

## Corporate Medical Policy

### Adoptive Immunotherapy

<b>File Name:</b>	adoptive_immunotherapy
<b>Origination:</b>	11/1993
<b>Last CAP Review:</b>	3/2012
<b>Next CAP Review:</b>	3/2013
<b>Last Review:</b>	3/2012

#### Description of Procedure or Service

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Adoptive immunotherapy is a method of activating lymphocytes for the treatment of cancer and other diseases. It involves the removal of lymphocytes from a patient with cancer, modification of the lymphocytes to increase their reactivity to the cancer, and transfer of the cells back into the patient to treat the cancer. Both non-specific and specific lymphocyte activation are used therapeutically. Non-specific, polyclonal proliferation of lymphocytes by cytokines (immune system growth factors), also called autolymphocyte therapy (ALT), increases the number of activated lymphocytes. Initially, this was done by harvesting peripheral lymphokine-activated killer (LAK) cells and activating them in vitro with the T-cell growth factor interleukin-2 (IL-2) and other cytokines. More recent techniques yield select populations of lymphocytes with specific reactivity to tumor antigens. Peripheral lymphocytes are propagated in vitro with antigen-presenting dendritic cells that have been pulsed with tumor antigens. Alternatively, tumor-infiltrating lymphocytes (TIL) from the tumor biopsy are propagated in vitro with IL-2 and anti-CD3 antibody, a T-cell activator. Expansion of TIL for clinical use is labor intensive and requires laboratory expertise. Only a few cancers are infiltrated by T cells in significant numbers; of these, TIL can be expanded in only approximately 50% of cases. These factors limit the widespread applicability of TIL treatment.

The spontaneous regression of certain cancers, such as renal cell cancer or melanoma, supports the idea that a patient's immune system can delay tumor progression and, on rare occasions, can eliminate the tumor altogether. These observations led to research interest in a variety of immunologic therapies designed to stimulate a patient's own immune system. The major research challenge in adoptive immunotherapy is to develop immune cells with anti-tumor reactivity in quantities sufficient for transfer to tumor-bearing patients. In current trials, two methods are studied: adoptive cellular therapy (ACT) and antigen-loaded dendritic cell infusions.

ACT is "the administration of a patient's own (autologous) or donor (allogeneic) anti-tumour lymphocytes following a lymphodepleting preparative regimen." Protocols vary, but include these common steps:

- 1) lymphocyte harvesting (either from peripheral blood or from tumor biopsy)
- 2) propagation of tumor-specific lymphocytes in vitro using various immune modulators
- 3) selection of lymphocytes with reactivity to tumor antigens with ELISA
- 4) lymphodepletion of the host with immunosuppressive agents
- 5) adoptive transfer (i.e., transfusion) of lymphocytes back into the tumor-bearing host

Dendritic cell-based immunotherapy uses autologous dendritic cells (ADC) to activate a lymphocyte-mediated cytotoxic response against specific antigens in vivo. ADCs harvested from the patient are either pulsed with antigen or transfected with a viral vector bearing a common cancer antigen. The activated ADCs are then transfused back into the patient, where they present antigen to effector lymphocytes

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(CD4+ T cells, CD8+ T cells, and in some cases, B cells). This initiates a cytotoxic response against the antigen and against any cell expressing the antigen. In cancer immunotherapy, ADCs are pulsed with tumor antigens; effector lymphocytes then mount a cytotoxic response against tumor cells expressing these antigens. [Note: See related policy: Cellular Immunotherapy for Prostate Cancer]

In an attempt to further regulate the host immune system, recent protocols utilize various cytokines (e.g., IL-7 and IL-15 instead of IL-2) to propagate lymphocytes. Protocols also differ in the extent of host lymphodepletion induced prior to transfusing the lymphocytes to the tumor-bearing host.

Note: Allogeneic stem-cell transplantation following nonmyeloablative conditioning of the recipient (known as reduced-intensity conditioning or RIC) may also be referred to as “adoptive immunotherapy” in the literature. However, RIC stem-cell transplantation relies on a donor-versus-malignancy effect of donor lymphocytes, while the adoptive immunotherapy techniques described in this policy enhance autoimmune effects primarily. The use of RIC in stem-cell transplantation is discussed for specific cancers in individual policies related to stem-cell transplantation.

## **Related Policies:**

Donor Leukocyte Infusion

Melanoma Vaccines

Cellular Immunotherapy for Prostate Cancer

***\*\*\*Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

## **Policy**

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**Adoptive Immunotherapy is considered investigational for all applications. BCBSNC does not cover investigational services or procedures.**

**Some patients may be eligible for coverage under Clinical Trials. Refer to the policy on Clinical Trial Services for Life-Threatening Conditions.**

## **Benefits Application**

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This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

## **When Adoptive Immunotherapy is covered**

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Not applicable..

