Oscar Clinical Guideline: Papzimeos (zopapogene imadenovec-drba) (PG275, Ver. 1)

Papzimeos (zopapogene imadenovec-drba)

Disclaimer

Clinical guidelines are developed and adopted to establish evidence-based clinical criteria for utilization management decisions. Clinical guidelines are applicable according to policy and plan type. The Plan may delegate utilization management decisions of certain services to third parties who may develop and adopt their own clinical criteria.

Coverage of services is subject to the terms, conditions, and limitations of a member's policy, as well as applicable state and federal law. Clinical guidelines are also subject to in-force criteria such as the Centers for Medicare & Medicaid Services (CMS) national coverage determination (NCD) or local coverage determination (LCD) for Medicare Advantage plans. Please refer to the member's policy documents (e.g., Certificate/Evidence of Coverage, Schedule of Benefits, Plan Formulary) or contact the Plan to confirm coverage.

Summary

Recurrent respiratory papillomatosis (RRP) is when benign tumors (papillomas) grow in the air passages leading from the nose and mouth into the lungs. RRP is caused by human papillomavirus (HPV) serotypes 6 and 11. There are two subtypes of RRP which are adult-onset and juvenile-onset. RRP is characterized by small papillomas forming in the respiratory tract such as larynx and vocal cords and, in rare cases, in the lungs. Symptoms of RRP include hoarseness to respiratory distress.

Most individuals clear the HPV virus without manifesting papillomas. However, once papillomas are formed, the mainstay of treatment is surgical removal. Once the papillomas have been removed, they can return; thus, multiple debulking surgeries may need to be performed during the course of the disease.

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

Definitions

"Debulking procedures" are to reduce the mass of benign (noncancerous) papillomas that grow on the mucosal surfaces of the respiratory tract. The goal is to alleviate airway obstruction and preserve vocal function.

"Documentation" refers to written information, including but not limited to:

- Up-to-date chart notes, relevant test results, and/or relevant imaging reports to support diagnoses; or
- Prescription claims records, and/or prescription receipts to support prior trials of formulary alternatives.

"Papillomas" are benign (noncancerous), wart-like growth that forms in the respiratory tract.

"[s]" indicates state mandates may apply.

Clinical Indications

Medical Necessity Criteria for Clinical Review

General Medical Necessity Criteria

Recurrent Respiratory Papillomatosis (RRP)

The Plan considers Papzimeos (zopapogene imadenovec-drba) medically necessary when ALL of the following criteria are met:

1. The medication is prescribed by or in consultation with an otolaryngologist, pulmonologist, or a specialist in the treatment of recurrent respiratory papillomatosis; *AND*
2. The member is 18 years of age or older; *AND*

3. The member has a diagnosis of recurrent respiratory papillomatosis defined as documentation of ALL of the following:
    a. Presence of laryngotracheal papillomas; *and*
    b. Histological diagnosis of papilloma confirmed by pathology report *and*
    c. Member has documented HPV serotype 6 or 11*; AND*
4. The member has had three (3) or more debulking procedures to remove laryngotracheal papillomas in the 12 months prior to treatment with Papzimeos (zopapogene imadenovec-drba); *AND*
5. Surgical debulking of visible papilloma will be performed prior to initial administration to establish minimal residual disease; *AND*
6. IF present, visible papillomas will be removed to maintain minimal residual disease prior to the third and fourth administration of Papzimeos (zopapogene imadenovec-drba)*; AND*
7. The member is unable to use, or has tried and failed ONE of the following[s]:
    a. bevacizumab*; or*
    b. cidofovir*; or*
    c. HPV vaccination series if ≤45 years of age*; AND*
8. Papzimeos will not be used in combination with other medications used for the treatment of RRP (e.g., bevacizumab, cidofovir)*; AND*
9. The member has a negative serology test for hepatitis B (HBV) and hepatits C (HCV)*; AND*
10. The member has not received more than 4 doses (one-treatment course) of 5×10^{11} particle units (PU) of Papzimeos (zopapogene imadenovec-drba).

<u>If the above prior authorization criteria are met, the requested product will be authorized for up to 4 doses for a treatment course of 12 weeks per lifetime, with an approval duration of up to 4-months.</u>

Experimental or Investigational / Not Medically Necessary[s]

Papzimeos (zopapogene imadenovec-drba) for any other indication or use is considered not medically necessary by the Plan, as it is deemed to be experimental, investigational, or unproven. Non-covered indications include, but are not limited to, the following:

- Re-treatment after 4 doses over 12 weeks [Papzimeos (zopapogene imadenovec-drba) is indicated for a one-time treatment of 4 doses over 12 weeks . There is no evidence to support the safety or efficacy of repeat administration after 4 doses over 12 weeks.]
- Juvenile onset recurrent respiratory papillomatosis (RRP).

Applicable Billing Codes

Table 1	
CPT/HCPCS codes considered medically necessary if criteria are met:	
Code	*Description*
C9399	Papzimeos Unclassified drugs or biologicals
J3590	Papzimeos Unclassified biologics

Table 2	
ICD-10 diagnosis codes considered medically necessary with Table 1 (CPT/HCPCS) codes if criteria are met:	
Code	*Description*
D14.1	Benign Neoplasm Of Larynx

References

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3. Recurrent respiratory papillomatosis or laryngeal papillomatosis. National Institute on Deafness and Other Communication Disorders. No. 10-4307. September 2017. Available at: https://www.nidcd.nih.gov/health/recurrent-respiratory-papillomatosis. Accessed November 18, 2025.
4. Recurrent respiratory papillomatosis. National Organization for Rare Disorders. June 2023. Available at: https://rarediseases.org/rare-diseases/recurrent-respiratory-papillomatosis/. Accessed November 18, 2025.
5. Sidell DR, Nassar M, Cotton RT, Zeitels SM, de Alarcon A. High-dose sublesional bevacizumab (avastin) for pediatric recurrent respiratory papillomatosis. Ann Otol Rhinol Laryngol. 2014 Mar;123(3):214-21. doi: 10.1177/0003489414522977.
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7. UptoDate. Common causes of hoarseness in children. Available at: https://www.uptodate.com/contents/common-causes-of-hoarseness-in-children. Accessed November 18, 2025.
8. UptoDate. Human papillomavirus vaccination. Available at: https://www.uptodate.com/contents/human-papillomavirus-vaccination. Accessed November 18, 2025.

Clinical Guideline Revision / History Information

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