Pharmacy Management Drug Policy

SUBJECT: Papzimeos™ (zopapogene imadenovec-drba)
POLICY NUMBER: PHARMACY-140
EFFECTIVE DATE: 01/2026
LAST REVIEW DATE: 01/16/2026

If the member's subscriber contract excludes coverage for a specific service or prescription drug, it is not covered under that contract. In such cases, medical or drug policy criteria are not applied. This drug policy applies to the following line/s of business:

Policy Application

Category:	☒ Commercial Group (e.g., EPO, HMO, POS, PPO)	☒ Medicare Advantage
	☒ On Exchange Qualified Health Plans (QHP)	☐ Medicare Part D
	☒ Off Exchange Direct Pay	☒ Essential Plan (EP)
	☒ Medicaid & Health and Recovery Plans (MMC/HARP)	☒ Child Health Plus (CHP)
	☐ Federal Employee Program (FEP)	☐ Ancillary Services
	☒ Dual Eligible Special Needs Plan (D-SNP)	

DESCRIPTION:

Papzimeos™ (zopapogene imadenovec-drba) is a non-replicating adenoviral vector-based immunotherapy indicated for the treatment of adults with recurrent respiratory papillomatosis. The recommended dose of Papzimeos is 5 x 10^{11} particle units (PU) per injection and is administered via subcutaneous injection four (4) times over a 12-week interval, with doses given on Day 1, Week 2, Week 6 and Week 12. Surgical debulking of visible papilloma should be performed prior to the initial administration of Papzimeos. To maintain minimal residual disease during treatment, visible papilloma should be removed, if present, prior to the third and fourth administration of Papzimeos.

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.

Recurrent respiratory papillomatosis (RRP) is a rare disease in which benign (noncancerous) tumors called papillomas grow in the air passages leading from the nose and mouth into the lungs (respiratory tract). Although the tumors can grow anywhere in the respiratory tract, they most often affect the larynx and vocal cords - a condition called laryngeal papillomatosis. RRP is caused by the human papilloma virus (HPV). Two specific subtypes, HPV 6 and HPV 11, account for more than 90% of cases of RRP.[4] Surgical debulking of the papillomas is the standard treatment, however once the tumors have been removed, they often grow back. It is common for patients to require multiple surgeries during their lifetime. About 20% of patients with RRP require adjunctive medical treatment in addition to surgery to control the disease.[5] The most common symptom is hoarseness, although patients can also experience difficulties speaking and breathing due to airway obstruction. The specific symptoms, course of the disease, and severity of RRP can vary greatly from one person to another. Although rare, RRP can lead to dysplasia and malignant transformation in about 15% of patients.[6]

Papzimeos was FDA-approved on August 14, 2025. The efficacy of Papzimeos was evaluated in a single-arm, phase I/II trial of adult patients aged 18 years or older with RRP who required three or more surgical debulking procedures in the 1 year before treatment [NCT04724980]. Thirty-eight (38) patients received Papzimeos on Day 1 following surgical debulking of disease, and on Days 15, 43,

and 85. The primary outcome measure was complete response rate, defined as the percentage of patients who did not require an intervention to control RRP in the 12 months after treatment. A total of thirty-five (35) patients were treated at a dose of 5 x 10^{11} PU and were included in the efficacy evaluation. Eighteen of the thirty-five patients achieved a complete response at 12 months resulting in a complete response rate of 51% [95% confidence interval (CI) 34 to 69%]. Among the eighteen patients with a complete response in the ongoing study, 15 maintained a complete response at 24 months yielding a complete response rate of 43% (95% CI 26 to 61%) at 2 years. Adverse events were mild and included injection site reactions, fatigue, chills, and fever.

POLICY:

Papzimeos (zopapogene imadenovec-drba) - Medical
1. Patient must be ≥ 18 years of age **AND** 2. Must be prescribed by, or in consultation with, a board-certified otolaryngologist (ENT), laryngologist, or head and neck surgical oncologist experienced in the management of recurrent respiratory papillomatosis (RRP) **AND** 3. Must have a diagnosis of histologically confirmed laryngotracheal recurrent respiratory papillomatosis (RRP) **AND** 4. Must have HPV serotype 6 or 11 positivity documented by polymerase chain reaction/in situ hybridization (PCR/ISH) from airway lesions a. Archival tissue obtained from prior surgical debulking procedures is acceptable provided that the sample is representative of the current disease site and histology. Additionally, there must be no indication of a non-HPV-driven or transformed malignancy. 5. Documentation of eligible disease severity and prior treatment history must meet ONE of the following (a or b): a. ≥3 surgical interventions in the prior 12 months **OR** b. ≥2 surgical interventions in the prior 12 months with at least one of the following: i. Extensive anatomic involvement, such as multi-site laryngotracheal disease, pulmonary spread, or a Derkay total score ≥20 (or equivalent qualitative description of high burden) ii. Rapid recurrence requiring repeat surgery or visible regrowth within ≤12 weeks of prior debulking iii. Documentation of clinically significant functional impairment, confirmed by the treating ENT, as evidenced by: 1. Airway compromise, such as, stridor, dyspnea, respiratory distress, or direct visualization of airway obstruction on laryngoscopy or bronchoscopy 2. Severe dysphonia or voice dysfunction, supported by Voice Handicap Index (VHI-10) score in the severe range or equivalent 6. Papzimeos is indicated for a one-time treatment cycle of 4 doses and therefore will not be authorized for retreatment. Retreatment will be considered experimental/investigational when any FDA approved gene therapy, or any other gene therapy under investigation, has been previously administered. 7. Papzimeos will not be authorized for patients: a. Currently receiving another investigational or systemic immunotherapy for RRP b. With prior or concurrent use of investigational gene, cell, or immunotherapy for RRP c. With a history of severe adverse reaction to adenoviral or other viral vector-based therapies (e.g., anaphylaxis, cytokine release syndrome, severe systemic inflammatory response)

POLICY GUIDELINES:

1. Prior authorization is contract dependent.
2. Clinical documentation must be submitted for each request (initial and recertification) unless otherwise specified (e.g., provider attestation required). Supporting documentation includes, but is not limited to, progress notes documenting previous treatments/treatment history, diagnostic testing, laboratory test results, genetic testing/biomarker results, and imaging.
    - Continued approval at time of recertification will require documentation that the drug is providing ongoing benefit to the patient in terms of improvement or stability in disease state or condition. Such documentation may include progress notes, imaging or laboratory findings, and other objective or subjective measures of benefit which support that continued use of the product is medically necessary. Also, ongoing use of the requested product must continue to reflect the current policy's preferred formulary.
3. Doses and frequency should be in accordance with the FDA label or recognized compendia (for off-label uses). When services are performed in excess of established parameters, they may be subject to review for medical necessity.
4. This policy does not apply to Medicare Part D and D-SNP pharmacy benefits. The drugs in this policy may apply to all other lines of business including Medicare Advantage.
5. For members with Medicare Advantage, medications with a National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) will be covered pursuant to the criteria outlined by the NCD and/or LCD. NCDs/LCDs for applicable medications can be found on the CMS website at https://www.cms.gov/medicare-coverage-database/search.aspx. Indications that have not been addressed by the applicable medication's LCD/NCD will be covered in accordance with criteria determined by the Health Plan (which may include review per the Health Plan's Off-Label Use of FDA Approved Drugs policy). Step therapy requirements may be imposed in addition to LCD/NCD requirements.
6. Not all contracts cover all Medical Infusible drugs. Refer to specific contract/benefit plan language for exclusions of Injectable Medications.
7. Unless otherwise indicated within drug specific criteria, the drugs listed in this policy are administered by a healthcare professional and therefore are covered under the medical benefit.
8. All requests will be reviewed to ensure they are being used for an appropriate indication and may be subject to an off-label review in accordance with our Off-Label Use of FDA Approved Drugs Policy (Pharmacy-32).
9. All utilization management requirements outlined in this policy are compliant with applicable New York State insurance laws and regulations. Policies will be reviewed and updated as necessary to ensure ongoing compliance with all state and federally mandated coverage requirements.
10. Manufacturers may either discontinue participation in, or may not participate in, the Medicaid Drug Rebate Program (MDRP). Under New York State Medicaid requirements, physician-administered drugs must be produced by manufacturers that participate in the MDRP. Products made by manufacturers that do not participate in the MDRP will not be covered under Medicaid Managed Care/HARP lines of business. Drug coverage will not be available for any product from a non-participating manufacturer. For a complete list of New/Reinstated & Terminated Labelers please visit: https://www.medicaid.gov/medicaid/prescriptiondrugs/medicaid-drug-rebate-program/newreinstated-terminated-labeler-information/index.html
11. Administration, Retreatment, and Treatment with Additional or Other Gene/Cellular Therapies
    a. One-Time Administration
        i. Most gene and cellular therapies, whether autologous, allogeneic ("off-the-shelf"), or in vivo gene-transfer therapies, are designed and studied as one-time treatments.
        ii. Repeat dosing, reinfusion, or sequential therapy with other gene or cellular products has not been established as safe, effective, or clinically appropriate.

b. Retreatment/Repeat Administration
   i. Retreatment with the same gene or cellular therapy product is considered experimental and investigational because:
      1. Clinical trials evaluated these therapies as single-administration interventions
      2. Safety, efficacy, and durability of a second administration have not been established
      3. Risks of immune activation, insertional mutagenesis, or vector immunity may be increased with repeat dosing

c. Treatment with an Additional or Other Gene/Cellular Therapy
   i. Treatment with an additional or different gene or cellular therapy after prior exposure to any gene or cellular therapy is also considered experimental and investigational, unless supported by evidence demonstrating (1-4):
      1. Anticipated clinical benefit beyond available standard therapies
      2. Safety of sequential administration
      3. Justification for selecting a second gene/cellular intervention after a prior one
      4. Meets the criteria established in the Off-Label Use of FDA Approved Pharmacy Management Drug Policy (Pharmacy-32)
   ii. This includes, but is not limited to:
      1. Switching between CAR-T products (e.g., CD19 → CD19 or CD19 → BCMA)
      2. Switching between autologous and allogeneic cellular therapies
      3. Sequential use of CAR-T, TCR-T, NK-cell therapies, or other genetically engineered cell therapies
      4. Receiving a gene therapy after previous gene or cellular therapy exposure
      5. Receiving an in vivo gene therapy following any prior vector-based therapy

d. Prior Gene/Cell Therapy Exposure
   i. An individual is generally not eligible for additional gene or cellular therapy if they have previously received:
      1. Any autologous cellular therapy (e.g., CAR-T, TCR-T, TIL),
      2. Any allogeneic genetically modified cellular therapy,
      3. Any in vivo gene therapy (e.g., AAV, lentiviral vector)
      4. Any ex vivo gene-modified cell product
      5. Are being considered for any other gene or cellular therapy without documented evidence supporting safety and anticipated benefit.
      e. Coverage Determination
   ii. Absent peer-reviewed evidence demonstrating safety and benefit, retreatment or sequential therapy is considered investigational and will not be covered.

CODES:

Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.
Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.

Code Key:
Experimental/Investigational = (E/I),
Not medically necessary/ appropriate = (NMN).

HCPCS:

J3590 (NOC) Papzimeos

UPDATES:

Date	Revision
01/16/2026	Effective & Posted
01/13/2026	Created
11/13/2025	P&T Committee Approval

REFERENCES:

1. Papzimeos [package insert]. Germantown, MD: Precigen. Inc.; Revised August 2025
2. Murono S, Current treatment options for recurrent respiratory papillomatosis: A narrative review. *Auris Nasus Larynx*. 2025;52(4):307-313
3. Fortes HR, von Ranke FM, Escuissato DL, et al. Recurrent respiratory papillomatosis: A state-of-the-art review. *Respiratory Medicine.* 2017;126:116-121
4. Katsenos S, becker H. Recurrent respiratory papillomatosis: a rare chronic disease, difficult to treat, with potential to lung cancer transformation: apropos of two cases and a brief literature review. *Case Rep. Oncol.* 2011; 4(1):162-171
5. Norberg SM, Valdez J, Napoer S, et al. PRGN-2012 gene therapy in adults with recurrent respiratory papillomatosis: a pivotal phase I/II clinical trial. *Lancet Respir Med.* 2025;13(4)318-326
6. Karatayli- Ozgursoy S, Bishop JA, Hillel A, Akst L, Best SR. Risk Factors for Dysplasia in Recurrent Respiratory Papillomatosis in an Adult and Pediatric Population. *Ann Otol Rhinol Laryngol.* 2016;125(3):235-241.
7. NCT04724980. Adjuvant PRGN-2012 in adult patients with recurrent respiratory papillomatosis. National Library of Medicine. National Center for Biotechnology Information. Available at https://www.clinicaltrials.gov/study/NCT04724980?intr=nct04724980&rank=1. Accessed January 2, 2026.
8. Donne AJ, Keltie K, Belilios E, et al. Current Practice, Safety and Efficacy of Interventions for Recurrent Respiratory Papillomatosis: Evidence From a UK Registry. *Clin Otolaryngol.* 2025;50(2):271-279
9. Hock K, Kennedy A, Howell R, et al. Surgery and Adjuvant Therapy Improve Derkay Scores in Adult and Pediatric Respiratory Papillomatosis. *Laryngoscope.* 2022;132(12):2420-2426
10. Bertino G, Pedretti F, Mauramati S, et al. Recurrent Laryngeal papillomatosis: multimodal therapeutic strategies. Literature review and multicentre retrospective study. *ACTA Otorhinolaryngologica Italica.* 2023;43. DOI: 10.14639/0392-100X-suppl.1-43-2023-14

