



Drug Coverage Policy

Effective Date 5/1/2025

Coverage Policy Number IP0407

Policy Title Proleukin

Oncology (Injectable) - Proleukin

- Proleukin® (aldesleukin intravenous infusion – Prometheus Laboratories)

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 guidelines:

- **Cutaneous melanoma** (version 1.2025 – December 20, 2024) clinical practice guidelines recommend Proleukin for unresectable or metastatic disease as a single agent for second-line or subsequent therapy for disease progression, or as part of tumor-infiltrating lymphocyte therapy after progression on anti-programmed death receptor-1 therapy and BRAF targeted therapy if BRAF *V600E* mutation positive (category 2A).^{2,4} Proleukin may be considered for patients with small brain tumors and without significant peritumoral edema (category 2B) or for intralesional therapy as primary or second-line treatment of unresectable stage III disease with clinical satellite/in-transit metastases, or local satellite/in-transit recurrence (category 2B).
- **Hematopoietic cell transplantation** (version 2.2024 – August 30, 2024) clinical practice guidelines recommend Proleukin as additional therapy, in combination with systemic corticosteroids, for steroid-refractory chronic graft-vs-host disease.^{2,5}
- **Kidney cancer** (version 3.2025 – January 9, 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 prescription benefit coverage of Proleukin. All approvals are provided for the duration noted below.

Proleukin is considered medically necessary when the following is met:

FDA-Approved Indications

-
- 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, iv, and v):
- 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. Proleukin will be used as a single agent; AND
 - v. Proleukin 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. Proleukin will be directly injected into metastatic, recurrent, or unresectable cutaneous, subcutaneous, or nodal 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.

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) Proleukin will be used as a single agent; AND
- D) Proleukin 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) Proleukin will be used in combination with systemic corticosteroids; AND
- D) Proleukin 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/m² administered subcutaneously once daily.

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Receipt of sample product does not satisfy any criteria requirements for coverage.

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]. San Diego, CA: Prometheus Laboratories; January 2024.
2. The NCCN Drugs and Biologics Compendium. © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed on January 27, 2025. Search term: aldesleukin.
3. The NCCN Kidney Cancer Clinical Practice Guidelines (version 3.2025 – January 9, 2025). © 2025 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed January 27, 2025.
4. The NCCN Cutaneous Melanoma Clinical Practice Guidelines (version 1.2025 – December 20, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed January 27, 2025.
5. The NCCN Hematopoietic Cell Transplantation Clinical Practice Guidelines (version 2.2024 – August 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: <http://www.nccn.org>. Accessed January 27, 2025.
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. 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" Added criteria for: (1) Cutaneous Melanoma, (2) Renal Cell Carcinoma	5/1/2025

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

"Cigna Companies" refers to operating subsidiaries of The Cigna Group. All products and services are provided exclusively by or through such operating subsidiaries, including Cigna Health and Life Insurance Company, Connecticut General Life Insurance Company, Evernorth Behavioral Health, Inc., Cigna Health Management, Inc., and HMO or service company subsidiaries of The Cigna Group. © 2025 The Cigna Group.