

Proleukin® (aldesleukin, IL-2) (Intravenous/Subcutaneous)

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Date of Origin: 07/26/2016

Dates Reviewed: 07/2016, 01/2017, 01/2018, 01/2019, 01/2020, 01/2021, 01/2022

Customization Dates: 04/01/2022

Effective Dates: 04/01/2022

I. Length of Authorization

- Coverage for Renal Cell Carcinoma (RCC) and Melanoma will be provided for two (2) months and may be renewed.
- Coverage for Hematopoietic Cell Transplantation (HSCT) will be provided for four (4) months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- 22 million IU single-dose vial: 1 vial per day

B. Max Units (per dose and over time) [HCPCS Unit]:

HSCT

- Initially 84 billable units per 112 days, maintenance is 1 billable unit per day

All other indications

- 88 billable units per 68 days

III. Initial Approval Criteria¹

Coverage is provided in the following conditions:

Submission of medical records (chart notes) related to the medical necessity criteria is **REQUIRED** on all requests for authorizations. Records will be reviewed at the time of submission. Please provide documentation related to diagnosis, step therapy, and clinical markers (i.e. genetic and mutational testing) supporting initiation when applicable. Medical records may be submitted via direct upload through the PA web portal or by fax.

- Patient is at least 18 years of age; **AND**

- Patient must have normal cardiac function (i.e., normal ejection fraction and unimpaired wall motion) as determined by thallium stress testing prior to initiating therapy; **AND**
- Patient must have normal pulmonary function determined by formal pulmonary function testing (i.e., FEV1 >2 liters or ≥75% of predicted for height and age) prior to initiating therapy; **AND**
- Patient must have a baseline serum creatinine of ≤1.5 mg/dL prior to initiating therapy; **AND**
- Pre-existing bacterial infections will be adequately treated prior to initiation of therapy; **AND**

Universal Criteria ¹

- Patient has an ECOG performance status of 0-1; **AND**
- Proleukin will be administered in a hospital setting under close supervision of a qualified physician; **AND**
- Patient must not have an organ allograft; **AND**
- Patient must not have untreated or active CNS metastases; **AND**

Renal Cell Carcinoma † Φ ^{1-3,6}

- Patient has metastatic disease; **AND**
- Used as a single agent

Melanoma † Φ ^{1,2,4,6}

- Patient has unresectable or metastatic disease; **AND**
- Used as a single agent: **AND**
 - Used as first line therapy †; **OR**
 - Used as subsequent therapy ‡; **AND**
 - Patient has disease progression or used after maximum clinical benefit from BRAF targeted therapy; **AND**
 - Patient does not have inadequate organ reserves

Hematopoietic Cell Transplantation ‡ ^{2,5}

- Patient has received a hematopoietic stem cell transplant; **AND**
- Used for steroid-refractory chronic GVHD; **AND**
- Used in combination with systemic corticosteroids as additional therapy following no response to first-line therapies

† FDA-labeled indication(s); ‡ Compendia approved indication(s); Φ Orphan Drug

IV. Renewal Criteria¹

Coverage can be renewed based upon the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), performance status, etc. identified in section III; **AND**
- Disease response with treatment as defined by stabilization of disease or decrease in size of tumor or tumor spread; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: capillary leak syndrome (CLS), sustained ventricular tachycardia (≥ 5 beats), cardiac arrhythmias not controlled or unresponsive to management; chest pain with ECG changes, consistent with angina or myocardial infarction; cardiac tamponade, intubation for >72 hours, renal failure requiring dialysis >72 hours, coma or toxic psychosis lasting >48 hours, repetitive or difficult to control seizures; bowel ischemia/perforation, GI bleeding requiring surgery, serious manifestations of eosinophilia, etc.; **AND**
- Patient must not have developed moderate to severe lethargy or somnolence

V. Dosage/Administration^{1,5}

Indication	Dose
Melanoma & Renal Cell Carcinoma	600,000 IU/kg (0.037 mg/kg) administered intravenously every 8 hours for a maximum of 14 doses. Following 9 days of rest, the schedule is repeated for another 14 doses, for a maximum of 28 doses per course, as tolerated. Each treatment course should be separated by a rest period of at least 7 weeks from the date of hospital discharge.
Hematopoietic Cell Transplantation/GVHD	1 million IU/m ² subcutaneously daily for 12 weeks, followed by a 4 week treatment break after the initial treatment period. Thereafter, patients showing improvement can continue treatment at the same dose (1 million IU/m ² subcutaneously daily) indefinitely.

