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MEDICAL POLICY – 8.01.36

Extracorporeal Photopheresis

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Effective Date:	Jan. 1, 2021	RELATED MEDICAL POLICIES:
Last Revised:	Dec. 1, 2020	5.01.532 Cutaneous T-Cell Lymphomas (CTCL): Systemic Therapies
Replaces:	8.01.501	

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

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Introduction

Extracorporeal photopheresis is a treatment of white blood cells. Blood is withdrawn and a specialized machine separates the whole blood into its different components — red blood cells, white blood, cells, platelets, and plasma. White blood cells are kept back and the rest of the blood is returned to the patient. The white blood cells are mixed with medication that makes them sensitive to ultraviolet light. After being exposed to ultraviolet light, the white blood cells are returned to the patient. White blood cells are part of the immune system, and treating them in this way stimulates the immune system. High quality medical studies have shown this technique is successful in treating a number of conditions. These include organ rejection after a heart transplant, graft-versus-host disease, and cutaneous T-cell lymphoma in certain situations. It has also been proposed to treat a number of autoimmune conditions, like Crohn disease or multiple sclerosis. Because more medical studies are needed to show if it works for other conditions, using this technique for autoimmune conditions is 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

Indication	Medical Necessity
Organ rejection after solid organ transplant	**Extracorporeal photopheresis may be considered medically necessary to treat cardiac allograft rejection, including acute rejection, that is either recurrent or that is refractory to standard immunosuppressive drug treatment.** **Extracorporeal photopheresis is considered investigational in all other situations related to treatment or prevention of rejection in solid organ transplantation.**
Graft-versus-host disease	**Extracorporeal photopheresis may be considered medically necessary as a technique to treat:** • Acute graft-versus-host disease (GVHD) that is refractory to medical therapy • Chronic GVHD that is refractory to medical therapy **Extracorporeal photopheresis is considered investigational as a technique to treat acute GVHD or chronic GVHD that is either previously untreated or is responding to established therapies.**
Cutaneous T-cell lymphoma	**Extracorporeal photopheresis may be considered medically necessary as a technique to treat:** • Late stage (III/IV) cutaneous T-cell lymphoma • Early stage (I/II) cutaneous T-cell lymphoma that is progressive and refractory to established nonsystemic therapies **Extracorporeal photopheresis is considered investigational as a technique to treat early stage (I/II) cutaneous T-cell lymphoma that is either previously untreated or responsive to established nonsystemic therapies.**

Indication	Investigational
Autoimmune diseases	**Extracorporeal photopheresis is considered investigational as a technique to treat either the cutaneous or visceral manifestations of autoimmune diseases, including but not limited to:** • Autoimmune bullous disorders • Crohn's disease • Diabetes • Multiple sclerosis • Pemphigus • Psoriasis • Rheumatoid arthritis • Scleroderma • Severe atopic dermatitis • Systemic lupus erythematosus
Other	**Extracorporeal photopheresis is considered investigational for all other indications.**

Documentation Requirements
The patient's medical records submitted for review should document that medical necessity criteria are met. The record should include clinical documentation of: • Diagnosis/condition • History and physical examination documenting the severity of the condition • The medical therapy that has been attempted

Coding

Code	Description
Reviewed for Medical Necessity	
CPT	
36522	Photopheresis, extracorporeal

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Organ Rejection After Solid Organ Transplant

A regimen of immunosuppressive therapy is standard of care for the treatment of solid organ rejection. Therefore, refractory rejection is defined as rejection that fails to respond adequately to a standard regimen of immunosuppressive therapy.

Recurrent allograft rejection is defined as having at least two rejection episodes after standard immunosuppressive therapy.

There is no standard schedule for extracorporeal photopheresis (ECP) and reported schedules vary by the organ type. However, most reported cardiac and lung schedules initiate therapy with two consecutive days of ECP in month 1, followed by biweekly therapy on two consecutive days in months 2 and 3, then monthly on two consecutive days in months 4 through 6.

Graft-Versus-Host Disease

Methylprednisolone is considered first-line treatment of acute graft-versus host disease (GVHD). For chronic GVHD, an alternating regimen of cyclosporine and prednisone is commonly used; other therapies include antithymocyte globulin, corticosteroid monotherapy, and cytotoxic immunosuppressive drugs such as procarbazine, cyclophosphamide, or azathioprine. Therefore, refractory disease is defined as GVHD that fails to respond adequately to a trial of any of these therapies.

Treatment schedule and duration of ECP for GVHD have not been optimally defined. Guidelines and consensus statements have generally recommended 1 cycle (ie, ECP on two consecutive days) weekly for acute GVHD and every 2 weeks for chronic GVHD. Treatment duration is based on clinical response (see **Practice Guidelines and Position Statements** section); discontinuation is generally recommended for no or minimal response.

