



Nonprofit corporations and independent licensees
of the Blue Cross and Blue Shield Association

Medical benefit drug policies are a source for BCBSM and BCN medical policy information only. These documents are not to be used to determine benefits or reimbursement. Please reference the appropriate certificate or contract for benefit information. This policy may be updated and therefore subject to change.

P&T Date: 10/09/2025

Papzimeos™ (zopapogene imadenovec-drba)

HCPCS: J3404

Policy:

Requests must be supported by submission of chart notes and patient specific documentation.

- A. Coverage of the requested drug is provided when all the following are met:
 - a. FDA approved indication
 - b. FDA approved age
 - c. Presence of laryngotracheal papillomas with or without pulmonary recurrent respiratory papillomatosis (RRP)
 - d. Must have had three or more tumor debulking interventions in the year prior to treatment
 - e. Have not received prior treatment with any other viral vector immunotherapy or are being considered for treatment with any other viral vector immunotherapy for the treatment of RRP
 - f. Trial and failure, contraindication, OR intolerance to the preferred drugs as listed in BCBSM/BCN's utilization management medical drug list.
- B. Quantity Limitations, Authorization Period and Renewal Criteria
 - a. Quantity Limits: Align with FDA recommended dosing
 - b. Authorization Period: 4 months
 - c. Renewal Criteria: Not applicable as no further authorization will be provided

***Note: Coverage and approval duration may differ for Medicare Part B members based on any applicable criteria outlined in Local Coverage Determinations (LCD) or National Coverage Determinations (NCD) as determined by Center for Medicare and Medicaid Services (CMS). See the CMS website at <http://www.cms.hhs.gov/>. Determination of coverage of Part B drugs is based on medically accepted indications which have supported citations included or approved for inclusion determined by CMS approved compendia.

Background Information:

- Recurrent respiratory papillomatosis (RRP) is a rare disorder characterized by the development of papillomas in the respiratory tract. Papillomas can develop anywhere along the respiratory tract, but most often affect the larynx and the vocal cords. Less often, the disorder affects the oral cavity, trachea, and bronchi. Only in rare cases do these growths spread to affect the lungs. While the papillomas are noncancerous, in extremely rare cases they can undergo malignant transformation. In RRP, papillomas tend to grow back after they have been removed.
- RRP is caused by the human papillomavirus (HPV). This virus is common in human beings with some studies estimating that as many as 75% - 80% of men and women will be affected by HPV at some point during their lives if they are not vaccinated against the virus. Most individuals who are infected with HPV never develop any symptoms. There are more than 150 different subtypes of HPV with two specific subtypes, HPV 6 and HPV 11, accounting for more than 90% of cases of RRP.
- Certain risk factors have been identified for the development of RRP. Being a firstborn child, having a vaginal delivery with prolonged labor, and having a mother under 20 years of age are all risk factors for juvenile-onset RRP. If the mother has active genital warts, the risk of passing on HPV is approximately 1 in 250 - 400. Adult-onset RRP may be worsened by tobacco exposure, gastroesophageal reflux, or radiation therapy.
- The specific symptoms, course of the disease, and severity of RRP can vary greatly from one person to another. In some people, the disease may resolve without treatment or it may remain stable requiring only periodic intervention. In other people, the disease may be aggressive requiring frequent medical intervention and potentially more than 100 surgeries during a person's lifetime. The most common presenting symptom of RRP is hoarseness. Affected individuals may develop stridor due to obstruction of the airway. Some individuals may exhibit dysphonia or aphonia. Affected infants may also have a weak cry, episodes of choking, and failure to thrive. Additional symptoms that can develop include a chronic cough, dysphagia, dyspnea, the sensation of a foreign body in the throat, and choking episodes. If left untreated, papillomas can eventually compromise the airways, resulting in life-threatening breathing difficulties. If RRP spreads to the lungs, affected individuals can potentially experience recurrent pneumonia, chronic lung disease, and progressive pulmonary failure. In extremely rare cases, papillomas can become cancerous developing into squamous cell carcinoma.
- RRP is classified into two subtypes, juvenile-onset and adult-onset.
 - Juvenile-onset typically develops before the age of 12 and tends to be more aggressive with more recurrences, but improves later in childhood. It is most often diagnosed between the ages of 2 and 4.
 - Adult-onset RRP can also be aggressive, although severe disease is less common in the adult population. Patients with adult-onset disease typically present in their twenties or thirties, with a "second peak" around age 60.
- There are no treatment guidelines for adult-onset RRP. In 2020, the International Pediatric Otolaryngology Group (IPOG) published consensus recommendations for the treatment of juvenile-onset disease. These recommendations state treatment is directed toward removing papillomas, decreasing the spread of disease, creating a safe and patent airway, preserving nearby anatomical structures, improving voice quality if necessary, and increasing the time between surgical procedures. Specific therapeutic procedures and interventions may vary, depending upon numerous factors, such as frequency of disease recurrences; specific location and spread of the disease; papilloma size; the presence or absence of certain symptoms; an individual's age and general health; and/or other elements. The mainstay of treatment is surgical removal of papillomas. Some individuals may require surgery every few weeks while others may only require surgery twice a year or only a few times during their life depending on the frequency of recurrence. Surgical techniques used to treat individuals with RRP include "cold" excision, microdebridement, various pulsed dye lasers, or carbon dioxide lasers.

