Medical Drug Clinical Criteria

Subject:	Proleukin (aldesleukin)		
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Overview

This document addresses the use of Proleukin (aldesleukin). Proleukin is a recombinant interleukin-2 (IL-2) primarily used to treat renal cell cancer and melanoma. Although the exact antitumor mechanism is unknown, it is believed that Proleukin works by interacting with IL-2 receptors to cause an immune reaction leading to proliferation and differentiation of B and T-cells in the body.

The FDA approved indications for Proleukin include metastatic renal cell cancer and metastatic melanoma.

Interleukin-2 agents are also used in the treatment of pediatrics with high-risk neuroblastoma, in combination with dinutuximab (Unituxin), granulocyte-macrophage colony-stimulating factor (GM-CSF), and 13-cis-retinoic acid (Unituxin 2020).

Proleukin has black box warnings that limits its use to only administration in a hospital setting under the supervision of a qualified physician. These box warnings include use restricted to patients with normal cardiac and pulmonary functions as defined by thallium stress testing and formal pulmonary function testing, and adverse effects, such as capillary leak syndrome resulting in cardiac issues and other abnormalities, and impaired neutrophil function leading to increased risk of disseminated infection. Proleukin should also not be given to patients who develop moderate or severe lethargy or somnolence due to risk of coma.

Other Uses

The National Comprehensive Cancer Network (NCCN) panel provides a category 2A recommendation for use of Proleukin in conjunction with systemic steroids for hematopoietic stem cell transplant (HSCT) recipients with chronic graft-versus-host disease (GVHD) who are refractory to steroids alone. The recommendation was based on small phase 1 and 2, open label observational studies where the author(s) concluded that more trials are needed to determine efficacy and long-term durability (Koreth 2011, 2016, Whangbo 2019). Therefore, at this time, there is insufficient evidence to add such indication to the criteria. Also, while NCCN does provide Proleukin (or interleukin-2) with a 2A recommendation, the discussion within the NCCN Hematopoietic Cell Transplantation guidelines states that it is strongly recommended that individuals with steroid-refractory GVHD participate in a well-designed clinical trial.

NCCN provides a category 2A recommendation for the use of Proleukin in cutaneous melanoma as a high dose single-agent therapy in metastatic or unresectable disease as second-line or subsequent therapy. The studies referenced within the NCCN Melanoma, cutaneous guideline discuss interleukin-2 studies in non-comparative studies, including phase 2 trials, and retrospective/observational analyses. The guidelines note that high dose IL-2 is associated with significant toxicities and requires careful selection of patients close monitoring, and adherence to administration and management protocols. This usage is restricted to institutions to ensure appropriate care and management is available. Due to low response rates and high toxicity, IL-2 is not a preferred option for second-line or subsequent systemic therapy since immune checkpoint inhibitors or BRAF-targeted therapy options are considered more effective and safe.

Definitions and Measures

Melanoma: A type of cancer that begins in the melanocytes. Melanoma is also referred to as malignant melanoma and cutaneous melanoma.

Metastasis: The spread of cancer from one part of the body to another; a metastatic tumor contains cells that are like those in the original (primary) tumor and have spread.

Clinical Criteria

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Proleukin (aldesleukin)

Requests for Proleukin (aldesleukin) may be approved if the following criteria are met:

I. Individual has metastatic malignant melanoma; **AND**
II. ECOG (Eastern Cooperative Oncology Group) performance status 0-1;

OR
III. Individual has metastatic renal cell cancer; **AND**
IV. ECOG (Eastern Cooperative Oncology Group) performance status 0-1;

OR
V. Individual is using in the treatment of high-risk neuroblastoma in pediatrics after response to induction therapy and stem cell transplantation (Unituxin 2020); **AND**
   A. Individual is using in combination with isotretinoin, dinutuximab, sargramostim (Ladenstein 2018).

Proleukin (aldesleukin) may not be approved for any of the following:

I. Individual has an abnormal thallium stress test; **OR**
II. Individual has an abnormal pulmonary function test; **OR**
III. Individual with organ allografts; **OR**
IV. Individual has active systemic infections; **OR**
V. When the above criteria are not met, and for all other indications.

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

J9015	Injection, aldesleukin, per single use vial

ICD-10 Diagnosis

C43.0-C43.9	Malignant melanoma of skin
C64.1-C64.9	Malignant neoplasm of kidney
C74.90	Malignant neoplasm of unspecified part of unspecified adrenal gland

Document History

Revised: 09/12/2022
Document History:

- 09/12/2022 – Select Review: Clarify use in pediatric high-risk neuroblastoma by removing language "and with or without Proleukin". Coding reviewed: Added ICD-10-CM C74.90.
- 05/20/2022 – Annual Review: Update renal cell and melanoma criteria with ECOG scores. Update criteria for pediatric high-risk neuroblastoma to allow for combination use with or without Proleukin. Coding Reviewed. No changes.
- 05/21/2021 – Annual Review: Update references. Coding reviewed: No changes.
- 08/21/2020 – Annual Review: Update references. Coding reviewed: Added HCPCS J9015, Added ICD-10-CM C43.0-C43.9, C64.1-C64.9
- 11/15/2019 – Annual Review: Update non-approvable criteria to restrict use in those with active infections per label.

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Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.