Cutaneous T-Cell Lymphoma Staging

Cutaneous T-cell lymphoma staging is based on the tumor, node, metastases (TNM) classification system (see **Table 1**).

Table 1. Cutaneous T-Cell Lymphoma Staging

Stage	Tumor T, N, and M Categories
IA	T1N0M0
IB	T2N0M0
IIA	T1-2N1M1
IIB	T3N0-1M0
III	T4N0-1M0
IVA	T1-4N2-3M0
IVB	T1-4N0-3M1

Sézary Syndrome

According to the World Health Organization–European Organization for Research and Treatment of Cancer, Sézary syndrome is defined by the triad of erythroderma, generalized lymphadenopathy, and the presence of neoplastic T cells (Sézary cells) in the skin, lymph nodes, and peripheral blood. The International Society of Cutaneous Lymphomas recommends an absolute Sézary cell count of at least 1000 cells per cubic millimeter, in the presence of immunophenotypical abnormalities (CD4/CD8 ratio >10; loss of any or all of the T-cell antigens CD2, CD3, CD4, and CD5; or both), or the demonstration of a T-cell clone in the peripheral blood by molecular or cytogenetic methods.

Benefit Application

Refer to contract or benefit language for specific language regarding extracorporeal photopheresis and chronic graft versus host disease.

Evidence Review

Description

Extracorporeal photopheresis (ECP) is a leukapheresis-based immunomodulatory procedure that involves the following three steps:

- Patient blood is collected into a centrifuge system that separates the leukocyte-rich portion (buffy coat) from the rest of the blood.
- The photosensitizer agent 8-methoxypsoralen is added to the lymphocyte fraction, which is then exposed to ultraviolet A (320-400 nm wavelength) light at a dose of 1-2 J/cm^2.
- The light-sensitized lymphocytes are reinfused into the patient.

The use of ECP has been investigated for patients needing treatment for organ rejection after solid organ transplant, graft-versus-host disease (GVHD), autoimmune diseases, and T-cell lymphoma.

Background

Organ Rejection Treatment After Solid Organ Transplant

The standard treatment for organ transplant rejection is immunosuppression, with the particular regimen dictated by the organ being transplanted. As organ transplantation success rates have improved, more patients are facing the morbidity and mortality associated with immunosuppressive therapies developed to prevent rejection of the transplanted organ. Immunosuppressive therapies are used to lower the responsiveness of the recipient's immune system, decreasing the chance of rejection. Unfortunately, portions of the immune system responsible for the prevention of viral, fungal, and bacterial infection also are affected. This can, in turn, lead to serious infections, including opportunistic infections.

Although first approved for the treatment of cutaneous T-cell lymphoma (CTCL), extracorporeal photopheresis (ECP) has more recently been used as a supplement to conventional therapies in the area of solid organ transplantation.[1] Reports of the successful use of ECP in human cardiac transplant recipients were published in 1992[2,3] and use in other transplant patients followed. Although the specific mechanism of action of ECP is unknown, the reinfusion of treated leukocytes seems specifically to suppress the patient's immune response to the donor organ, although maintaining the body's ability to respond to other antigens.[4] The specificity of ECP to target the immune response to the transplanted organ allows ECP to decrease organ rejection without the increased risk of infection, common with immunosuppressive drugs.[5]

Graft-Versus-Host Disease

Given that graft-versus-host disease (GVHD) is an immune mediated disease, ECP can be used to treat GVHD after a prior allogeneic cell transplant. In fact, GVHD can be categorized in two ways: (1) as an acute disease, occurring within the first 100 days after infusion of allogeneic cells; or (2) as a chronic disease, which develops sometime after 100 days. Acute GVHD is commonly graded from I to IV, ranging from mild disease, which is characterized by a skin rash without involvement of the liver or gut, to grades III and IV, which are characterized by generalized erythroderma, elevated bilirubin levels, or diarrhea. Grade III acute GVHD is considered severe, and grade IV is considered life-threatening. Chronic GVHD typically presents with more diverse symptomatology resembling autoimmune diseases such as progressive systemic sclerosis, systemic lupus erythematosus, or rheumatoid arthritis. Chronic GVHD may affect the mouth, eyes, respiratory tract, musculoskeletal system, and peripheral nerves, as well as the skin, liver, or gut — the usual sites of acute GVHD.

Autoimmune Disease

The use of ECP as a treatment of autoimmune disease is based on the premise that pathogenic lymphocytes form an expanded clone of cells, which are damaged when exposed to ultraviolet light in the presence of agent 8-methoxypsoralen. It is hypothesized that the resulting damage induces a population of circulating suppressor T-cells targeted against the light-damaged cells. It is further hypothesized that these suppressor T-cells are targeted at a component of the cell that is common to the entire clone of abnormal cells (ie, not just the light-sensitized cells), thus inducing a systemic effect. However, although scleroderma and other autoimmune diseases are associated with the presence of circulating autoantibodies, it is unknown how these antibodies are related to the pathogenesis of the disease. As discussed in this policy, photopheresis is not associated with consistent changes in autoantibody levels.

