

MEDICAL POLICY – 8.01.01

Adoptive Immunotherapy

BCBSA Ref. Policy: 8.01.01


Effective Date: Jan. 1, 2024
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Replaces: N/A

RELATED MEDICAL POLICIES:

8.01.53	Cellular Immunotherapy for Prostate Cancer
8.01.63	Chimeric Antigen Receptor Therapy for Hematologic Malignancies
8.01.520	Hematopoietic Cell Transplantation for Acute Lymphoblastic Leukemia

Select a hyperlink below to be directed to that section.

[POLICY CRITERIA](#) | [CODING](#) | [RELATED INFORMATION](#)
[EVIDENCE REVIEW](#) | [REFERENCES](#) | [HISTORY](#)

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Introduction

The immune system is made up of several different disease-fighting cells. When someone has cancer, their immune system sometimes doesn't work as it should. Adoptive immunotherapy is a treatment that uses the person's own immune cells in order to destroy cancer. Specific types of immune system cells are withdrawn from the person to be treated. They're modified in a lab and then given back to the individual. Adoptive immunotherapy is being studied. The US Food and Drug Administration (FDA) has approved two adoptive immunotherapy treatments. Any other application of adoptive immunotherapy is considered investigational (unproven).

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Treatment	Investigational
Other applications	All adoptive immunotherapy techniques intended to enhance autoimmune effects are considered investigational for the indications included, but not limited to, cancers associated with Epstein-Barr virus, <i>Cytomegalovirus</i> -associated cancers, nasopharyngeal cancer, renal cell carcinoma, gastric cancer, colorectal cancer, hepatocellular carcinoma, non-small-cell lung cancer, melanoma, glioblastoma multiforme, medullary thyroid cancer, pancreatic cancer, and cancers treated with autologous peripheral T lymphocytes containing tumor antigen-specific T cell receptors.

Coding

Code	Description
CPT	
36511	Therapeutic apheresis; for white blood cells
HCPCS	
S2107	Adoptive immunotherapy i.e., development of specific antitumor reactivity (e.g., tumor-infiltrating lymphocyte therapy) per course of treatment

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Related Information

N/A

Evidence Review



Description

The spontaneous regression of certain cancers (e.g., renal cell carcinoma, melanoma) supports the idea that an individual's immune system can delay tumor progression and, on rare occasions, can eliminate tumors altogether. These observations have led to research into various immunologic therapies designed to stimulate an individual's own immune system. Adoptive immunotherapy is a method of activating lymphocytes and/or other types of cells for the treatment of cancer and other diseases. Cells are removed from the individual, processed for some period of time, and then infused back into the individual.

Background

Health Disparities in Certain Cancers

Hepatic tumors can arise as primary liver cancer (hepatocellular cancer) or by metastasis to the liver from other tissues. A study from 2016 determined that the incidence of liver cancer was higher among White individuals, Black individuals, and Hispanic individuals born after 1938.¹ The incidence of hepatocellular carcinoma was twice as high for US-born Hispanic men compared to Hispanic men born outside of the US. This may be due to the increased risk of smoking, hepatitis B or C infection, and diabetes among US-born Hispanic individuals.

Based on data from 2015 through 2019, kidney cancer is more common in men than women and occurs more often in American Indian and Alaskan Native individuals, followed by Black individuals.² American Indians and Alaska Natives have higher death rates from kidney cancer than any other racial or ethnic group. A cohort study by Howard et al (2021) included 158,445 individuals with localized kidney cancer from the National Cancer Database between 2010 and 2017.³ Investigators found that that female individuals were treated more aggressively compared with male individuals, with lower adjusted odds of undertreatment and higher adjusted odds of overtreatment. They also found that Black and Hispanic individuals had higher adjusted odds of undertreatment, and overtreatment compared to White individuals, and uninsured status was associated with lower adjusted odds of overtreatment and higher adjusted odds of undertreatment. These results suggest that sex, race and ethnicity, and socioeconomic status are associated with disparities in guideline-based treatment for localized kidney cancer, specifically, with increased rates of non-guideline based treatment for women and Black and Hispanic individuals.



Adoptive Immunotherapy

Adoptive immunotherapy uses “activated” lymphocytes as a treatment modality. Both nonspecific and specific lymphocyte activation are used therapeutically. The nonspecific, polyclonal proliferation of lymphocytes by cytokines (immune system growth factors), also called autolympocyte therapy, increases the number of activated lymphocytes.

