Utilization Review Policy 382

POLICY: Papillomatosis – Gene Therapy – Papzimeos Utilization Management Medical Policy
- Papzimeos™ (zopapogene imadenovec-drba subcutaneous injection – Precigen)

EFFECTIVE DATE: 02/01/2026
LAST REVISION DATE: 09/10/2025

COVERAGE CRITERIA FOR: All UCare Plans

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]

Dosing Information

The recommended dose of Papzimeos is 5 x 10^{11} particle units (PU) per injection administered as a subcutaneous (SC) injection four times over a 12-week interval.[1] The recommended dosing schedule is as follows: an initial dose on Day 1, followed by a second dose administered two weeks later, a third dose six weeks after the initial administration, and a final fourth dose 12 weeks after the initial administration. The second dose should occur no less than 11 days after the initial dose.

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.

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Papzimeos. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication(s). Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). 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.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Papzimeos is recommended in those who meet the following criteria:

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; AND
   - **C)** Patient has or will undergo debulking procedure prior to administration; AND
   - **D)** The medication is prescribed by, or in consultation with a pulmonologist, oncologist, thoracic surgeon, or otolaryngologist.

   Dosing. Approve the following dosing regimens (A, B, C, and D):
   - **A)** 5×10^{11} particle units per injection subcutaneously on Day 1; AND
   - **B)** 5×10^{11} particle units per injection subcutaneously 2 weeks after initial administration; AND
     Note: The second dose should occur no less than 11 days after the initial administration.
   - **C)** 5×10^{11} particle units per injection subcutaneously 6 weeks after initial administration; AND
   - **D)** 5×10^{11} particle units per injection subcutaneously 12 weeks after initial administration.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Papzimeos is not recommended in the following situations:

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

2. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Papzimeos™ subcutaneous injection [prescribing information]. Germantown, MD: Precigen; 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].

HISTORY

Type of Revision	Summary of Changes	Review Date
New Policy	--	09/10/2025
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	12/08/2025