Appendix:

Derkay Score

The Derkay Staging System is a severity scale used to quantify the severity of RPP and is based on the laryngeal structures involved. Derkay's score is composed of a for-site score and a clinical score. The for-site score takes into account the amount of disease (0: none surface; 2: raised; 3: bulky) in the different laryngeal and extra-laryngeal subsites. The clinical score takes into consideration voice qual presence of stridor, urgency of intervention and presence of respiratory distress.[10]

STAGING ASSESSMENT FOR RECURRENT LARYNGEAL PAPOLLOMATOSIS

PATIENTS INITIALS : _____ DATE OF SURGERY_____SURGEON_____
PATIENT ID #_____ INSTITUTION _____
1. How long since the last papilloma surgery? _____days_____weeks_____months
_____years_____don't know
_____this is the child's first surgery
2. Counting today's surgery, how many papilloma surgeries in the past 12 months?_____
3. Describe the patient's voice today :
nomal_____(0) abnormal_____(1) aphonic _____(2)
4. Describe the patient's stridor today :
absent_____(0) present with activity_____(1) present at rest _____(2)
5. Describe the urgency of today's intervention :
scheduled _____(0) elective _____(1) urgent_____(2) emergent_____(3)
6. Describe today's level of respiratory distress :
none_____ (0) mild_____ (1) mod_____ (2) severe_____ (3) extreme_____ (4)
Total score of questions 3 – 6 = _____

FOR EACH SITE, SCORE AS: 0=NONE, 1 – SURFACE LESION, 2 – RAISED LEASION, 3 – BULKY LESION
LARYNX
Epiglottis
Lingual surface_____ Laryngeal surface_____
Aryepiglottic folder : Right _____ Left_____
False vocal cords : Right _____ Left_____
True vocal cords : Right _____ Left _____
Arytenoids : Right _____Left
Anterior commissure _____ Posterior commissure_____
Subglottis _____
TRACHEA :
Upper one-third _____
Middle one-third _____
Lower one-third _____
Bronchi : Right _____ Left_____
Tracheotomy stoma _____
OTHER :
Nose _____
Palate _____
Pharynx _____
Esophagus _____
Lungs _____
Other _____

TOTAL SCORE ALL SITES : _____TOTAL CLINICAL SCORE :_____

Voice Handicap Index-10 (VHI-10)

The VHI-10 is a validated self-assessment tool designed to quantify the psychosocial impact of voice disorders on patients. It evaluates perceived handicap associated with dysphonia by capturing functional, physical and emotional aspects through a concise questionnaire consisting of 10 items, Each item is rated on a 5-point Likert scale from 0 (never) to 4 (always), allowing for a total score between 0 and with higher scores indicating a greater perceived voice handicap. A score above 11 typically suggests a significant voice disorder requiri clinical attention.

Voice Handicap Index (VHI)-10

Instructions: These are statements that many people have used to describe their voices and the effects of their voices on their lives. Circle the response that indicates how frequently you have the same experience.

0-Never 1-Almost Never 2-Sometimes 3-Almost Always 4-Always

• My voice makes it difficult for people to hear me.	0	1	2	3	4
• People have difficulty understanding me in a noisy room.	0	1	2	3	4
• My voice difficulties restrict personal and social life.	0	1	2	3	4
• I feel left out of conversations because of my voice.	0	1	2	3	4
• My voice problem causes me to lose income.	0	1	2	3	4
• I feel as though I have to strain to produce voice.	0	1	2	3	4
• The clarity of my voice is unpredictable.	0	1	2	3	4
• My voice problem upsets me.	0	1	2	3	4
• My voice makes me feel handicapped.	0	1	2	3	4
• People ask, "What's wrong with your voice?"	0	1	2	3	4

Rosen, CA. et al. Development and Validation of the Voice Handicap Index-10. *Laryngoscope* 2004; 114: 1549-56.