T Lymphocytes and Killer Cells

Initially, this treatment was performed by harvesting peripheral lymphokine-activated killer cells and activating them in vitro with the T-cell growth factor interleukin-2 (IL-2) and other cytokines. More recent techniques have yielded select populations of cytotoxic T lymphocytes with specific reactivity to tumor antigens. Peripheral lymphocytes are propagated in vitro with antigen-presenting dendritic cells (DC) that have been pulsed with tumor antigens. Alternatively, innate tumor-infiltrating lymphocytes (TIL) from the tumor biopsy are propagated in vitro with interleukin-2 and anti-CD3 antibody, a T-cell activator. The 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. Recently, cytokine-induced killer cells have been recognized as a new type of anti-tumor effector cells, which can proliferate rapidly in vitro, with stronger anti-tumor activity and a broader spectrum of targeted tumors than other reported anti-tumor effector cells.⁴

Cellular Therapy and Dendritic Cell Infusions

The major research challenge in adoptive immunotherapy is to develop immune cells with anti-tumor reactivity in quantities sufficient for transfer to tumor-bearing individuals. In current trials, two methods are studied: adoptive cellular therapy and antigen-loaded dendritic cell infusions.

Adoptive cellular therapy is “the administration of an individual’s own (autologous) or donor (allogeneic) anti-tumor lymphocytes following a lymphodepleting preparative regimen.”⁵ 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 enzyme-linked immunosorbent assay
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 DC (ADC) to activate a lymphocyte-mediated cytotoxic response against specific antigens in vivo. ADCs harvested from the individual are either pulsed with antigen or transfected with a viral vector bearing a common cancer antigen. The activated ADCs are then re-transfused back into the individual, where they present antigen to effector lymphocytes (CD4-positive T cells, CD8-positive 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 (see [Related Policies](#) for dendritic cell-based immunotherapy for prostate cancer).

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

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

Chimeric antigen receptor T-cell therapies for certain hematologic malignancies (e.g., tisagenlecleucel, axicabtagene ciloleucel) are discussed in a separate policy (see [Related Policies](#) above).

Summary of Evidence

Cytotoxic T Lymphocytes

For individuals with Epstein-Barr virus (EBV)-associated cancers who receive cytotoxic T lymphocytes (CTL), the evidence includes two small, prospective noncomparative cohort studies. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. The cohort studies have shown a treatment response



to infused cytotoxic T lymphocytes directed against cancer-associated viral antigens. To establish efficacy, the following are needed: large, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with Cytomegalovirus-associated cancers who receive CTL, the evidence includes a single case series. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. In the absence of an RCT comparing CTL with the standard of care, no conclusions can be made. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Cytotoxic-Induced Killer Cells

For individuals with nasopharyngeal carcinoma who receive CIK cells, the evidence includes a single RCT. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. The RCT reported a numerically favorable but statistically insignificant effect on progression-free survival (PFS) and overall survival. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with renal cell carcinoma (RCC) who receive CIK cells, the evidence includes multiple RCTs. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. The largest of the RCTs reported statistically significant gains in progression-free survival and overall survival with CIK cell-based immunotherapy compared with interleukin (IL)-2 plus interferon- α -2. This body of evidence is limited by the context of the studies (non-U.S.) and choice of a nonstandard comparator. The other two RCTs have also reported response rates in favor of CIK therapy with inconsistent effect on survival. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The



evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with gastric cancer who receive CIK cells, the evidence includes 2 meta-analyses encompassing non-randomized trials. Relevant outcomes are OS, DSS, QOL, and treatment-related mortality and morbidity. Both meta-analyses reported statistically significant effects on OS, disease-free survival (DFS), and PFS in favor of immunotherapy versus no immunotherapy. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with colorectal cancer who receive CIK cells, the evidence includes a single RCT and one cohort study. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Results of the RCT showed a statistically significant effect on overall survival in favor of immunotherapy vs chemotherapy alone. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with hepatocellular carcinoma who receive CIK cells, the evidence includes several RCTs. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Several RCTs from Asia have generally reported some benefits in response rates and/or survival. The results of a meta-analysis of these trials have also shown a statistically significant 41% reduction in the hazard of death, but there was considerable heterogeneity across the included studies. This body of evidence is limited by the context of the studies (non-U.S.), small sample sizes, heterogeneous treatment groups, and other methodologic weaknesses. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with non-small-cell lung cancer (NSCLC) who receive CIK cells, the evidence includes multiple RCTs and a systematic review. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. A single systematic review of RCTs reported some benefits in median time to progression and median



survival time. The trials assessed in the systematic review were limited by the context of the studies (non-U.S.), small sample sizes, heterogeneous treatment groups, and other methodologic weaknesses. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Tumor-Infiltrating Lymphocytes

