Utilization Review Policy 263

POLICY: Oncology (Injectable) – Proleukin Utilization Management Medical Policy
- Proleukin® (aldesleukin injection for intravenous use – Prometheus Laboratories)

EFFECTIVE DATE: 1/1/2022
REVIEW DATE: 02/11/2026

COVERAGE CRITERIA FOR: All UCare Plans

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, 2026) 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]

POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Proleukin. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indications. Extended approvals are allowed if the patient continues to meet the Criteria and Dosing. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. Because of the specialized skills

required for evaluation and diagnosis of patients treated with Proleukin as well as the monitoring required for adverse events and long-term efficacy, approval requires Proleukin to be prescribed by or in consultation with a physician who specializes in the condition being treated.
Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Proleukin is recommended in those who meet one of the following criteria:

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, 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.

---

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 ALL of 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. Approve up to 1 million International Units/m^2 administered subcutaneously no more frequently than once daily.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Proleukin is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

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, 2026.
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.

HISTORY

Type of Revision	Summary of Changes	Review Date
Annual Revision	No criteria changes.	01/18/2023
Annual Revision	No criteria changes.	01/17/2024
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/16/2024
Annual Revision	**Renal Cell Carcinoma:** Condition of approval changed from kidney cancer to renal cell carcinoma. The descriptor "relapsed" removed from the patient has metastatic disease. Removed requirement that the patient has clear cell histology.	02/05/2025
UCare P&T Review	Policy reviewed and approved by UCare P&T committee. Annual review process	09/15/2025
Annual Revision	**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	02/11/2026

	changed to "the medication will be directly injected into unresectable or borderline resectable lesions."	