Papzimeos™ (Zopapogene Imadenovec-Drba)

Policy Number: 2026D0141A
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Instructions for Use

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Application

UnitedHealthcare Commercial

This Medical Drug Policy applies to UnitedHealthcare Commercial benefit plans.

UnitedHealthcare Individual Exchange

This Medical Drug Policy applies to Individual Exchange benefit plans.

Coverage Rationale

See Benefit Considerations

Papzimeos™ (zopapogene imadenovec-drba) has been added to the Review at Launch program. Some members may not be eligible for coverage of this medication at this time. Refer to the Medical Benefit Drug Policy titled Review at Launch for New to Market Medications for additional details.

Papzimeos is proven and medically necessary for the treatment of recurrent respiratory papillomatosis in patients who meet all of the following criteria:

- Diagnosis of recurrent respiratory papillomatosis (RRP); **and**
- Patient is 18 years of age or older; **and**
- Patient has required surgery (i.e., surgical resection of papillomas, laser ablation of papillomas) to remove laryngotracheal papillomas prior to treatment with Papzimeos; **and**
- Surgical debulking of present visible papilloma will be performed prior to the initial, third, and fourth dose of Papzimeos; **and**
- Prescribed by or in consultation with a specialist knowledgeable in the treatment of recurrent respiratory papillomatosis (e.g., otolaryngologist, pulmonologist, oncologist); **and**
- Patient has not received a previous complete treatment course (i.e., four doses over a 12-week interval) with Papzimeos; **and**
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Authorization will be issued for no more than one treatment course (i.e., four doses) per lifetime

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
C9399	Unclassified drugs or biologicals
J3490	Unclassified drugs
J3590	Unclassified biologics

Diagnosis Code	Description
D14.1	Benign neoplasm of larynx
J38.7	Other diseases of larynx

Background

Papzimeos is a non-replicating adenoviral vector-based immunotherapy designed to express a fusion antigen of selected regions of human papillomavirus (HPV) proteins expressed in HPV 6- and HPV 11-infected cells. Papzimeos is designed to generate an immune response directed against HPV 6 and HPV 11 proteins in patients with recurrent respiratory papillomatosis.

Benefit Considerations

Some Certificates of Coverage allow for coverage of experimental/investigational/unproven treatments for life-threatening illnesses when certain conditions are met. The member specific benefit plan document must be consulted to make coverage decisions for this service. Some states mandate benefit coverage for off-label use of medications for some diagnoses or under some circumstances when certain conditions are met. Where such mandates apply, they supersede language in the benefit document or in the medical or drug policy.

Clinical Evidence

Papzimeos was evaluated in an open-label, single-arm study in 38 adults with recurrent respiratory papillomatosis (RRP). Patients received Papzimeos on days 1, 15, 43, and 85. The primary efficacy endpoint was the percentage of patients with a complete response to Papzimeos treatment, defined as no requirement of surgical intervention in the 12 months after treatment. In the 35 patients that received a dose of $5X10^{11}$ particle units (PU) per injection, the median age at RRP diagnosis was 35 years (range 1-68) and median age at the start of treatment was 49 years (range 20-88). 23 (66%) patients were diagnosed with adult-onset RRP and 12 (34%) with juvenile-onset disease. Most patients were male [20 (57%) of 35] and required up to hundreds of lifetime clinically indicated interventions to control RRP [median 40 (range 3 to > 400)]. Four (11%) of 35 patients had pulmonary RRP evaluable by RECIST criteria. The median number of previous medical treatments for RRP was 2 (range 1-8). The median number of clinically indicated interventions in the 12 months before the study treatment was 4 (3-10). The median pretreatment anatomic Derkay score was 8 (3-31). The median pretreatment VHI-10 score was 24 (6-40), indicating severe dysphonia. At the dose of $5X10^{11}$ PU per injection, 18 of 35 patients received a complete response at 12 months [complete response rate 51% (95% CI: 34, 69)]. At the dose of $1X10^{11}$ PU per injection, no patient (0 of 3) received a complete response. Warnings and precautions for Papzimeos include injection site reactions and thrombotic events. The most common adverse reactions (≥ 5%) with Papzimeos use were injection site reactions, fatigue, chills, pyrexia, myalgia, and nausea.

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Papzimeos is a non-replicating adenoviral vector-based immunotherapy indicated for the treatment of adults with recurrent respiratory papillomatosis.

References

1. Papzimeos [prescribing information]. Germantown, MD: Precigen, Inc; August 2025.
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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;128:109697. doi:10.1016/j.ijporl.2019.109697.
5. Sidell DR, Balakrishnan K, Best SR, et al. Systemic Bevacizumab for Treatment of Respiratory Papillomatosis: International Consensus Statement. Laryngoscope. 2021;131(6):E1941-E1949. doi:10.1002/lary.29343.
6. American Academy of Otolaryngology – Head and Neck Surgery (AAO-HNS). Position statement: Recurrent respiratory papillomatosis and Gardasil vaccination. AAO-HNS. April 5, 2021. Accessed December 1, 2025. https://www.entnet.org/resource/position-statement-recurrent-respiratory-papillomatosis-and-gardasil-vaccination/.

Policy History/Revision Information

Date	Summary of Changes
02/01/2026	• New Medical Benefit Drug Policy

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Benefit Drug Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Benefit Drug Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.