For individuals with melanoma who receive tumor infiltrating lymphocytes (TILs) , the evidence includes a meta-analysis of randomized trials. Relevant outcomes are OS, DSS, QOL, and treatment-related mortality and morbidity. The meta-analysis evaluating TIL with IL-2 in patients with cutaneous melanoma reported an objective response rate of 41%. Pooled 1-year OS rates ranged from 46.1% to 56.5% depending on the IL-2 dose level. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with EBV-associated nasopharyngeal carcinoma who receive TILs, the evidence includes an RCT evaluating TILs as adjuvant therapy. Relevant outcomes are OS, DSS, QOL, and treatment-related mortality and morbidity. The RCT evaluating TILs as adjuvant therapy following standard chemoradiation in individuals with EBV-associated nasopharyngeal carcinoma found no difference in PFS or other clinical outcomes compared to patients who received standard chemoradiation alone. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Dendritic Cells

For individuals with glioblastoma multiforme who receive dendritic cells (DC), the evidence includes a systematic review of observational studies. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Because of the observational and noncomparative nature of the available evidence, it is difficult to draw any meaningful conclusions. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. Interim results from one such RCT have been published but are not



informative because the individuals were unblinded and results combined for the treatment and placebo arms. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with non-small-cell lung cancer who receive dendritic cells, the evidence includes two RCTs and a meta-analysis. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. The RCTs have generally reported some benefits in response rates and/or survival. The meta-analysis of these trials also reported a statistically significant reduction in the hazard of death. Most trials were from Asia and did not use standard of care as the control arm. This body of evidence is limited by the context of the studies (non-U.S.), small sample sizes, heterogeneous treatment groups, and other methodologic weaknesses. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with medullary thyroid cancer who receive dendritic cells, the evidence includes one prospective noncomparative study. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. A small prospective noncomparative study in ten medullary thyroid cancer individuals treated with autologous dendritic cells has been published. There are no RCTs comparing dendritic cell-based adoptive immunotherapy with standard of care and, therefore, no conclusions can be made. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with pancreatic cancer who receive dendritic cells, the evidence includes a small prospective noncomparative study. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. The study reported on treatment outcomes for five individuals with pancreatic cancer. Because of the noncomparative nature of the available evidence and small sample base, it is difficult to draw any meaningful conclusions. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.



Genetically Engineered T Cells

Peripheral T Lymphocytes

For individuals with cancers who receive autologous peripheral T lymphocytes containing tumor antigen-specific T-cell receptors, the evidence includes multiple small observational studies. The relevant outcomes are overall survival, disease-specific survival, quality of life, and treatment-related mortality and morbidity. Multiple observational studies have examined autologous peripheral T lymphocytes containing tumor antigen-specific T-cell receptors in melanoma, Hodgkin and non-Hodgkin lymphoma, prostate tumors, and neuroblastoma. Because of the noncomparative nature of the available evidence and a small sample size, it is difficult to draw any meaningful conclusion. To establish efficacy, the following are needed: larger, well-conducted, multicentric trials with adequate randomization procedures, blinded assessments, centralized oversight, and the use of an appropriate standard of care as the control arm showing treatment benefit. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this review are listed in [Table 1](#).

Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Tumor-infiltrating lymphocytes			
NCT01174121	A Phase II Study Using Short-Term Cultured, Autologous Tumor-Infiltrating Lymphocytes Following a Lymphodepleting Regimen in Metastatic Cancers Plus the Administration of Pembrolizumab	332	Dec 2024
NCT01319565	A Prospective Randomized Study of Cell Transfer Therapy for Metastatic Melanoma Using Short-Term Cultured Tumor Infiltrating Lymphocytes Plus IL-2 Following Either a Non-	102	Jun 2025



