CLINICAL GUIDELINES FOR MEDICAL NECESSITY

MEDICAL ONCOLOGY

Aldesleukin (Proleukin®)

Version: 1.0

EFFECTIVE DATE: 1/1/2024

Please note the following:

Aldesleukin (Proleukin ®)

Note: For Medicare members/enrollees, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Please refer to the CMS website at http://www.cms.gov for additional information.

Note: For Medicaid members/enrollees, circumstances when state Medicaid coverage provisions conflict with the coverage provisions within this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Aldesleukin (Proleukin): Discussion

Aldesleukin is recombinant analog of the endogenous cytokine interleukin-2 (IL-2). Interleukin-2 is a critical cytokine in the adaptive immune process and interacts with specific T cell receptors to activate intracytoplasmic pathways that lead to the proliferation and differentiation of immature T lymphoblasts into mature and reactive T cells that play an important role in immune responses to foreign proteins, viruses and bacteria and tumor cells. Aldesleukin induces the enhancement of lymphocyte mitogenesis and stimulation of long-term growth of human interleukin-2 dependent cell lines, the enhancement of lymphocyte cytotoxicity, the induction of killer cell (lymphokine-activated (LAK) and natural (NK)) activity; and the induction of interferon-gamma production. [1,2]

Aldesleukin is approved by the Food and Drug Administration (FDA) for the treatment of metastatic renal cell cancer and metastatic melanoma.[2]

IL-2–based immunotherapy has achieved long-lasting complete or partial remissions in a small subset of patients with renal cell carcinoma (RCC), but high-dose IL-2 is associated with substantial toxicity and attempts to characterize tumor or patient factors for best response to this therapy have been unsuccessful.[3]

For patients with stage III in-transit melanoma where resection is not feasible, prior resections have been unsuccessful, or who refuse surgery, intralesional aldesleukin injections are useful. High-dose IL-2 for metastatic melanoma remains an option in the second-line or subsequent setting because it can provide long-term survival for a small percentage of patients, however, it is not a preferred option as it is considered less safe and less effective than immune checkpoint inhibitors or BRAF-targeted therapy.[4]

Low-dose IL2 has durable clinical activity in treating steroid-refractory chronic graft-versus-host disease (GVHD) with improvement in multiple sites of cGVHD, including the liver, skin, GI tract, lungs, and joints/muscle/fascia. Extended IL-2 therapy is well tolerated and is generally safe for long-term use.[5]

The National Comprehensive Cancer Network (NCCN) endorses aldesleukin for the following: kidney cancer, melanoma, and hematopoietic cell transplantation.[3,4,5.]

Aldesleukin should be restricted to patients with normal cardiac and pulmonary functions as defined by thallium stress testing and formal pulmonary function testing.

Aldesleukin should be administered in a hospital setting under the supervision of a qualified physician experienced in the use of anticancer agents. An intensive care facility and specialists skilled in cardiopulmonary or intensive care medicine must be available.

Aldesleukin administration has been associated with capillary leak syndrome (CLS) which is characterized by a loss of vascular tone and extravasation of plasma proteins and fluid into the extravascular space. CLS results in hypotension and reduced organ perfusion which may be severe and can result in death. CLS may be associated with cardiac arrhythmias (supraventricular and ventricular), angina, myocardial infarction, respiratory insufficiency requiring intubation, gastrointestinal bleeding or infarction, renal insufficiency, edema, and mental status changes.

Aldesleukin treatment is associated with impaired neutrophil function (reduced chemotaxis) and with an increased risk of disseminated infection, including sepsis and bacterial endocarditis.[2]

Aldesleukin: Definitions

- **BRAF target therapy -** Targeted therapy drugs that block the activity of the MEK protein and the mutated BRAF protein.
- **Capillary Leak Syndrome (CLS) –** Capillary leak syndrome is characterized by a loss of vascular tone and extravasation of plasma proteins and fluid into the extravascular space. CLS results in hypotension and reduced organ perfusion which may be severe and can result in death.
- **Food and Drug Administration (FDA)** – The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
- **Graft-versus-host disease (GVHD)** - Graft-versus-host disease (GVHD) is a potentially serious complication of allogeneic stem cell transplantation that occurs when the graft's immune cells recognize the host as foreign and attack the recipient's body cells. GVHD can be mild, moderate, or severe. In some cases, it can be life-threatening.
- **National Comprehensive Cancer Network (NCCN) -** An alliance of thirty-two leading cancer centers devoted to patient care, research, and education. The NCCN guidelines are utilized for Radiation Therapy and Medical Oncology standards. NCCN consensus clinical standards are periodically updated and NantHealth, Inc. reviews these and updates its policies within a timely manner.

