

Corporate Medical Policy: Zopapogene imadenovec-drba (Papzimeos™) “Notification”

POLICY EFFECTIVE APRIL 1, 2026

Restricted Product(s):

- zopapogene imadenovec-drba (Papzimeos™) subcutaneous injection for administration by a healthcare professional

FDA Approved Use:

- For the treatment of adults with recurrent respiratory papillomatosis

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

1. The patient is 18 years of age or older; **AND**
2. The patient has a confirmed histological diagnosis of **recurrent respiratory papillomatosis (RRP) [medical record documentation required]; AND**
3. The patient has either human papillomavirus (HPV) type 6 or 11 **[medical record documentation required]; AND**
4. The patient has the presence of laryngotracheal papillomas **[medical record documentation required]; AND**
5. The patient has required 3 or more interventions (i.e., surgery, systemic therapies [i.e., bevacizumab, intralesional cidofovir]) in the last 12 months for control of RRP **[medical record documentation required]; AND**
6. The patient will undergo surgical debulking of visible papilloma prior to the initial, third, and fourth administration of the requested agent **[medical record documentation required]; AND**
7. If the patient is less than 46 years of age, the patient has received HPV vaccination that protects against HPV type 6 or 11 **[medical record documentation required]; AND**
8. ONE of the following **[medical record documentation required, including lab results within the past 3 months]:**
 - a. The patient’s hepatitis B surface antigen is negative; **OR**
 - b. The patient has been previously vaccinated against hepatitis B virus (HBV) (i.e., HBV surface antibody [Ab]-positive) AND is negative for other markers of prior HBV infection (e.g., negative for HBV core Ab); **OR**
 - c. The patient is negative for HBV DNA; **AND**
9. ONE of the following **[medical record documentation required, including lab results within the past 3 months]:**
 - a. The patient’s hepatitis C virus (HCV) antibody is negative; **OR**
 - b. The patient’s HCV antibody is positive and BOTH of the following:
 - i. The patient’s HCV viral load is undetectable; **AND**
 - ii. The patient is negative for HCV RNA; **AND**

10. ONE of the following **[medical record documentation required]**:
- The patient does NOT have a condition that requires systemic treatment with corticosteroids (i.e., > 10 mg daily prednisone equivalents) or other immunosuppressive medications; **OR**
 - The patient does have a condition that requires systemic treatment with corticosteroids (i.e., > 10 mg daily prednisone equivalents) or other immunosuppressive medications, but the medication will be stopped at least 14 days prior to receiving the initial administration of the requested agent; **AND**
11. The patient has NOT received any previous gene therapy, including the requested agent **[medical record documentation required]; AND**
12. The prescriber is a specialist in the area of the patient's diagnosis (e.g., otolaryngologists) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]; AND**
13. The requested dose is within FDA labeled dosing for the requested indication, and the requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below) **[medical record documentation required]; AND**
14. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting**, Site of Care Criteria applies (outlined below).*

Duration of Approval: 365 days (1 year); one treatment course (4 injections) per lifetime

** Please note, for certain identified gene and cellular therapies such as zopapogene imadenovec-drba (Papzimeos™), when coverage is available and the individual meets medically necessary criteria, distribution from a specialty pharmacy provider due to cost (distribution channel restriction) may be required in order for coverage to be provided. **Please contact Blue Cross NC** to coordinate this therapy.

FDA Label Reference				
Medication	Indication	Dosing	HCPCS	Maximum Units*
zopapogene imadenovec-drba (Papzimeos™) subcutaneous (SC) injection	Recurrent respiratory papillomatosis	SC: 5×10 ¹¹ particle units (PU) (1 mL) per injection four times over a 12-week interval. - 2 nd dose: 2 weeks after initial* - 3 rd dose: 6 weeks after initial - 4 th dose: 12 weeks after initial *Second administration should occur no less than 11 days after initial	C9399** J3490** J3590**	4 injections (1 treatment course per lifetime)

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FDA Label Reference

Medication	Indication	Dosing	HCPCS	Maximum Units*
		<p>Prior to the initial administration, perform a surgical debulking of visible papilloma to establish minimal residual disease.</p> <p>To maintain minimal residual disease during treatment, remove visible papilloma, if present, prior to the third and fourth administration.</p>		

***Maximum units allowed for duration of approval**

****Non-specific assigned HCPCS codes, must submit requested product NDC**

Other revenue codes that may be applicable to this policy: 0891, 0892

***Site of Care Medical Necessity Criteria**

1. For requests for injection or infusion administration in an **inpatient setting**, the injection or infusion may be given if the above medical necessity criteria are met AND the inpatient admission is NOT for the sole purpose of administering the injection or infusion; **OR**
2. For requests for injection or infusion administration in an **outpatient hospital setting**, the injection or infusion may be given if the above medical necessity criteria are met AND ONE of the following must be met:
 - a. History of a severe adverse event following the injection or infusion of the requested medication (i.e., anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure); **OR**
 - b. Conditions that cause an increased risk for severe adverse event (i.e., unstable renal function, cardiopulmonary conditions, unstable vascular access); **OR**
 - c. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); **OR**
 - d. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; **OR**
 - e. New to therapy, defined as initial injection or infusion OR less than 3 months since initial injection or infusion; **OR**
 - f. Re-initiation of therapy, defined as ONE of the following:
 - i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; **OR**
 - ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; **OR**

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- g. Requirement of a change in the requested restricted product formulation; **AND**
3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional.

References: all information referenced is from FDA package insert unless otherwise noted below.

1. National Organization for Rare Disorders (NORD). Recurrent respiratory papillomatosis. Updated June 8, 2023.
2. American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS). Position statement: recurrent respiratory papillomatosis and Gardasil vaccination. AAO-HNS website.
3. Balai E, et al. Adjuvant treatments for recurrent respiratory papillomatosis: a descriptive review and proposed management guideline in adults. *J Laryngol Otol.* 2024;138:1133–1143.
4. Rosenberg T, Philipson 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; 15;219(7):1016-102.
5. Gazia F, et al. Use of intralesional cidofovir in the recurrent respiratory papillomatosis: a review of the literature. *Eur Rev Med Pharmacol Sci.* 2020;24(2):956–962.
6. Ballestas SA, et al. Long-term follow-up of parenteral bevacizumab in patients with recurrent respiratory papillomatosis. *Laryngoscope.* 2023;133(10):2725–2733.
7. Pogoda L, et al. Bevacizumab as a treatment option for recurrent respiratory papillomatosis: a systematic review. *Eur Arch Otorhinolaryngol.* 2022;279(9):4229–4240.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q3 annually.

April 2026: Coding change: Added the following applicable revenue codes associated with policy HCPCS code(s): 0891 (Special Processed Drugs – FDA Approved Cell Therapy) and 0892 (Special Processed Drugs – FDA Approved Gene Therapy). **Policy notification given 2/1/2026 for effective date 4/1/2026.**

December 2025: Criteria change: Reformatted criteria about histological diagnosis and presence of laryngotracheal papillomas for clarity with no change to intent. Adjusted requirement that the patient has had 3 or more debulking procedures in the past 12 months, plus has tried and failed either bevacizumab or intralesional cidofovir to the patient has required 3 or more interventions (i.e., surgery, systemic therapies) in the last 12 months. Reformatted surgical debulking requirements prior to administration into one criterion point. Removed requirement of no history of significant cardiovascular disease.

September 2025: Original medical policy criteria issued.