NCT No.	Trial Name	Planned Enrollment	Completion Date
	Myeloablative Lymphocyte Depleting Chemotherapy Regimen Alone or in Conjunction With 12Gy Total Body Irradiation (TBI)		
NCT02278887	Randomized Phase III Study Comparing a Non-myeloablative Lymphocyte Depleting Regimen of Chemotherapy Followed by Infusion of Tumor Infiltrating Lymphocytes and Interleukin-2 to Standard Ipilimumab Treatment in Metastatic Melanoma	168	Sep 2023
NCT05727904 ^a	A Phase 3, Multicenter, Randomized, Open-label, Parallel Group, Treatment Study to Assess the Efficacy and Safety of the Lifileucel (LN-44, Autologous Tumor Infiltrating Lymphocytes [TIL]) Regimen in Combination With Pembrolizumab Compared With Pembrolizumab Monotherapy in Participants with Untreated, Unresectable or Metastatic Melanoma	670	Mar 2030
Autologous dendritic cells			
NCT00338377 ^a	Lymphodepletion Plus Adoptive Cell Transfer With or Without Dendritic Cell Immunization in Patients With Metastatic Melanoma	1230	Feb 2030
NCT01204684	A Phase II Clinical Trial Evaluating Autologous Dendritic Cells Pulsed With Tumor Lysate Antigen +/- Toll-like Receptor Agonists for the Treatment of Malignant Glioma	60	Jan 2025
Dendritic cells/cytokine-induced killer cells			
NCT02487992	The Randomized, Controlled, Multicenter Clinical Trial of CIK Plus S-1 and Bevacizumab as Maintenance Treatment for Patients With Advanced Colorectal Cancer	1200	Jul 2045

NCT: national clinical trial.

^a Denotes industry-sponsored or cosponsored trial.

Practice Guidelines and Position Statements

Current guidelines from the National Comprehensive Cancer Network do not include recommendations for adoptive immunotherapy to treat cancers of the bladder,⁴⁴ central nervous system,⁴⁴ head and neck,⁴⁴ hepatobiliary system,⁴⁴ kidney,⁴⁴ pancreatic,⁴⁵ stomach,⁴⁶ thyroid,⁴⁷ melanoma,⁴⁸ or non-small-cell lung cancer.⁴⁹



Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

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History

Date	Comments
01/97	Add to Therapy Section - New Policy
05/19/98	Replace policy. Policy updated; new indications
12/10/02	Replace policy. Policy updated; new references added. No change in policy statement.
04/15/03	Replace policy. Policy reviewed with CPT codes added. No change in policy statement.
01/01/04	Replace policy. CPT code updates only.
05/11/04	Replace policy. Policy updated; no change in policy statement. Additional discussion of dendritic cell therapy.
06/14/05	Replace policy. Policy updated with literature search; no change in policy statement.
02/06/06	Codes Updated. No other changes.
06/16/06	Replace policy. Policy updated with literature search; no change in policy statement; Scope and Disclaimer updated.
06/12/07	Replace policy. Policy updated; no change in policy statement. Reviewed and recommended by OAP on May 24, 2007.
01/13/09	Replace policy. Policy updated with literature search. Policy statement updated to include "adoptive cellular therapy (ACT) for the administration of lymphokine-activated killer cells (LAK) tumor-infiltrating lymphocytes (TIL), or antigen-loaded dendritic cells (ADCs)" as an investigational indication. Investigational statement deleted. References added. Reviewed and recommended by OAP on August 21, 2008.
12/08/09	Cross Reference Update - No other changes.
05/11/10	Cross Reference Update - No other changes.
06/13/11	Replace policy. Policy updated with literature search; reference numbers 33–48 added; no change in policy statements. ICD-10 codes added to policy.
02/14/12	Replace policy. Policy updated with literature search; references 23 and 24 added and other references renumbered or removed. No change in policy statements.
08/15/12	Update Related Policies: remove 2.03.04, as it was archived.



