Molina Clinical Policy
Tudriqev (vusolimogene oderparepec): MEDICARE
Policy No. 486b

Last Approval: 08/19/2026
Next Review Due By: August 2027

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of the Federal government or CMS for Medicare. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

This policy covers the use of Tudriqev (vusolimogene oderparepec; RP1) in combination with nivolumab for the treatment of adults with advanced, unresectable cutaneous melanoma who experienced disease progression while on an anti-PD-1 (programmed cell death protein 1) therapy.

Melanoma is a malignancy of melanocytes that accounts for the majority of skin cancer deaths. It is the fifth most common cancer in the USA. There are almost 15,000 new patients diagnosed with the most advanced forms of melanoma (stage III/IV) annually. The five-year survival rate for stage IV melanoma is 29.8% as of 2017 (Saginala et al. 2021). One of the most important predictors of clinical outcomes is the TNM (tumor, node, metastasis) staging system by the American Joint Committee on Cancer. When lesions become advanced, and spread, or become unresectable or metastatic, medical therapies can be used for adjuvant therapy. Development of medical therapies including targeted treatments and immunotherapy have decreased overall mortality but outcomes in this setting remain poor. Current treatment options include targeted therapies such as BRAF inhibitors like vemurafenib, dabrafenib, encorafenib. These slow or shrink melanomas with BRAF mutations. MEK inhibitors also treat melanomas with BRAF mutations and include trametinib, cobimetinib and binimetinib. For those with KIT gene mutations, KIT inhibitors may be used (imatinib, dasatinib, nilotinib).

Immunotherapies such as immune checkpoint inhibitors (ICI) act at immune checkpoints and are first-line therapy for advanced melanoma. Immune checkpoints normally turn down an immune response to protect the body's healthy cells. Immunotherapies such as ICIs are used to turn up the immune system response when cancer is present by targeting proteins called PD-1 on T -cells and CTLA-4. Types of immunotherapies include Pembrolizumab, Nivolumab, ipilimumab, Atezolizumab, and Nivolumab/Relatlimab. Combinations of targeted therapies and immunotherapies are often used in the treatment of melanomas. Only about half of patients respond to first-line checkpoint blockade, and options after progression on anti–PD-1–based therapy are limited.

There is currently a tumor-infiltrating lymphocyte (TIL) therapy available for melanoma that is restricted to patients with adequate cardiac, pulmonary, and renal function, and good performance status.

Tudriqev (vusolimogene oderparepec; RP1) is a genetically modified herpes simplex virus type 1 (HSV-1) designed to express a fusogenic protein (Galv-GP-R) along with a granulocyte-macrophage colony-stimulating factor. The fusogenic protein causes melanoma cells to fuse together, thus rendering them metabolically incapable of survival. After melanoma cell death, new antigens are released and the GM-CSF recruits immune cells (antigen presenting cells) which take up the released antigens that then prime T cells to recognize non-injected melanoma cells. While Tudriqev (vusolimogene oderparepec; RP1) is administered via intratumoral injection it appears to have an additional systemic effect.

RELATED POLICIES / PROCEDURES

MCP-450: Amtagvi (lifileucel)

COVERAGE POLICY

All Gene Therapy requests require Molina Medical Director review.

Tudriqev (vusolimogene oderparepec) may be **considered medically necessary** for the treatment of adults with advanced, unresectable cutaneous melanoma when the ALL following criteria are met:

1. Member is ≥ 18 years of age

2. Histologically confirmed diagnosis of advanced, unresectable cutaneous melanoma

3. Confirmed disease progression while on anti-PD-1-based therapy (e.g., nivolumab or pembrolizumab) for at least 8 consecutive weeks (maybe in combination with other therapies such as anti-CTLA-4 therapy)
    a. Disease progression is defined by ONE of the following:
        i. Clinical progression - a decline in performance status directly attributed to disease or increased disease related symptoms, or new symptomatic visceral / CNS disease
        ii. Radiographic progression - documented progression on two radiographic assessments > 4 weeks apart, with further growth relative to the first scan

4. At least 1 tumor lesion must be accessible to intratumoral injection and be measurable per RECIST v1.1* for response assessment
    *See Supplemental Information section for definitions

5. Members who progressed on adjuvant anti–PD-1 must have biopsy-confirmed progression while receiving adjuvant therapy

6. Member must have known and documented BRAF mutation status.
    a. If BRAF V600 mutation-positive, a BRAF/MEK inhibitor–based regimen should have been received or considered (BRAF/MEK-targeted therapy is not required before anti-PD-1 therapy or before vusolimogene.)

7. Member must continue to meet criteria for nivolumab approval (efficacy data exists for the combination of Tudriqev and nivolumab. Nivolumab is authorized separately under its own policy).

8. ECOG performance status ≤ 1

9. Member must have adequate hematologic function, as defined by the following:
    a. White blood cell count (WBC) ≥ 2.0×10^9/L
    b. Absolute neutrophil count (ANC) ≥ 1.5×10^9/L
    c. Platelet count ≥ 100×10^9/L
    d. Hemoglobin ≥ 9 g/dL or ≥ 5.6 mmol/L without erythropoietin dependency and without packed red blood cell (pRBC) transfusion within 2 weeks of dosing

10. Member must have adequate hepatic function, as defined by the following:
    a. Total bilirubin ≤ 1.5 × upper limit of normal (ULN) *or* ≤3.0 × ULN for patients with documented Gilbert syndrome
    b. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) ≤ 3.0 × ULN *or* ≤5.0 × ULN if liver metastases are present
    c. Alkaline phosphatase (ALP) ≤ 2.5 × ULN *or* ≤ 5.0 × ULN, if liver or bone metastases are present

11. Member must have adequate renal function, as defined by blood creatinine ≤ 1.5 × ULN *or* measured or calculated creatinine clearance ≥ 30 mL/minute for patients with creatinine levels > 1.5 x ULN

12. Member must have adequate coagulation function, as defined by the following:
    a. Prothrombin time (PT) *or* international normalization ratio (INR) ≤ 1.5 × ULN

b. Partial thromboplastin time (PTT) *or* activated partial thromboplastin time (aPTT) ≤ 1.5 × ULN. (Note: Patients who are on chronic anticoagulant therapy may receive therapy if INR < 2.5 × ULN)

13. Absence of systemic infection requiring intravenous (IV) antibiotics or other serious infection within 14 days prior to dosing, unless documented infectious disease consultation and clearance

14. Absence of active significant herpetic infections or prior complications of HSV-1 infection (e.g., herpetic keratitis or encephalitis)

15. Absence of conditions requiring treatment with immunosuppressive doses (> 10 mg daily prednisone or equivalent) of systemic corticosteroids other than for corticosteroid replacement therapy within 14 days of dosing

16. For female Members of childbearing potential: Negative beta-human chorionic gonadotropin (β-hCG) test

17. Members of reproductive potential must have attestation of willingness to adhere to a highly effective contraception method until 90 days after the last dose of Tudriqev

18. Prescribed and administered by, or in consultation with, a physician experienced in intratumoral oncolytic immunotherapy at a center capable of image-guided injection

Administration

1. **SETTING:** This gene therapy is administered in-vivo. For in-vivo route*, outpatient administration* is generally anticipated. Inpatient admission is not required in the absence of complicating factors. The FDA label specifies monitoring for 2–4 hours post-injection for visceral lesions, which is feasible in an outpatient procedural setting but not a standard clinic room.

2. This Oncolytic gene therapy is provided at highly specialized facilities by, or in consultation with, a physician experienced in intratumoral oncolytic immunotherapy at a center capable of image-guided injection

3. Refer to MHI Policy & Procedure: Specialty Medication Administration Site of Care Policy: MHI Pharm 11

Limitations and Exclusions

QUANTITY LIMITATIONS:

- Initial course is 8 doses administered every 14 days: Week 1 at 10^6 PFU/mL, then 10^7 PFU/mL for doses 2–8.
- Initial authorization duration: 4 months (accommodates 8 biweekly doses plus permitted interruptions).
- Quantity limit per treatment visit: 1 mL per cm of the largest dimension of each injected tumor, not to exceed 10 mL total across all lesions per dose.

CONTINUATION OF THERAPY: Tudriqev (vusolimogene oderparepec) may be considered medically necessary for the continuation of therapy when ALL the following criteria are met:

1. Continuation of therapy is allowed in the absence of confirmed disease progression. Documentation should include date and result of most recent tumor assessment, including whether progression was unconfirmed or confirmed and the date of any confirmatory scan.
    a. Disease progression while on Tudriqev is defined and confirmed as ONE of the following is present, and necessitates Tudriqev discontinuation:
        i. Radiographic confirmed progression: RECIST v1.1 progression on one imaging study, followed by a confirmatory scan performed 4–8 weeks later demonstrating further increase in the lesion category in which progression was first identified (≥5 mm further increase in the sum of new target lesions, or any further increase in new non-target lesions), or new RECIST v1.1 progression in a lesion category that had not previously progressed.
        ii. Clinically relevant progression: progression accompanied by a decline in performance status and/or a determination that alternative systemic therapy is required.
    b. Disease progression is NOT considered confirmed, and therapy may continue when the following any of the following are documented:
        i. A single scan shows progression that has not yet been confirmed, and the patient remains

clinically stable. Repeat imaging in 4–8 weeks is required. (Note: oncolytic virus injection can cause inflammatory changes that mimic new lesions on imaging. That is why follow-up confirmation is needed)

ii. New lesions appear or existing lesions enlarge in a clinically stable patient without confirmatory imaging. Progression prior to response is a recognized pattern with intralesional oncolytic herpesvirus therapy

2. At least one injectable lesion remains that is safely accessible by direct or image-guided injection, and is not excluded by labeled anatomic restrictions (no brain or spinal cord tumors; no scalp tumors with moderate-to-extensive bone erosion; avoid tumors encasing, invading, or occluding major vessels, major nerve structures, or airways).
    a. If no injectable lesion remains, continuation is not authorized regardless of response status.

3. Documented absence of unacceptable toxicity attributable to Tudriqev, including recurrent injection-procedure complications (e.g, hemorrhage, infection, visceral injury such as pneumothorax) or immune-mediated events precluding safe continuation.

4. Dosing interval remains every 14 days at 10^7 PFU/mL. Higher frequency is not supported by the label

5. Maximum total is 24 total doses of Tudriqev per patient: 8 initial doses plus up to 16 additional doses at 10^7 PFU/mL every 2 weeks. Documentation must exhibit number of Tudriqev doses administered to date and cumulative volume per visit. (Note: Per IGNYTE trial; Requests beyond 24 cumulative doses have not been studied and are not supported by literature.)

6. Documentation of Nivolumab status (continuing, completed 24 months, or discontinued with reason)

DURATION of APPROVAL:
Initial authorization duration: 4 months (accommodates 8 biweekly doses plus permitted interruptions).
Reauthorization duration: up to 6 months at a time, not to exceed 2 years

DOCUMENTATION REQUIREMENTS: Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational, or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

The Ignyte study is the primary evidence for accelerated approval. Ignyte study (NCT03767348) is an open-Label, multicenter, non-randomized, non-placebo controlled, prospective phase 1/2 Study of RP1 as a single agent and in combination with PD1 Blockade in patients with unresectable melanoma**.** Phase 2 portion was conducted in stage IIIb-IV unresectable melanoma. The pivotal cohort in the Ignyte phase ½ study consisted of 140 patients with advanced cutaneous melanoma and confirmed progression on ≥8 weeks of anti–PD-1 ± anti–CTLA-4 (anti–PD-1 last).

The efficacy of RP1 in combination with nivolumab in the failed cutaneous melanoma cohort was determined by ORR (overall response rate = complete response + partial response). Response assessed by blinded independent central review per RECIST v1.1, which is the only blinded element. ORR was 32.9% (95% CI 25.2–41.3), with 15.0% complete response (Wong et al. 2025).

Key secondary endpoints were median DOR (duration of response) which was 33.7 months (95% CI 14.1–NR); OS (overall survival) 75.3% at 1 year and 63.3% at 2 years; updated 3-year landmark analysis (Wong et al. 2026) showed median OS 32.2 months and 3-year OS 45.5% (81.8% in responders vs 22.5% in non-responders). Supportive lesion-level analysis: among 46 responders, 93.5% of injected and 79.0% of non-injected measured lesions had >30% reduction, supporting a systemic effect rather than local debulking only.

Treatment-related adverse events occurred in 90% of patients, with grade 3/4 events reported in 12.9%. The most common treatment-related adverse events were fatigue, chills, pyrexia, and nausea. Serious treatment-related toxicities were uncommon, and no treatment-related deaths were observed.

Interim data from the ongoing IGNYTE-3, (NCT06264180) phase 3 confirmatory trial also contributed to the FDA approval. That phase 3 trial interim data has not been published in a peer reviewed journal yet.

SUPPLEMENTAL INFORMATION

RECIST 1.1 (Response Evaluation Criteria in Solid Tumors) is a standardized method used in oncology clinical trials and practice to measure whether a tumor is responding to treatment, remaining stable, or progressing. It provides objective rules for interpreting changes in tumor size on imaging studies such as CT or MRI scans, measured serially (Eisnhauer et al. 2009).

At baseline, investigators identify and measure selected target lesions (up to 5 total, with a maximum of 2 per organ). The sum of their longest diameters is calculated and then compared with measurements obtained during follow-up imaging

RECIST 1.1 Response Categories

Response	Definition
Complete Response (CR)	Disappearance of all target lesions; pathological lymph nodes must decrease to <10 mm short axis.
Partial Response (PR)	At least a 30% decrease in the sum of target lesion diameters compared with baseline.
Stable Disease (SD)	Neither sufficient shrinkage for PR nor sufficient increase for PD.
Progressive Disease (PD)	At least a 20% increase in the sum of target lesion diameters, with an absolute increase of at least 5 mm, or appearance of new lesions.

Example
A patient has target lesions totaling 100 mm at baseline:

- Follow-up total = 65 mm → 35% decrease → Partial Response (PR)
- Follow-up total = 100 mm ± small change → Stable Disease (SD)
- Follow-up total = 122 mm → 22% increase and >5 mm absolute increase → Progressive Disease (PD)
- All lesions disappear → Complete Response (CR)

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology)

Code	Description
96405	Chemotherapy administration; intralesional, up to and including 7 lesions
96406	Chemotherapy administration; intralesional, more than 7 lesions

HCPCS (Healthcare Common Procedure Coding System)

Code	Description
C9399	Unclassified drugs or biologicals [when specified as Tudriqev (vusolimogene oderparepvec-wtpg)]
J3590	Unclassified biologics [when specified as Tudriqev (vusolimogene oderparepvec-wtpg)]

CODING DISCLAIMER: Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

08/19/2026 New policy. IRO peer review completed on 8/11/26 by a physician board certified in Medical Oncology.

REFERENCES

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