T-Cell Lymphoma

Cutaneous T-Cell Lymphoma

According to the National Cancer Institute, CTCL is a neoplasia of malignant T lymphocytes that initially presents as skin involvement. CTCL is extremely rare, with an estimated incidence of approximately 0.4 per 100,000 annually, but because most are low-grade malignancies with long

survival, overall prevalence is much higher. Two CTCL variants, mycosis fungoides and the Sézary syndrome, account for approximately 60% and 5% of new cases of CTCL, respectively.

CTCL is included in the Revised European-American Lymphoma classification as a group of low-grade T-cell lymphomas, which should be distinguished from other T-cell lymphomas that involve the skin, such as anaplastic large cell lymphoma, peripheral T-cell lymphoma, adult T-cell leukemia/lymphoma (usually with systemic involvement), and subcutaneous panniculitis T-cell lymphoma. In addition, a number of benign or very indolent conditions can be confused with mycosis fungoides, further complicating diagnosis.

Mycosis fungoides typically progresses from an eczematous patch/plaque stage, covering less than 10% of the body surface (T1), to a plaque stage, covering 10% or more of the body surface (T2), and finally to tumors (T3) that frequently undergo necrotic ulceration. Sézary syndrome is an advanced form of mycosis fungoides with generalized erythroderma (T4) and peripheral blood involvement (B1) at presentation. The cytologic transformation from a low-grade lymphoma to a high-grade lymphoma sometimes occurs during the course of these diseases and is associated with poor prognosis. A common cause of death during the tumor phase is sepsis from Pseudomonas aeruginosa or Staphylococcus aureus caused by chronic skin infection with staphylococcus species and subsequent systemic infections.

The natural history of mycosis fungoides is typically indolent. Symptoms may present for long periods (mean, 2-10 years) as waxing and waning cutaneous eruptions. The prognosis of patients with mycosis fungoides or Sézary syndrome is based on the extent of disease at presentation and its stage. Lymphadenopathy and involvement of peripheral blood and viscera increase in likelihood with worsening cutaneous involvement and define poor prognostic groups. Median survival after diagnosis varies according by stage. Median survival in patients with stage IA disease exceeds 20 years, with most deaths in this group typically unrelated to mycosis fungoides. In contrast, median survival in patients with stage III or IV disease is less than 5 years; more than 50% of these patients die of their disease.

Appropriate therapy of CTCL depends on a variety of factors, including stage, the patient's overall health, and the presence of symptoms. In general, therapies can be categorized into topical and systemic treatments that include ECP. In contrast to more conventional lymphomas, CTCL is usually not curable (unless caught in its earliest stages). Thus, systemic cytotoxic chemotherapy is avoided except for advanced stage cases. Partial or complete remission is achievable, although most patients require lifelong treatment and monitoring.

Summary of Evidence

Graft Rejection After Solid Organ Transplant

Heart Transplant

For individuals who are heart transplant recipients who experience acute graft rejection refractory to immunosuppression who receive ECP, the evidence includes a small RCT. The relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. The small RCT, while suggesting similar outcomes for ECP and corticosteroids, is insufficient to permit conclusions on the utility of ECP. Studies with more patients and longer follow-up are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are heart transplant recipients who experience recurrent and/or refractory graft rejection who receive ECP, the evidence includes a comparative study and small case series. The relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. Current evidence is consistent on the beneficial effect of ECP for cardiac transplant patients with graft rejection refractory to standard therapy. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who are heart transplant recipients who require prophylaxis to prevent graft rejection who receive ECP, the evidence includes a small RCT. The relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. The small randomized trial is insufficient to permit conclusions on the utility of ECP. Studies with more patients and longer follow-up are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

Lung Transplant

For individuals who are lung transplant recipients who experience acute graft rejection who receive ECP, the evidence includes a small retrospective study and small case series. The relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. Current evidence is very limited and any conclusions drawn lack certainty. A prospective, randomized trial is needed specifically evaluating the treatment of patients with acute graft rejection. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who are lung transplant recipients with BOS refractory to corticosteroids who receive ECP, the evidence includes a prospective study and numerous retrospective analyses. The relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. Studies have shown inconsistent results across BOS grades. Prospective, RCTs are necessary with analyses stratified by syndrome grade. The evidence is insufficient to determine the effects of the technology on health outcomes.

