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Title

**Interleukin-2 (IL-2)
Proleukin[®] (Aldesleukin)**

Description

Interleukin-2 (IL-2) is a protein that occurs naturally in your body and plays an important role in activating your immune system. The immune system protects the body from foreign substances, cells, and tissues by responding to and resisting diseases. PROLEUKIN[®] therapy is a genetically engineered or recombinant version of IL-2. PROLEUKIN[®] therapy possesses the same properties as naturally occurring IL-2 and helps activate the immune system to recognize and eliminate certain kinds of cancer cells.

Your immune system is composed of various types of cells that kill and remove foreign substances from the body. IL-2 activates specialized defense cells called T cells and natural killer (NK) cells to help attack and destroy invading germs or diseases. IL-2 can also stimulate these cells to attack and destroy cancerous tumors.

PROLEUKIN[®] therapy differs from other treatments for metastatic melanoma and metastatic kidney cancer because it's an immunotherapy. Instead of directly inhibiting cancer cells, it works to activate the body's immune system to help kill them.

Labeled indications approved by the U.S. Food and Drug Administration (FDA) include the treatment of metastatic renal cell carcinoma and metastatic malignant melanoma.

PROLEUKIN[®] (aldesleukin) for injection is a recombinant human interleukin-2 (rhIL-2) for treatment in adults with metastatic melanoma and metastatic kidney cancer. PROLEUKIN[®] therapy is a form of immunotherapy that uses the body's natural immune system to fight cancer. PROLEUKIN[®] has been used for over 10 years in the treatment of metastatic melanoma and over 15 years in the treatment of metastatic kidney cancer (renal cell carcinoma). Studies have demonstrated that PROLEUKIN[®] therapy offers the possibility of a complete and long-lasting response in these diseases.*

* A complete response is defined as the disappearance of all signs of cancer in response to treatment.

When services are covered for commercial products and Medicare HMO Blue, Medicare PPO Blue, and Blue Medicare PFFS PlusRx.

We cover Proleukin[®] (Aldesleukin) for adults (18 years and older) with a documented diagnosis of metastatic renal cell carcinoma.

We cover Proleukin[®] (Aldesleukin) for adults (18 years and older) with a documented diagnosis of metastatic melanoma.

We cover perilymphatic injection of IL-2 in patients with resectable, non-metastatic squamous cell cancer of the oral cavity and oropharynx.

When services are not covered for commercial products and Medicare HMO Blue, Medicare PPO Blue, and Blue Medicare PFFS PlusRx.

We do not cover Proleukin® (Aldesleukin) for the treatment of other conditions not listed above because they are considered investigational.

We do not cover IL-2 in combination with chemotherapy or in combination with interferon alfa as a treatment of metastatic melanoma and renal cell cancer.

We do not cover IL-2 as a therapy to maintain remission after high-dose chemotherapy for a variety of malignancies, including multiple myeloma, leukemia, lymphoma, multiple myeloma, or breast cancer.

We do not cover other oncologic applications of IL-2 monotherapy, including but not limited to the following:

- colorectal cancer;
- hepatocellular carcinoma;
- small-cell and non-small-cell lung cancers;
- acute leukemia;
- myelodysplastic syndromes;
- multiple myeloma;
- non-Hodgkin's and Hodgkin's lymphoma;
- Ewing's sarcoma;
- soft tissue sarcoma;
- osteosarcoma;
- bladder
- brain
- breast
- esophagus
- ovary
- pancreas
- prostate
- small bowel
- stomach
- testes
- thyroid

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

PROLEUKIN® 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.

PROLEUKIN® 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.

PROLEUKIN® 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® therapy. Patients with indwelling central lines are particularly at risk for infection with gram positive microorganisms. Antibiotic prophylaxis with oxacillin, nafcillin, ciprofloxacin, or vancomycin has been associated with a reduced incidence of staphylococcal infections.

Individual consideration

All our medical policies are written for the majority of people with a given condition. Each policy is based on medical science. For many of our medical policies, each individual’s unique clinical circumstances may be considered in light of current scientific literature. For consideration of an individual patient, physicians may send relevant clinical information to:

For services already billed

Blue Cross Blue Shield of Massachusetts
 Provider Appeals
 P. O. Box 986065
 Boston, MA 02298

Prior to performance of service

Blue Cross Blue Shield of Massachusetts
 Case Creation/Medical Policy
 One Enterprise Drive
 Quincy, MA 02171
 Tel: 1-800-327-6716
 Fax: 1-888-641-5330

For medications provided and billed by a Home Infusion Provider or a Specialty Retail Pharmacy, all prior authorization requests should be sent to:

Blue Cross Blue Shield of Massachusetts
 Clinical Pharmacy Operations
 25 Technology Place
 Hingham, MA 02043
 Tel: (800) 366-7778
 Fax: (888) 641-5355

Managed care guidelines

- Prior authorization **is** required when these medications are processed under the home infusion therapy or retail pharmacy benefit.
- Prior authorization **is not** required when these drugs are purchased by the physician and administered in the office in accordance with this medical policy.