## **When Adoptive Immunotherapy is not covered**

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1. Adoptive immunotherapy is considered investigational for all applications, including, but not limited to, use of adoptive cellular therapy (ACT) for the administration of lymphokine-activated killer cells (LAK), tumor-infiltrating lymphocytes (TIL), or antigen-loaded dendritic cells (ADC).

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## Policy Guidelines

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Clinical studies using adoptive immunotherapy are small, early-stage investigations of novel immunologic treatments for a variety of cancers. The impact on patient outcomes (e.g., increased survival, improved quality of life) has yet to be clarified in large, randomized, controlled clinical trials.

## Billing/Coding/Physician Documentation Information

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This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at [www.bcbsnc.com](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable Code: S2107, 36511, 37799, 96365*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

## Scientific Background and Reference Sources

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BCBSA Medical Policy Reference Manual - 12/95

BCBSA Medical Policy Reference Manual - 4/98

Medical Policy Advisory Group - 3/99

Specialty Matched Consultant Advisory Panel - 10/2000

Medical Policy Advisory Group - 10/2000

Specialty Matched Consultant Advisory Panel - 6/2002

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.01, 12/17/03.

ECRI. (1994) Interleukin-2 for the treatment of renal cell carcinoma. Executive Briefing. Retrieved on 4/ 7/2004 from [https://members.ecri.org/members/\\_elements/exec\\_brief/exec\\_docs/oexb36.asp](https://members.ecri.org/members/_elements/exec_brief/exec_docs/oexb36.asp).

ECRI. (1994) Interleukin-2 for the treatment of malignant melanoma. Executive Briefing. Retrieved on 4/ 7/2004 from [https://members.ecri.org/members/\\_elements/exec\\_brief/exec\\_docs/oexb35.asp](https://members.ecri.org/members/_elements/exec_brief/exec_docs/oexb35.asp).

Specialty Matched Consultant Advisory Panel - 5/2004

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.01, 3/15/05.

Specialty Matched Consultant Advisory Panel - 3/2006

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.01, 3/7/06.

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Specialty Matched Consultant Advisory Panel - 3/2008

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.01, 1/14/2010

Specialty Matched Consultant Advisory Panel -5/2010

Specialty Matched Consultant Advisory Panel -5/2011

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.01.01, 12/8/2011

Specialty Matched Consultant Advisory Panel – 3/2012

## Policy Implementation/Update Information

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- 11/93 Evaluated: Investigational in treatment of advanced renal cell carcinoma
- 7/96 Reaffirmed: National Association reviewed 12/95. No changes.
- 3/99 Revised: Added investigational indications. Reaffirmed by MPAG.
- 6/99 Reformatted, Description of Procedure or Service revised, Medical Term Definitions added.
- 7/00 System coding changes.
- 10/00 Specialty Matched Consultant Advisory Panel review. No change recommended in criteria. Medical Policy Advisory Group review. No change in criteria. Approve.
- 11/01 Coding format change.
- 6/02 Specialty Matched Consultant Advisory Panel. No changes. Approve.
- 1/03 Code S2107 added and code 36520 deleted from Billing/Coding section. System coding changes.
- 12/03 Benefits Application and Billing/Coding Sections updated for consistency.
- 6/10/04 Specialty Matched Consultant Advisory Panel review. No change to criteria. References added. Notification given 6/10/2004. Effective date 8/12/2004.
- 4/10/06 Specialty Matched Consultant Advisory Panel review 3/15/2006. No change to policy. Added information pertaining to dendritic cells to "Description of Procedure or Service" section. Added reference to dendritic cells under #1 in the "When not covered" section. Rationale added to "Policy Guidelines" section. References added.
- 6/2/08 Specialty Matched Consultant Advisory Panel review 3/17/2008. No change to policy statement. Added reference to Clinical Trials policy in "Policy" section. References added. (btw)
- 8/3/10 Specialty Matched Consultant Advisory Panel review 5/24/2010. "Description" section revised. No change to policy statement. The "When Not Covered" section revised no change to policy intent. Added CPT codes 36511, 37799, and 96365 to the "Billing/Coding" section. References added. (btw)
- 5/24/11 Specialty Matched Consultant Advisory Panel review 4/27/11. No changes to policy statement. (btw)

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4/17/12 Specialty Matched Consultant Advisory Panel review 3/21/2012. Description section revised.  
Updated Policy Guidelines section. No change to policy intent. Reference added. (btw)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.