- Since the publication of the 2020 consensus recommendations, Papzimeos has been approved for the treatment of adults with RRP. Safety and efficacy were evaluated in the PRGN-2012-201 trial, an open-label, single-arm, Phase I/II study of 38 patients with histological and clinically diagnosed RRP who required three or more interventions in the year prior to treatment with Papzimeos. Participants received adjuvant Papzimeos on day 1 following surgical debulking of disease, and on days 15, 43, and 85. Of the 38 patients, 3 were treated with Papzimeos at a dose of 1×10^{11} particle units (PU) per injection. Thirty-five patients were treated at a dose of 5×10^{11} PU per injection and were included in the efficacy evaluation. The primary endpoint 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. Eighteen of 35 patients achieved a complete response at 12 months, resulting in a complete response rate of 51% (95% CI: 34%, 69%). Of the 18 patients with a complete response in the ongoing study, 15 demonstrated continued complete response at 24 months yielding a complete response rate of 43% (95% CI: 26%, 61%) at 2 years for the 35 patients in the efficacy population.
- Papzimeos is given via subcutaneous (SQ) injection 4 times over the course of 12 weeks. There is no data to support retreatment following the initial 12-week course of therapy.
- Papzimeos has not been studied and there is no data to support use in combination with other medications used to treat RRP.

References:

1. Papzimeos [prescribing information]. Germantown, MD: Precigen, Inc.; August 2025.
2. 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 - 26.
3. Clinicaltrials.gov. Adjuvant PRGN-2012 in adult patients with recurrent respiratory papillomatosis (NCT04724980). Available at: <https://clinicaltrials.gov/study/NCT04724980>. Accessed on August 18, 2025.
4. National Organization of Rare Disorders. Recurrent respiratory papillomatosis. 2023 June 8. Available at: <https://rarediseases.org/rare-diseases/recurrent-respiratory-papillomatosis/>. Accessed on August 18, 2025.
5. 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 Jan; 128: 109697.

