POLICY NUMBER UM_1067	**SUBJECT** Proleukin™ (aldesleukin)		**DEPT/PROGRAM** UM	**PAGE 1 OF 4**
DATE REVIEWED 02/20/11, 12/07/11, 09/18/13, 10/06/14, 12/18/15, 12/19/16, 10/09/17, 09/04/18, 08/08/19	**APPROVAL DATE** August 14, 2019	**EFFECTIVE DATE** August 14, 2019	**REVISION DATES** (latest version listed last) 02/20/11, 12/07/11, 12/18/15, 10/11/17, 09/21/18, 08/14/19	
PRIMARY BUSINESS OWNER: UM **APPROVED BY:** Dr. Andrew Hertler		**COMMITTEE/BOARD APPROVAL** Utilization Management Committee		
URAC STANDARDS		**ADDITIONAL AREAS OF IMPACT**		
CMS REQUIREMENTS	**STATE/FEDERAL REQUIREMENTS**		**APPLICABLE LINES OF BUSINESS** Oncology	

I. PURPOSE

To define and describe the accepted indications for Proleukin (aldesleukin) usage in the treatment of cancer.

II. DEFINITIONS

Proleukin (aldesleukin): is an antineoplastic agent and is in the class of response biologic modifiers. It is a recombinant formulation of interleukin-2 (IL-2). Proleukin (aldesleukin) is a nonglycosylated biosynthetic interleukin-2 (also known as T-cell growth factor), which differs only slightly in amino acid sequence from the natural compound.

Proleukin (aldesleukin) interacts with the high-affinity IL-2 receptor expressed on cells of the immune system and stimulates a cytokine cascade involving various interferons, interleukins, and tumor necrosis factors. Proleukin (aldesleukin) along with other cytokines induce proliferation and differentiation of B and T-cells, monocytes, macrophages, and cytotoxic lymphocytes which include natural killer (NK) cells, cytotoxic T-cells, tumor-infiltrating lymphocytes (TIL), and lymphokine-activated killer (LAK) cells. Proleukin (aldesleukin)'s antitumor activity is believed to result from activation of cytotoxic lymphocytes, however, the exact mechanism is unknown. Whether Proleukin (aldesleukin) acts directly or through second messengers is also unclear, however, Proleukin (aldesleukin) does elevate production of interleukin-1, tumor necrosis factors alpha and beta, interferon gamma, and interleukin-6.

Proleukin (aldesleukin) is indicated for the treatment of adults with metastatic renal cell carcinoma (metastatic RCC) and metastatic melanoma.

Aldesleukin is available as Proleukin in 22 million IU per single use vial.

III. POLICY

New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century may be deemed as not approvable and therefore not reimbursable.

Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Proleukin (aldesleukin) may be considered medically necessary when any of the following selection criteria is met:

1. **Renal cell carcinoma (RCC)**
    a. The member has a diagnosis of metastatic renal cell carcinoma **AND**
    b. The member is at least 18 years of age and has PS ≤ 1 **AND**
    c. Proleukin (aldesleukin) is being used as first line therapy, as a high-dose single agent, for member with predominant clear cell histology with medically unresectable stage IV disease.
2. **Melanoma**
    a. The member has a diagnosis of metastatic/unresectable melanoma **AND**
    b. The member is at least 18 years of age and has PS 0-2 **AND**
    c. Proleukin (aldesluekin) is being used as second line or subsequent therapy as high-dose single agent.

Exclusion Criteria: Proleukin (aldesleukin) is not considered medically necessary when any of the following selection criteria is met:

1. High dose Proleukin (aldesleukin) is being used in member with active, untreated brain metastases.
2. High dose Proleukin (aldesleukin) is being administered outside a hospital setting.
3. Dosing exceeds single dose limit of Proleukin (aldesleukin) 600,000 International Units/kg or 16.8 MIU/kg (28 doses) per cycle.
4. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Proleukin (aldesleukin) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration**
    a. Dose: 600,000 IU/kg (0.037 mg/kg) administered every 8 hours by a 15-minute IV infusion for a maximum of 14 doses.
    b. Each course of treatment consists of two 5-day treatment cycles separated by a rest period.
    c. Following 9 days of rest, the schedule is repeated for another 14 doses, for a maximum of 28 doses per course, as tolerated.
2. **Dosage Adjustments**
    a. Hepatic Impairment: Hold the next dose for signs of hepatic failure including encephalopathy, increasing ascites, liver pain, or hypoglycemia. Resume therapy once all signs of hepatic failure have resolved; however, it is recommended that further treatment for that course be discontinued. Consider starting a new course of treatment at least 7 weeks after cessation of adverse event.
    b. Renal impairment:

i. Serum creatinine > 4.5 mg/dl: hold dose until SCr < 4 mg/dl and fluid and electrolyte status are stable.

ii. Serum creatinine ≥ 4 mg/dl in the presence of severe volume overload, acidosis, or hyperkalemia: hold dose until SCr < 4 mg/dl and fluid and electrolyte status are stable

iii. Persistent oliguria with urine output of < 10 ml/hour for 16—24 hours with a rising SCr: hold dose until urine output > 10 ml/hour with a decrease of SCr > 1.5 mg/dl or normalization of SCr.

3. **Monitoring**

a. Proleukin (aldesleukin) should be administered in a hospital setting under the supervision of a qualified physician experienced in the use of anticancer agents.

b. Therapy with Proleukin (aldesleukin) for injection should be restricted to member with normal cardiac and pulmonary functions as defined by thallium stress testing and formal pulmonary function testing. Extreme caution should be used in member with a normal thallium stress test and a normal pulmonary function test who have a history of cardiac or pulmonary disease.

c. Proleukin (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.

d. Contraindications:

i. Member has an abnormal thallium stress test or abnormal pulmonary function tests (FEV1 >2 liters or ≥75% of predicted for height and age) and has organ allografts.

ii. Retreatment in member who have experienced the following drug-related toxicities while receiving an earlier course of therapy:

iii. Sustained ventricular tachycardia (≥5 beats),

iv. Cardiac arrhythmias not controlled or unresponsive to management,

v. Chest pain with ECG changes, consistent with angina or myocardial infarction,

vi. Cardiac tamponade,

vii. Intubation for >72 hours,

viii. Renal failure requiring dialysis >72 hours,

ix. Coma or toxic psychosis lasting >48 hours,

x. Repetitive or difficult to control seizures,

xi. Bowel ischemia/perforation, and/or

xii. GI bleeding requiring surgery.

e. Proleukin (aldesleukin) treatment is associated with impaired neutrophil function (reduced chemotaxis) and with an increased risk of disseminated infection, including sepsis and bacterial endocarditis. Consequently, preexisting bacterial infections should be adequately

treated prior to initiation of Proleukin (aldesleukin) therapy. Member with indwelling central lines are particularly at risk for infection with gram positive microorganisms. Antibiotic prophylaxis has been associated with a reduced incidence of staphylococcal infections.

f. Proleukin (aldesleukin) administration should be withheld in member developing moderate to severe lethargy or somnolence; continued administration may result in coma.

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Proleukin® prescribing information. Prometheus Laboratories Inc. San Diego, CA.2019.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.