Date	Comments
09/28/12	Update Coding Section – ICD-10 codes are now effective 10/01/2014.
02/13/13	Replace policy. Policy updated with literature search; Two systematic reviews added; Primary studies added on cytokine-induced killer (CIK) cells; references 1, 3-6, 24, and 27 added and other references renumbered. The wording of the policy statement under adoptive cellular therapy was changed to include cytokine-induced killer (CIK) cells; however, the intent of both policy statements (i.e., investigational) is unchanged. Remove Related Policy 2.03.500 as it was archived.
07/25/13	Update Related Policies. Add 8.01.520.
02/24/14	Replace policy. Policy updated with literature search through November 8, 2013; references 3, 8, 27, and 31 added. No change in policy statements.
02/25/15	Annual Review. Policy updated with literature review through November 2, 2014; references 6-9, 12, 14-17, 41, 46, 52-53, and 56-65 added; reference 55 updated. Rationale reorganized and references renumbered. Cytotoxic T-lymphocytes and genetically engineered T cells added to investigational policy statements; “autologous” added to clarify antigen-loaded dendritic cells. ICD-9 and ICD-10 codes removed; these are not utilized in policy adjudication.
02/09/16	Annual Review. Policy updated with literature review through November 10, 2015; references 13 and 17-18 added. Section on lymphokine-activated killer cell deleted as this is an obsolete intervention. Policy statements unchanged.
01/01/18	Annual Review, approved December 12, 2017. Policy updated with literature review through April 2017. Policy statement changed for clarity as Kymriah™ (tisagenlecleucel) and Yescarta™ (axicabtagene ciloleucel) are addressed in policy 5.01.580. Removed codes 96365, 96367, 96368, and S2107.
11/01/18	Annual Review, approved October 19, 2018. Policy criteria for Chimeric Antigen Receptor (CAR) T Cell Therapies is now addressed in this policy; added codes J3590, Q2040, Q2041, S2107. Removed CPT code 37799. Policy 5.01.580 is now deleted. Policy updated with literature review through June 2018; several references added.
11/17/18	Minor update, added Documentation Requirements section.
01/01/19	Coding update, added 0537T, 0538T, 0539T, 0540T, and Q2042 (new codes effective 1/1/19).
04/01/19	Annual Review, approved March 19, 2019. Policy updated with literature review through October 2018; reference 31 added. Policy statements unchanged.
01/01/20	Coding update, removed HCPCS code Q2040 as it terminated 1/1/19.
07/01/20	Annual Review, approved June 9, 2020. Statements regarding use of tisagenlecleucel and axicabtagene ciloleucel were removed and added to new policy 8.01.63 Chimeric Antigen Receptor Therapy for Hematologic Malignancies, references updated. Policy Coverage section revised to ‘Other applications of adoptive immunotherapy not addressed in Related Policy 8.01.63 Chimeric Antigen Receptor Therapy for



Date	Comments
	Hematologic Malignancies are considered investigational'. Removed codes 0537T, 0538T, 0539T, 0540T, Q2041 and Q2042.
12/01/20	Interim Review, approved November 19, 2020. No changes to Coverage Criteria. Updated Evidence Review and References.
12/01/21	Annual Review, approved November 18, 2021. Policy updated with literature review through August 24, 2021; references updated. Policy section revised to "All adoptive immunotherapy techniques intended to enhance autoimmune effects are considered investigational for the indications included, but not limited to" as referenced in this policy.
01/01/23	Annual Review, approved December 23, 2022. Policy updated with literature review through August 24, 2022; references added. Policy statements unchanged. Changed the wording from "patient" to "individual" throughout the policy for standardization.
01/01/24	Annual Review, approved December 11, 2023. Policy updated with literature review through August 11, 2023; references added. Indication added (TIL in EBV-associated nasopharyngeal carcinoma). Policy statements unchanged.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2024 Premera All Rights Reserved.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.



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Washington residents: You can also file a civil rights complaint with the Washington State Office of the Insurance Commissioner, electronically through the Office of the Insurance Commissioner Complaint Portal available at <https://www.insurance.wa.gov/file-complaint-or-check-your-complaint-status>, or by phone at 800-562-6900, 360-586-0241 (TDD). Complaint forms are available at <https://fortress.wa.gov/oic/online-services/cc/pub/complaintinformation.aspx>.

Alaska residents: Contact the Alaska Division of Insurance via email at insurance@alaska.gov, or by phone at 907-269-7900 or 1-800-INSURAK (in-state, outside Anchorage).

Language Assistance

ATENCIÓN: si habla español, tiene a su disposición servicios gratuitos de asistencia lingüística. Llame al 800-722-1471 (TTY: 711).

PAUNAWA: Kung nagsasalita ka ng Tagalog, maaari kang gumamit ng mga serbisyo ng tulong sa wika nang walang bayad. Tumawag sa 800-722-1471 (TTY: 711).

注意: 如果您使用繁體中文，您可以免費獲得語言援助服務。請致電 800-722-1471 (TTY: 711)。

CHÚ Ý: Nếu bạn nói Tiếng Việt, có các dịch vụ hỗ trợ ngôn ngữ miễn phí dành cho bạn. Gọi số 800-722-1471 (TTY: 711).

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ВНИМАНИЕ: Если вы говорите на русском языке, то вам доступны бесплатные услуги перевода. Звоните 800-722-1471 (телетайп: 711).

LUS CEEV: Yog tias koj hais lus Hmoob, cov kev pab txog lus, muaj kev pab dawb rau koj. Hu rau 800-722-1471 (TTY: 711).

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УВАГА! Якщо ви розмовляєте українською мовою, ви можете звернутися до безкоштовної служби мовної підтримки. Телефонуйте за номером 800-722-1471 (телетайп: 711).

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