Aldesleukin: Policy

Aldesleukin will be considered for coverage when the following criteria are met:

Hematopoietic Cell Transplantation (HCT)

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. Additional low-dose therapy for chronic graft-versus-host disease (GVHD) in conjunction with systemic corticosteroids following no response (steroid-refractory disease) to first-line therapy options.[5]

Kidney Cancer (Clear Cell)

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. High-dose single-agent therapy for patients with an excellent performance status (PS<2)
   a) First-line therapy for relapse or stage IV favorable risk disease
   b) Subsequent therapy for relapse or stage IV disease. [3]

Melanoma (Cutaneous)

1. At least 18 years of age; AND
2. Prescribed by or in consultation with an oncologist; AND
3. Useful in certain circumstances for either:
   a) Intralesional therapy for initial and/or subsequent treatment of unresectable disease for one of the following:
      i. Stage III disease with clinical satellite/in-transit metastases
      ii. Local satellite/in-transit recurrence; OR
   b) High-dose single-agent therapy for metastatic or unresectable disease as second-line or subsequent therapy for one of the following:
      i. Disease progression, intolerance, and/or projected risk of progression with BRAF-targeted therapy
      ii. Disease progression, intolerance, and/or projected risk of progression with BRAF-targeted therapy in patients with small brain metastases and without significant peritumoral edema.

Note:

1. High-dose interleukin-2 should not be used for patients with inadequate organ reserve, poor performance status, or untreated or active brain metastases.[4]

2. Coverage of aldesleukin will be provided for an FDA-approved indication or National Comprehensive Cancer Network (NCCN) guidelines when it is a Category 1, 2A, or 2B recommendation or when all criteria are met.

Authorization Period and Renewal Criteria

1. Initial Authorization Period: 12 months
2. Renewal Criteria: No evidence of disease progression or unacceptable toxicity
3. Renewal Authorization Period: 12 months

Aldesleukin: References

1. LiverTox: Clinical and Research Information on Drug-Induced Liver Injury [Internet]. https://www.ncbi.nlm.nih.gov/books/NBK548091/. Accessed May 15, 2023.
2. Aldesleukin (Proleukin) Package Insert. https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/103293s5130lbl.pdf. Accessed May 15, 2023.
3. National Comprehensive Cancer Network Guidelines. Kidney Cancer (Version 4.2023). https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed May 15, 2023.
4. National Comprehensive Cancer Network Guidelines. Melanoma: Cutaneous (Version 2.2023). https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf. Accessed May 15, 2023.
5. National Comprehensive Cancer Network Guidelines. Hematopoietic Cell Transplantation (HCT) (Version 1.2023). https://www.nccn.org/professionals/physician_gls/pdf/hct.pdf. Accessed May 15, 2023.

Aldesleukin: Coding (CPT®, ICD 10 and HCPCS) *

*Procedure codes appearing in medical policy documents are only included as a general reference. This list may not be all inclusive and is subject to updates. In addition, the codes listed are not a guarantee of payment.

CODE	DESCRIPTION
C43.9	Malignant melanoma of skin, unspecified
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis
D89.813	Graft-versus-host disease, unspecified
J9015	Aldesleukin (Proleukin)

Aldesleukin: Revision and Review History

No.	Description	Date(s)
1	Original Effective Date:	1/1/2024
2	Policy Review Dates:	5/24/2023
3	Policy Revision Dates:	
4	Department Owner:	Medical Affairs
5	NH Advisory Committee Approval Dates:	6/27/2023
6	Revision Changes:	