Reference number(s)
4239-A

STANDARD MEDICARE PART B MANAGEMENT

PROLEUKIN (aldesleukin)

POLICY

I. INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

A. FDA-Approved Indications
1. Proleukin is indicated for the treatment of adults with metastatic renal cell carcinoma (metastatic RCC).
2. Proleukin is indicated for the treatment of adults with metastatic melanoma.

B. Compendial Uses
1. Relapsed or stage IV renal cell carcinoma
2. Unresectable cutaneous melanoma
3. Chronic graft-versus-host disease (GVHD)
4. Acute Myeloid Leukemia (AML)
5. Carcinomatous metastasis in skin
6. Glial tumor of the brain
7. Kaposi's Sarcoma
8. Malignant Effusion

All other indications will be assessed on an individual basis. Submissions for indications other than those enumerated in this policy should be accompanied by supporting evidence from Medicare approved compendia.

II. CRITERIA FOR INITIAL APPROVAL

A. Renal Cell Carcinoma
Authorization of 6 months may be granted for treatment of relapsed or stage IV renal cell carcinoma with clear cell histology for high-dose single-agent therapy.

B. Cutaneous Melanoma
Authorization of 6 months may be granted for treatment of cutaneous melanoma when used as one of the following:
1. Intravenously as high-dose single agent subsequent therapy for metastatic or unresectable disease.
2. Intralesionally for unresectable disease

C. Chronic graft-versus-host disease (GVHD)

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Authorization of 6 months may be granted for treatment of chronic graft-versus host-disease (GVHD) as additional therapy in conjunction with systemic corticosteroids following no response to first-line therapy options.

D. Acute Myeloid Leukemia (AML)
Authorization of 6 months may be granted for the treatment of AML when used as high-dose therapy.

E. Carcinomatous metastasis in skin
Authorization of 6 months may be granted for treatment of skin metastasis (carcinoma erysipeloids) from gastric carcinoma when used intralesionally.

F. Glial tumor of brain
Authorization of 6 months may be granted for treatment of refractory anaplastic astrocytoma when used intracerebrally in combination with lymphokine-activated killer cells.

G. **Kaposi's Sarcoma**
Authorization of 6 months may be granted for the treatment of classic Kaposi's Sarcoma not associated with human immunodeficiency virus when used intralesionally.

H. Malignant Effusion
Authorization of 6 months may be granted when given at a low dose for treatment of neoplastic fluid accumulation in members with advanced solid tumors.

III. CONTINUATION OF THERAPY

All members (including new members) requesting authorization for continuation of therapy must be currently receiving therapy with the requested agent.

A. Renal Cell Carcinoma or Cutaneous Melanoma
Authorization for 6 months may be granted when all of the following criteria are met:
1. The member is currently receiving therapy with the requested medication.
2. The member must be evaluated for response approximately 4 weeks after completion of a course of therapy and again immediately prior to the scheduled start of the next treatment course.
3. Additional courses of treatment should be given only if there is some tumor shrinkage following the last course.
4. Retreatment is not contraindicated.
5. Each treatment course should be separated by a rest period of at least 7 weeks from the date of hospital discharge.

B. Chronic graft-versus-host disease (GVHD)
Authorization for 12 months may be granted when all of the following criteria are met:
1. The member is currently receiving therapy with the requested medication.
2. The member is receiving benefit from therapy. Benefit is defined as:
   a. Improvement in symptoms, and
   b. No unacceptable toxicity

C. All other indications
Authorization for 12 months may be granted for all members who are continuing with the requested therapy when all of the following criteria are met:
1. The member is currently receiving therapy with the requested medication.

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2. The requested medication is being used to treat any other diagnosis or condition enumerated in Section II.
3. The member is receiving benefit from therapy. Benefit is defined as:
   a. No evidence of unacceptable toxicity while on the current regimen AND
   b. No evidence of disease progression while on the current regimen.

IV. SUMMARY OF EVIDENCE

The contents of this policy were created after examining the following resources:

1. The prescribing information for Proleukin.
2. The available compendium
   a. National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium
   b. Micromedex DrugDex
   c. American Hospital Formulary Service- Drug Information (AHFS-DI)
   d. Lexi-Drugs
   e. Clinical Pharmacology
3. NCCN Guideline: Cutaneous melanoma
4. NCCN Guideline: Hematopoietic cell transplantation
5. NCCN Guideline: Kidney cancer

After reviewing the information in the above resources, the FDA-approved indications listed in the prescribing information for Proleukin are covered in addition to the following:

1. Relapsed or stage IV renal cell carcinoma
2. Unresectable cutaneous melanoma
3. Chronic graft-versus-host disease (GVHD)
4. Acute Myeloid Leukemia (AML)
5. Carcinomatous metastasis in skin
6. Glial tumor of the brain
7. Kaposi's Sarcoma
8. Malignant Effusion

V. EXPLANATION OF RATIONALE

Support for FDA-approved indications can be found in the manufacturer's prescribing information.

Support for using Proleukin to treat renal cell carcinoma and cutaneous melanoma can be found in the NCCN Drugs and Biologics Compendium. Use of information in the NCCN Drugs and Biologics Compendium for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Support for using Proleukin to treat acute myeloid leukemia, carcinomatous metastasis in skin, glial tumor of brain, and Kaposi's sarcoma can be found in the Micromedex DrugDex database. Use of information in the DrugDex database for off-label use of drugs and biologicals in an anti-cancer chemotherapeutic regimen is supported by the Medicare Benefit Policy Manual, Chapter 15, section 50.4.5 (Off-Label Use of Drugs and Biologicals in an Anti-Cancer Chemotherapeutic Regimen).

Support for using Proleukin to treat chronic graft-versus-host disease can be found in the National Comprehensive Cancer Network's guideline for hematopoietic cell transplantation. The NCCN Guideline for

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hematopoietic cell transplantation supports the use of Proleukin in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options.

Support for using Proleukin to treat malignant effusion can be found in a study by Lissoni and colleagues. In a case-series study of patients with advanced solid tumors and neoplastic effusions (n=100), the intracavity administration of low-dose interleukin-2 (6,000,000 IU on days 1 and 7) resulted in an objective clinical response in 72% of patients with a median response duration of 5 months. A complete response was observed in 27% and a partial response in 45% of patients. The peritoneal site was significantly less responsive than the pleural or pericardial sites. The intracavity injection was well-tolerated.

VI. REFERENCES

1. Proleukin [package insert]. Yardley, PA: Clinigen, Inc.; September 2019.
2. The NCCN Drugs & Biologic Compendium 2023 National Comprehensive Cancer Network, Inc. http://www.nccn.org. Accessed May 11, 2023.
3. Micromedex (electronic version). Truven Health Analytics. Greenwood Village, Colorado, USA http://www.micromedexsolutions.com/. Accessed May 11, 2023.
4. Lissoni P, Mandala M, Curigliano G, et al: Progress report on the palliative therapy of 100 patients with neoplastic effusions by intracavitary low-dose interleukin-2. Oncology 2001; 60:308-312.

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