VI. Billing Code/Availability Information

HCPCS Code:

- J9015 – Injection, aldesleukin, per single use vial

NDC:

- Proleukin 22 million IU single-dose vial: 76310-0022-xx

VII. References

1. Proleukin [package insert]. Yardley, PA; Clinigen, Inc.; September 2019. Accessed December 2021.
2. Referenced with permission from the NCCN Drugs and Biologics Compendium (NCCN Compendium[®]) aldesleukin; Interleukin-2, recombinant. National Comprehensive Cancer Network, 2020. The NCCN Compendium[®] is a derivative work of the NCCN Guidelines[®]. NATIONAL COMPREHENSIVE CANCER NETWORK[®], NCCN[®], and NCCN GUIDELINES[®] are trademarks owned by the National Comprehensive Cancer Network,

Inc. To view the most recent and complete version of the Compendium, go online to NCCN.org. Accessed December 2021.

3. Fyfe G, Fisher RI, Rosenberg SA, et al. Results of treatment of 255 patients with metastatic renal cell carcinoma who received high-dose recombinant interleukin-2 therapy. *J Clin Oncol.* 1995 Mar;13(3):688-96.
4. Atkins MB, Lotze MT, Dutcher JP, et al. High-dose recombinant interleukin 2 therapy for patients with metastatic melanoma: analysis of 270 patients treated between 1985 and 1993. *J Clin Oncol.* 1999 Jul;17(7):2105-16.
5. 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 Jul 7;128(1):130-7. doi: 10.1182/blood-2016-02-702852. Epub 2016 Apr 12.
6. Buchbinder E, Dutcher J, Daniels G, et al. Therapy with high-dose Interleukin-2 (HD IL-2) in metastatic melanoma and renal cell carcinoma following PD1 or PDL1 inhibition. *J Immunother Cancer.* 2019 Feb 18;7(1):49. doi: 10.1186/s40425-019-0522-3.

Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
C43.0	Malignant melanoma of lip
C43.10	Malignant melanoma of unspecified eyelid, including canthus
C43.11	Malignant melanoma of right eyelid, including canthus
C43.12	Malignant melanoma of left eyelid, including canthus
C43.111	Malignant melanoma of right upper eyelid, including canthus
C43.112	Malignant melanoma of right lower eyelid, including canthus
C43.121	Malignant melanoma of left upper eyelid, including canthus
C43.122	Malignant melanoma of left lower eyelid, including canthus
C43.20	Malignant melanoma of unspecified ear and external auricular canal
C43.21	Malignant melanoma of right ear and external auricular canal
C43.22	Malignant melanoma of left ear and external auricular canal
C43.30	Malignant melanoma of unspecified part of face
C43.31	Malignant melanoma of nose
C43.39	Malignant melanoma of other parts of face
C43.4	Malignant melanoma of scalp and neck
C43.51	Malignant melanoma of anal skin
C43.52	Malignant melanoma of skin of breast
C43.59	Malignant melanoma of other part of trunk
C43.60	Malignant melanoma of unspecified upper limb, including shoulder
C43.61	Malignant melanoma of right upper limb, including shoulder
C43.62	Malignant melanoma of left upper limb, including shoulder

C43.70	Malignant melanoma of unspecified lower limb, including hip
C43.71	Malignant melanoma of right lower limb, including hip
C43.72	Malignant melanoma of left lower limb, including hip
C43.8	Malignant melanoma of overlapping sites of skin
C43.9	Malignant melanoma of skin, unspecified
C64.1	Malignant neoplasm of right kidney, except renal pelvis
C64.2	Malignant neoplasm of left kidney, except renal pelvis
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
C65.1	Malignant neoplasm of right renal pelvis
C65.2	Malignant neoplasm of left renal pelvis
C65.9	Malignant neoplasm of unspecified renal pelvis
D89.811	Chronic graft-versus-host disease
D89.812	Acute on chronic graft-versus-host disease
D89.813	Graft-versus-host disease, unspecified
T86.09	Other complications of bone marrow transplant

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Determinations (LCDs), and Local Coverage Articles (LCAs) may exist and compliance with these policies is required where applicable. They can be found at: <https://www.cms.gov/medicare-coverage-database/search.aspx>. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCD/LCA): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	Applicable State/US Territory	Contractor
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.

Medicare Part B Administrative Contractor (MAC) Jurisdictions

Jurisdiction	Applicable State/US Territory	Contractor
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC