# Drug Coverage Policy

**Effective Date ..... 5/1/2026**
**Coverage Policy Number.....IP0407**
**Policy Title.....Proleukin**

# Oncology (Injectable) - Proleukin

- Proleukin® (aldesleukin intravenous infusion – Iovance Biotherapeutics)

*The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.*

## OVERVIEW

Proleukin, a human recombinant interleukin-2 product, is indicated for the following: [1]

- **Metastatic melanoma**, in adults.
- **Metastatic renal cell carcinoma**, in adults.

### Dosing Information

The recommended dose of Proleukin is the same for metastatic melanoma and metastatic renal cell carcinoma.[1] Proleukin 600,000 International Units/kg (0.037 mg/kg) is administered by intravenous infusion over 15 minutes every 8 hours for a maximum of 14 doses. Following 9 days of rest the schedule is repeated to complete one course of therapy. Additional courses of therapy can be given

after at least 7 weeks of rest. Additional courses of therapy should only be given if there is evidence of tumor shrinkage after the previous course of therapy and there are no contraindications to retreatment.

**Guidelines**
Proleukin is addressed in the following National Comprehensive Cancer Network (NCCN) guidelines:

- **Cutaneous Melanoma:** NCCN guidelines (version 2.2025 – January 28, 2025) recommend Proleukin for unresectable or metastatic disease as a single agent for second-line or subsequent therapy for disease progression, intolerance, and/or projected risk of progression with BRAF-targeted therapy or as part of tumor-infiltrating lymphocyte therapy after progression on anti-programmed death receptor-1 therapy and BRAF/MEK targeted therapy if BRAF *V600E* mutation positive (category 2A).[2,4] In this setting, Proleukin may be considered for patients with small brain tumors and without significant peritumoral edema (category 2B). Proleukin is also recommended as intralesional therapy for initial and/or subsequent treatment of unresectable/borderline resectable disease as "useful in certain circumstances." (category 2B).
- **Hematopoietic Cell Transplantation:** NCCN guidelines (version 3.2025 – September 24, 2025) recommend Proleukin for chronic graft-vs-host disease as additional therapy, in combination with systemic corticosteroids, following no response (steroid-refractory) to first-line therapy options.[2,5]
- **Kidney cancer** (version 1.2026 – July 24, 2025) clinical practice guidelines no longer recommend Proleukin for the treatment of renal cell carcinoma.[2,3]

## Coverage Policy

**POLICY STATEMENT**
**Prior Authorization is required for benefit coverage of Proleukin. All approvals are provided for the duration noted below.**

Certain indications and/or approval conditions that are delegated to EviCore by Evernorth will follow Oncology Medications (1403) coverage policy for prior authorization medically necessity criteria. Note: Any listed preferred product requirements in this coverage policy, inclusive of oncology and/or oncology-related uses, are applicable as noted.

**Proleukin is considered medically necessary when the following is met:**

**FDA-Approved Indications**

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1. **Cutaneous Melanoma.** Approve for 1 year if the patient meets ONE of the following (A or B):
   - **A)** Intravenous Therapy. Approve if the patient meets ALL of the following (i, ii, iii, and iv):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** Patient has metastatic or unresectable disease; AND
     - **iii.** Patient has tried at least one other systemic therapy; AND
     - **iv.** The medication is prescribed by or in consultation with an oncologist; OR
   - **B)** Intralesional Therapy. Approve if the patient meets ALL of the following (i, ii, and iii):
     - **i.** Patient is ≥ 18 years of age; AND
     - **ii.** The medication will be directly injected into unresectable or borderline resectable lesions; AND
     - **iii.** The medication is prescribed by or in consultation with an oncologist or dermatologist.

   **Dosing.** Approve ONE of the following dosing regimens (A or B):
   - **A)** Intravenous Therapy (i, ii, and iii):

**i.** Each dose must not exceed 600,000 International Units/kg (0.037 mg/kg) given no more frequently than three times daily for a maximum of 14 doses to complete one cycle of treatment; AND
**ii.** A second cycle is given after a minimum of 9 days of rest to complete a course of therapy; AND
**iii.** Each additional course of therapy is given after at least 7 weeks of rest; OR

**B)** Intralesional Therapy (i and ii):
**i.** The dose to each individual lesion must not exceed 6 million International Units given by intralesional injection; AND
**ii.** The dose is given no more frequently than three times weekly.

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**2. Renal Cell Carcinoma.** Approve for 1 year if the patient meets ALL of the following (A, B, C, and D):
**A)** Patient is ≥ 18 years of age; AND
**B)** Patient has metastatic disease; AND
**C)** The medication will be used as a single agent; AND
**D)** The medication is prescribed by or in consultation with an oncologist.

**Dosing.** Approve the following dosing regimen (A, B, and C):
**A)** Each dose must not exceed 600,000 International Units/kg (0.037 mg/kg) given intravenously no more frequently than three times daily for a maximum of 14 doses to complete one cycle of treatment; AND
**B)** A second cycle is given after a minimum of 9 days of rest to complete a course of therapy; AND
**C)** Each additional course of therapy is given after at least 7 weeks of rest.

**Other Uses with Supportive Evidence**

**3. Graft-Versus-Host Disease**. Approve for 1 year if the patient meets the following (A, B, C, and D):
**A)** Patient has chronic graft-versus-host disease; AND
**B)** According to the prescriber, the patient has steroid-refractory disease; AND
**C)** The medication will be used in combination with systemic corticosteroids; AND
**D)** The medication will be prescribed by or in consultation with an oncologist or a physician associated with a transplant center.

**Dosing.** Up to 1 million International Units/$m^2$ administered subcutaneously once daily.

**Conditions Not Covered**

**Proleukin for any other use is considered not medically necessary. Criteria will be updated as new published data are available.**

## Coding Information

**Note:** 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

**Considered Medically Necessary when criteria in the applicable policy statements listed above are met:**

| HCPCS Codes | Description |
|---|---|
| J9015 | Injection, aldesleukin, per single use vial |

## References


1. Proleukin® intravenous infusion [prescribing information]. Philadelphia, PA: Iovance Biotherapeutics; January 2024.
2. The NCCN Drugs and Biologics Compendium. © 2026 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 3, 2026. Search term: aldesleukin.
3. The NCCN Kidney Cancer Clinical Practice Guidelines (version 1.2026 – July 24, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 3, 2025..
4. The NCCN Cutaneous Melanoma Clinical Practice Guidelines (version 2.2025 – January 28, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 3, 2025.
5. The NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines (version 3.2025 – September 24, 2025). © 2025 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed February 3, 2026.
6. Radny P, Caroli UM, Bauer J, et al. Phase II trial of intralesional therapy with interleukin-2 in soft-tissue melanoma metastases. *Br J Cancer*. 2003;89:1620-1626.
7. Weide B, Derhovanessian E, Pflugfelder A, et al. High response rate after intratumoral treatment with interleukin-2. Results from a Phase 2 study in 51 patients with metastasized melanoma. *Cancer*. 2010;116:4139-4146.
8. Koreth J, Kim HT, Jones KT, et al. Efficacy, durability, and response predictors of low-dose interleukin-2 therapy for chronic graft-versus-host disease. *Blood*. 2016;128:130-137.


## Revision Details

| Type of Revision | Summary of Changes | Date |
|---|---|---|
| Annual Review | **Graft-Versus-Host Disease.**<br>**Updated** initial authorization duration from 4 months to 1 year | 8/1/2024 |
| Annual Revision | **Updated title from** "Proleukin (for Non-Oncology Uses)" **to** "Oncology (Injectable) – Proleukin"<br><br>**Added** criteria for: (1) Cutaneous Melanoma, (2) Renal Cell Carcinoma | 5/1/2025 |
| Annual Revision | **Added** "Certain indications and/or approval conditions that are delegated to EviCore by Evernorth will follow Oncology Medications (1403) coverage policy for prior authorization medically necessity criteria. Note: Any listed preferred product requirements in this coverage policy, inclusive of oncology and/or oncology-related uses, are applicable as noted." | 5/1/2026 |

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| | **Cutaneous Melanoma:** The requirement that Proleukin will be used as a single agent was removed. The requirement that "Proleukin will be directly injected into metastatic, recurrent, or unresectable cutaneous, subcutaneous, or nodal lesions" was changed to "The medication will be directly injected into unresectable or borderline resectable lesions." | |

The policy effective date is in force until updated or retired.