Indemnity and PPO guidelines

- Prior authorization **is** required when these medications are processed under the home infusion therapy or retail pharmacy benefit.
- Prior authorization **is not** required when these drugs are purchased by the physician and administered in the office in accordance with this medical policy.

Coding information

Procedure codes are from current CPT, HCPCS Level II, Revenue Code, and/or ICD-9-CM manuals, as recommended by the American Medical Association, Centers for Medicare and Medicaid Services and American Hospital Associations. Blue Cross Blue Shield Association national codes may be developed when appropriate.

The following codes are included below for informational purposes. Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member’s contract

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benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

- **CPT code 96413** - Chemotherapy administration, intravenous infusion technique; up to 1 hour, single or initial substance/drug (new code effective 1/1/06)
- **CPT code 96415** - each additional hour, 1 to 8 hours (list separately in addition to code for primary procedure) (new code effective 1/1/06)
- **HCPCS code - J9015** - Aldesleukin, per single use vial

Other information

Blue Cross Blue Shield of Massachusetts (BCBSMA) members utilizing the retail pharmacy benefit will be required to fill their prescriptions for Proleukin[®] (Aldesleukin) at one of the four providers in our retail specialty pharmacy network, as listed below

Retail Specialty Pharmacy Contact Information:	Retail Specialty Pharmacy Contact Information:	Retail Specialty Pharmacy Contact Information:	Retail Specialty Pharmacy Contact Information:
Caremark, Inc.	CuraScript™ Pharmacy, Inc., a subsidiary of Express Scripts, Inc.	IVPCARE®, A Walgreens Specialty Company	SpecialtyScripts Pharmacy
Phone: 1-866-846-3096 Fax: 1-800-323-2445 Website: www.caremark.com	Phone: 1-888-823-9070 Fax: 1-888-773-7386 Website: www.curascript.com	Phone: 1-800-370-2510 Fax: 1-800-874-9179 Website: www.otnservices.com	Phone: 1-800-218-5688 Fax: 1-800-830-5292 Website: www.specialtyscripts.com
7:30 a.m. – 9:00 p.m. EST	8:00 a.m. – 9:00 p.m. EST (M-F); 9:00 a.m. – 1:00 p.m. EST (Sat.)	8:00 a.m. – 9:00 p.m. EST (M-F); 10:00 a.m. – 4:00 p.m. EST (Sat.)	8:30 a.m. – 7:00 p.m. EST

Policy update history

New policy, effective 6/1/09.

Footnotes

¹ Based upon BCBSA national policy 8.01.04 Oncologic Applications of Interleukin-2 (Aldesleukin) when used as Monotherapy issued 2/06.

References

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4. Negrier S, Caty A, Lesimple T et al. Treatment of patients with metastatic renal carcinoma with a combination of subcutaneous interleukin-2 and interferon alfa with or without fluorouracil. J Clin Oncol 2000; 18(24):4009-15.

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7. Rosenberg SA, Yang JC, Schwartzentruber DJ et al. Prospective randomized trial of the treatment of patients with metastatic melanoma using chemotherapy with cisplatin, dacarbazine, and tamoxifen alone or in combination with interleukin-2 and interferon alfa-2b. *J Clin Oncol* 1999; 17(3):968-75.
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9. Eton O, Legha SS, Bedikian AY et al. Sequential biochemotherapy versus chemotherapy for metastatic melanoma: results from a phase III randomized trial. *J Clin Oncol* 2002; 20(8):2045-52.
10. Hauschild A, Garbe C, Stolz W et al. Dacarbazine and interferon alpha with or without interleukin 2 in metastatic melanoma: a randomized phase III multicentre trial of Dermatologic Cooperative Oncology Group (DeCOG). *Br J Cancer* 2001; 84(8):1036-42.
11. Atzpodien J, Neuber K, Kamanabrou D et al. Combination chemotherapy with or without s.c. IL-2 and IFN-alpha: results of a prospectively randomized trial of the Cooperative Advanced Malignant Melanoma Chemoimmunotherapy Group (ACIMM). *Br J Cancer* 2002; 86(2):179-84.
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14. Blaise D, Attal M, Pico JL et al. The use of a sequential high dose recombinant interleukin 2 regimen after autologous bone marrow transplantation does not improve the disease free survival of patients with acute leukemia transplanted in first complete remission. *Leuk Lymphoma* 1997; 25(5-6):469-78.
15. Nagler A, Ackerstein A, Or R et al. Immunotherapy with recombinant interleukin-2 and recombinant interferon-alpha in lymphoma patients postautologous bone marrow or stem cell transplantation. *Blood* 1997; 89(11):3951-9.
16. Cortes JE, Kantarjian HM, O'Brien S et al. A pilot study of interleukin-2 for adult patients with acute myelogenous leukemia in first complete remission. *Cancer* 1999; 85(7):1506-13.
17. De Stefani A, Forni G, Ragona R et al. Improved survival with perilymphatic interleukin 2 in patients with resectable squamous cell carcinoma of the oral cavity and oropharynx. *Cancer* 2002; 95(1):90-7.
18. www.cancer.gov/search/clinical_trial

This document is designed for informational purposes only and is not an authorization, or an explanation of benefits, or a contract. Receipt of benefits is subject to satisfaction of all terms and conditions of the coverage. Medical technology is constantly changing, and we reserve the right to review and update our policies periodically.

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Home Infusion Therapy Prior Authorization Form

Please complete and fax with the physician's prescription to: (888) 641-5355. If the patient is a BCBSMA employee, please fax the form to: (617)246-4013. If the patient is a Blue MedicareRx member, please fax the request to Anthem Blue Cross Blue Shield at (866) 827-9822.

FOR TPN THERAPY, USE MEDICAL POLICY #296 REQUEST FORM

Company name:		Contact Name:	
Phone #:		Provider #:	
Fax#		Address:	
Patient name:		Address:	
Patient ID#:		DOB: ___/___/___	Diagnosis:
Prescribing Physician/addr:	_____	Telephone:	
PCP name/address:	_____	Telephone:	

Place of Service Home SNF MD office other (specify)

Primary Therapy

Primary drug name: _____ Approximate duration: ___/___/___ to ___/___/___
 Dose: _____
 Frequency: _____ Route of Administration: _____ pump: Y___ N___

Other Therapy

Other drug name: _____ Approximate duration: ___/___/___ to ___/___/___
 Dose: _____
 Frequency: _____ Route of Administration: _____ pump: Y___ N___

If this is a "drug only" authorization request, indicate other services the nursing agency is providing:

Nursing provided by: _____ Contact: _____
 Phone: _____
 Fax: _____

Request for 7 Day Coverage: Date of occurrence: _____ Request dates: _____
 Occurrence type: Hospitalization Death Change of Therapy

Physician signature: _____
 Date: _____

OR Copy of prescription REQUIRED with this request.

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Request for Outpatient Retail Pharmacy Prior Authorization
Fax to: Clinical Pharmacy Program (800) 583-6289 or
for Medicare HMO and Medicare PPO Blue: (866)463-7700

We plan to respond to your request within two business days of our receipt. To ensure that we can confirm your request (required by NCQA), please be sure to include your fax number.

We cannot process requests unless they contain all of the information requested below:	
Patient Information (REQUIRED)	
Name	
BCBSMA ID number	
Is the patient a BCBSMA employee? If yes, please fax request to: (617) 246-4013	Yes No
Date of Birth	
Patient's Diagnosis or ICD-9-CM code	
Physician Information (REQUIRED)	
Name	
Medical Specialty	
BCBSMA Provider number	
Telephone Number	
Fax Number	
Contact Name (if different from physician)	
Please select one of the three following sections to complete, depending on the nature of your request for the above-named patient.	
Formulary Exception Request	
Name of non-covered drug you want to prescribe	
Reason for Individual Consideration Request (please check one): <input type="checkbox"/> Treatment failure with the following covered drugs in class <input type="checkbox"/> Documented adverse reaction to the following covered drugs <input type="checkbox"/> Other clinical reason (please specify) _____	
Quality Care Dosing Override Request	
Drug name, strength and quantity requested:	
Clinical reason for override (please specify)	
Outpatient Retail Pharmacy Prior Authorization Request	
Drug name:	
Start/End date (must be one year or less):	
Associated Co-morbid diagnosis:	
For Epogen®/Procrit® only:	GFR:
	Is patient certified ESRD with Medicare? Yes No
MD Signature:	Date: