, a non-replicating adenoviral vector-based immunotherapy, is indicated for the treatment of **recurrent respiratory papillomatosis**, in adults.[1]

Disease Overview
Recurrent respiratory papillomatosis (RRP) is a chronic disease characterized by papillomatous growths in the airway.[2] Low-risk types of human papillomavirus (HPV), specifically HPV6 and HPV11, are associated with the pathogenesis of RRP. Laryngotracheal papillomas can cause dysphonia and airway obstruction, and pulmonary papillomas can cause post-obstructive pneumonias and death. There is no cure for RRP and no approved pharmacologic therapies. Current standard of care is surgical therapy or laser ablation to remove the lesions and preserve the normal structure of the larynx. Patients often require dozens to hundreds of procedures during their lifetime. However, these therapies do not address the chronic HPV infection. There are an estimated 27,000 cases in the US and 1,000 new cases annually, but data on incidence is limited.[3]

Guidelines
There are no guidelines for the management and treatment of RRP. However, several organizations have issued consensus statements and position papers. The Department of Otolaryngology – Head and Neck Surgery published a consensus statement (2024) on the administration of systemic bevacizumab (Avastin®, biosimilars [intravenous infusion]) as a nonsurgical treatment option for patients with RRP.[7] The statement recommends systemic Avastin as a first-line therapy and advises evaluating all patients for treatment eligibility to minimize or eliminate the need for surgery. Treatment is expected to be indefinite. The document adopts a neutral stance on Avastin biosimilars, neither endorsing nor discouraging their use.

The American Academy of Otolaryngology issued a position statement (2021) on Gardasil®-9 (Human Papillomavirus 9-valent vaccine intramuscular injection [recombinant]) vaccination.[4] The statement encourages the use of Gardasil-9 HPV vaccination in all patients 9 to 45 years of age, highlighting a potential benefit for both the prevention and treatment of RRP since the vaccine covers subtypes most commonly implicated in RRP, as well as other conditions. This recommendation has also been endorsed by both the National Institute on Deafness and Other Communication Disorders and Centers for Disease Control and Prevention's Advisory Committee on Immunization Practices.[5,6]

Finally, the American Laryngological, Rhinological, and Otological Society published a consensus statement on pulmonary RRP (2025), in which 33 recommendation statements were made for screening, diagnosis, management, and treatment.[8] Regarding therapy, the statement emphasizes systemic Avastin as a commonly used option and encourages consideration of clinical trials exploring other systemic treatments.

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POLICY STATEMENT
Prior Authorization is required for benefit coverage of Papzimeos. All approvals are provided for one treatment course. Note: a treatment course consists of four subcutaneous doses administered over 12 weeks. Because of the specialized skills required for evaluation and diagnosis of patients treated with Papzimeos as well as the monitoring required for adverse events and long-term efficacy, approval requires Papzimeos to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Documentation: Documentation is required where noted in the criteria as **[documentation required]**. Documentation may include, but is not limited to, chart notes, laboratory tests, claims records, and/or other information.

Papzimeos is considered medically necessary when the following criteria are met:

FDA-Approved Indication

1. **Recurrent Respiratory Papillomatosis.** Approve for a total of four doses, enough to complete one treatment, if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 18 years of age; AND
   - **B)** Diagnosis of Recurrent Respiratory Papillomatosis has been confirmed by biopsy **[documentation required]**; AND
   - **C)** Patient has or will undergo debulking procedure prior to administration **[documentation required]**; AND
   - **D)** The medication is prescribed by, or in consultation with a pulmonologist, oncologist, thoracic surgeon, or otolaryngologist.

Conditions Not Covered

Papzimeos for any other use is considered not medically necessary, including the following (this list may not be all inclusive; criteria will be updated as newly published data are available):

1. **Recurrent Respiratory Papillomatosis – Re-Treatment**. The use of Papzimeos beyond four doses given over 12 weeks has not yet been established.[1]

Coding Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
C9399	Unclassified drugs or biologicals (Code effective until 3/31/2026)
J3404	Injection, zopapogene imadenovec-drba suspension, per therapeutic dose (Code effective 4/1/2026)
J3490	Unclassified drugs (Code effective until 3/31/2026)
J3590	Unclassified biologics (Code effective until 3/31/2026)

References

1. Papzimeos™ subcutaneous injection [prescribing information]. Germantown, MD: Precigen; August 2025.
2. Norberg SM, Valez 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;13: 318-326.
3. Ivancic R, Iqbal H, DeSilva B, et al. Current and future management of recurrent respiratory papillomatosis. *Laryngoscope Investigative Otolaryngology*. 2018;3: 22-34.
4. Position statement: recurrent respiratory papillomatosis and Gardasil vaccination. American Academy of Otolaryngology – Head and Neck Surgery. Available at: https://www.entnet.org/resource/position-statement-recurrent-respiratory-papillomatosis-and-gardasil-vaccination/. Updated on April 5, 2021. Accessed on August 18, 2025.

5. Recurrent respiratory papillomatosis or laryngeal papillomatosis. National Institute on Deafness and Other Communication Disorders. Available at: https://www.nidcd.nih.gov/health/recurrent-respiratory-papillomatosis. Updated on November 28, 2017. Accessed on August 18, 2025.
6. Meites E, Szilagyi PG, Chesson HW, et al. Human papillomavirus vaccination for adults: updated recommendations of the advisory committee on immunization practices. *MMWR*. 2019;68(32): 698-702.
7. Best SR, Bock JM, Fowler NB, et al. A consensus statement on the administration of systemic bevacizumab in patients with recurrent respiratory papillomatosis. *Laryngoscope*. 2024;134:5041-5046.
8. Kohli N, Pai SI, Buckingham J, et al. A clinical consensus statement on pulmonary recurrent respiratory papillomatosis. *Laryngoscope*. 2025 Aug 1. [Online ahead of print].

Revision Details

Summary of Changes	Review Date	Effective Date
New policy.	10/9/2025	12/1/2025
Coding Information: **Added** HCPCS code: J3404 (Code effective 4/1/2026) Updated the description for C9399, J3490 & J3590 to include the note "Code effective until 3/31/2026"	-	3/15/2026
Policy Title: **Removed** "Gene Therapy" from the policy title. No criteria changes.	3/26/2026	4/1/2026

The policy effective date is in force until updated or retired.