Policy History												
#	Date	Change Description										
1.2	Effective Date: 05/11/2026	UM medical management system update for MAPPO and BCNA <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>Yes</td></tr><tr><td>BCNA</td><td>Yes</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	Yes	BCNA	Yes
Line of Business	PA Required in Medical Management System (Yes/No)											
BCBS	Yes											
BCN	Yes											
MAPPO	Yes											
BCNA	Yes											
1.1	Effective Date: 10/09/2025	New Policy										
1.0	Effective Date: 08/28/2025	UM medical management system update for BCBS and BCN <table><tr><th>Line of Business</th><th>PA Required in Medical Management System (Yes/No)</th></tr><tr><td>BCBS</td><td>Yes</td></tr><tr><td>BCN</td><td>Yes</td></tr><tr><td>MAPPO</td><td>No</td></tr><tr><td>BCNA</td><td>No</td></tr></table>	Line of Business	PA Required in Medical Management System (Yes/No)	BCBS	Yes	BCN	Yes	MAPPO	No	BCNA	No
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BCBS	Yes											
BCN	Yes											
MAPPO	No											
BCNA	No											

* The prescribing information for a drug is subject to change. To ensure you are reading the most current information it is advised that you reference the most updated prescribing information by visiting the drug or manufacturer website or <http://dailymed.nlm.nih.gov/dailymed/index.cfm>.

Blue Cross Blue Shield/Blue Care Network of Michigan

Medication Authorization Request Form



This form is to be used by participating physicians to obtain coverage for **drugs covered under the medical benefit**. For commercial members only, please complete this form and submit via fax to 1-877-325-5979. If you have any questions regarding this process, please contact BCBSM Provider Relations and Servicing or the Medical Drug Helpdesk at 1-800-437-3803 for assistance.

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PATIENT INFORMATION	PHYSICIAN INFORMATION
Name	Name
ID Number	Specialty
D.O.B. ☐ Male ☐ Female	Address
Diagnosis	City /State/Zip
Drug Name	Phone/Fax: P: () - F: () -
Dose and Quantity	NPI
Directions	Contact Person
Date of Service(s)	Contact Person Phone / Ext.

STEP 1: DISEASE STATE INFORMATION

- Is this request for: ☐ Initiation ☐ Continuation Date patient started therapy: _____
- Administered by patient or a medical professional? ☐ patient (self) ☐ health care professional (physician, nurse, etc.)
- Site of administration? ☐ Provider office/Home infusion ☐ Other: _____
☐ Hospital outpatient facility (go to #4) Reason for Hospital Outpatient administration: _____
☐ Hospital inpatient facility for Car-T therapy only (for example: Kymriah, Yescarta, or Tecartus) (go to #5)
- Please specify location of administration if hospital outpatient infusion: _____
- Please specify location of administration if hospital inpatient infusion: _____
- Please provide the NPI number for the place of administration: _____
- Initiation AND Continuation of therapy:**
 - What is the patient's diagnosis? _____
 - What other medication has the patient received for their condition? Please list _____
 - Please describe the response to previous therapies: _____
 - Will the patient be receiving any other treatment for the listed condition while on this medication? Please list: _____
 - Please list any labs values important for diagnosing or monitoring this patient's condition: _____
- Continuation of therapy:**
 - Has the patient progressed while on this medication? ☐ yes ☐ no
 - How has the patient's condition changed while on this medication?

☐ Improved: Please describe: _____
☐ Stable: please describe: _____
☐ Worsened; Please describe: _____
☐ Other; Please describe: _____

Chart notes are required for the processing of all requests. Please add any other supporting medical information necessary for our review (required)

Coverage will not be provided if the prescribing physician's signature and date are not reflected on this document.

☐ Request for expedited review: I certify that applying the standard review time frame may seriously jeopardize the life or health of the member or the member's ability to regain maximum function

Physician's Name	Physician Signature	Date
Step 2: Checklist	☐ Form Completely Filled Out ☐ Provide chart notes	☐ Attach test results
Step 3: Submit	By Fax: BCBSM Specialty Pharmacy Mailbox 1-877-325-5979	By Mail: BCBSM Specialty Pharmacy Program P.O. Box 312320, Detroit, MI 48231-2320

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7/26/2018, 9/18/2018; 1/31/2020; 3/17/2020; 8/9/2021