

Medical Drug Clinical Criteria

Subject: Papzimeos (zopapogene imadenovec-drba)

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Overview

This document addresses the use of Papzimeos (zopapogene imadenovec-drba), a non-replicating adenoviral vector-based immunotherapy, for the treatment of adults with recurrent respiratory papillomatosis (RRP).

Recurrent respiratory papillomatosis (RRP) is a disease in which benign (noncancerous) tumors called papillomas grow in the air passages leading from the nose and mouth into the lungs (respiratory tract). RRP is caused by two types of human papilloma virus (HPV): HPV 6 and HPV 11. HPV infections are common, but most individuals clear the virus without manifesting papillomas, dysplasia, or invasive cancers. Preventative HPV vaccination (Gardasil 9 in the U.S.) is highly effective in preventing infection but fails to consistently provide clinical benefit to those already infected and diagnosed with RRP. Once RRP develops, there is currently no cure. The mainstay of treatment is repeated surgical removal of papillomas. Once the tumors have been removed, they can still return. It is common for patients to require multiple surgeries during their lifetime. The specific symptoms, course of the disease, and severity of RRP can vary greatly from one person to another. The most common presenting symptom of RRP is hoarseness.

RRP is a disorder caused by chronic HPV infection. Viral antigen-specific T-cells are essential in controlling chronic infection. Therapeutic vaccines are one immunotherapy strategy that may enhance T-cell responses.

Papzimeos is a gorilla adenovirus therapeutic vaccine containing DNA encoding full length HPV 6 antigens E2, E4, E6 and E7. It is a gene-based therapeutic vaccine that induces HPV-specific immunity to target papillomas. Immunotherapy, aimed at activating HPV-specific T-cell responses, might result in control or elimination of papillomas and durable clinical benefit. Papzimeos is administered as adjuvant treatment following surgical debulking. Papzimeos is delivered as a 4 dose (12-week) course of treatment.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Papzimeos (zopapogene imadenovec-drba)

Requests for Papzimeos (zopapogene imadenovec-drba) may be approved if the following criteria are met:

- I. Individual has a diagnosis of recurrent respiratory papillomatosis (RRP); **AND**
- II. Documentation is provided that individual has received surgical debulking of laryngotracheal papillomas.

Papzimeos (zopapogene imadenovec-drba) may not be approved for the following:

- I. Individual has had a previous treatment course with Papzimeos; **OR**
- II. When the above criteria are not met and for all other indications.

Approval Duration: One treatment course (12 weeks)

Quantity Limits

Papzimeos (zopapogene imadenovec-drba) Quantity Limits

Drug	Limit
Papzimeos (zopapogene imadenovec-drba) 5x10 ¹¹ particle units (PU) suspension	4 injections per 12 weeks (treatment course); one time treatment course

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

C9399	Unclassified drugs or biologicals [when specified as Papzimeos (zopapogene imadenovec-drba)]
J3590	Unclassified biologics [when specified as Papzimeos (zopapogene imadenovec-drba)]

ICD-10 Diagnosis

All diagnosis pend.

Document History

New: 08/18/2025

Document History:

- 08/18/2025 – Annual Review: Add new criteria document for new agent Papzimeos. Coding Reviewed: Added HCPCS NOC C9399, J3590, and all diagnosis pend for Papzimeos.

References

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- 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.

Federal and state laws or requirements, contract language, and Plan utilization management programs or policies may take precedence over the application of this clinical criteria.

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