Liver Transplant

For individuals who are liver transplant recipients who experience graft rejection and receive ECP, the evidence includes a small nonrandomized study, a retrospective study, and a case series. The relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. Current evidence does not permit conclusions on the utility of ECP in this population. There is a need for RCTs comparing immunosuppressive therapy alone with immunosuppressive therapy with ECP. The evidence is insufficient to determine the effects of the technology on health outcomes.

Kidney Transplant

For individuals who are kidney transplant recipients who experience recurrent graft rejection who receive ECP, the evidence includes a small prospective study and numerous case reports. The relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. Current evidence does not permit conclusions on the effect of ECP on net health outcome. RCTs, comparing immunosuppressive therapy with immunosuppressive therapy using ECP and examining histologic confirmation of treatment response, are needed. The evidence is insufficient to determine the effects of the technology on health outcomes.

Graft-Versus-Host Disease

For individuals who have acute or chronic GVHD refractory to medical treatment who receive ECP, the evidence includes systematic reviews, retrospective studies, and case series. The relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. Current evidence has consistently shown that ECP reduces the incidence of GVHD that is unresponsive to standard therapy. Additionally, there is a lack of other treatment options for these patients; adverse events related to ECP are minimal; and, if there is a response

to ECP, patients may be able to reduce or discontinue treatment with corticosteroids and other immunosuppressive agents. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Additional Information

Clinical input obtained in 2014 supported the use of ECP in patients with refractory acute GVHD.

Other Indications, Not Related to Solid Organ Transplant

Autoimmune Disease

For individuals who have autoimmune diseases (eg, cutaneous or visceral manifestations of autoimmune diseases including but not limited to scleroderma, systemic lupus erythematosus, rheumatoid arthritis, pemphigus, psoriasis, multiple sclerosis, diabetes, autoimmune bullous disorders, severe atopic dermatitis, and Crohn's disease) who receive ECP, the evidence includes isolated RCTs, small prospective and retrospective studies, and case reports. The relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. The current literature assessing the various autoimmune diseases is not sufficiently robust to support conclusions. The evidence is insufficient to determine the effects of the technology on health outcomes.

Cutaneous T-Cell Lymphoma

For individuals who have advanced-stage (stage III or IV) CTCL who receive ECP, the evidence includes a systematic review and numerous small case series. The relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. Evidence from these small case series has shown a favorable response to ECP treatment and an increase in survival in a proportion of these patients. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have refractory or progressive early-stage (stage I or II) CTCL who receive ECP, the evidence includes a systematic review. The relevant outcomes are overall survival, change in disease status, and treatment-related mortality and morbidity. Given the unfavorable prognosis for patients with early-stage CTCL that progresses on nonsystemic therapies, the relative lack of adverse events with ECP compared with other systemic treatments, and the good

response rates often observed with ECP, this therapy is an option for those with refractory or progressive early-stage CTCL. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this policy are listed in **Table 2**.

Table 2. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
Graft-versus-host disease			
NCT03204721	Prevention of Graft-versus-host Disease in Patients Treated With Allogeneic Stem Cell Transplantation: Possible Role of Extracorporeal Photopheresis	158	Dec 2021 (ongoing)
NCT03112603a	A Phase III Randomized Open-label Multi-center Study of Ruxolitinib vs. Best Available Therapy in Patients with Corticosteroid-refractory Chronic Graft vs Host Disease After Allogeneic Stem Cell Transplantation (REACH3)	329	March 2022 (ongoing)
NCT00637689	Improving Outcomes Assessment in Chronic GVHD	601	Feb 2025 (ongoing)
NCT01460914	Outcomes of Cutaneous T-Cell Lymphoma and Chronic Graft-Versus-Host Disease in Patients Treated with Extracorporeal Photopheresis	100	Oct 2050 (ongoing)
Cutaneous T-cell lymphoma			
NCT01460914	Outcomes of Cutaneous T-Cell Lymphoma and Chronic Graft-Versus-Host Disease in Patients Treated with Extracorporeal Photopheresis	100	Oct 2050 (ongoing)
Unpublished			
Solid organ transplants			
NCT01824368	Extracorporeal Photopheresis in Liver Transplantation. Phase 2 Clinical Trial in Safety and Efficacy in Patients With Gradual Decrease of Immunosuppression (FEC-TH)	10	Apr 2016 (completed)
Autoimmune disorders			

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT02296346[a]	Open-Label Study to Evaluate the Efficacy of ECP in Secondary Progressive Multiple Sclerosis	13/66	May 2018 (terminated)

CTCL: cutaneous T-cell lymphoma; GVHD: graft-versus-host disease; NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored trial.

Clinical Input from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received through two academic medical centers and five Blue Distinction Centers for Transplant when this policy was under review in 2014. Respondents agreed unanimously that extracorporeal photopheresis should not be medically necessary for previously untreated acute graft-versus-host disease but should be medically necessary for acute graft-versus-host disease that is refractory to medical therapy.

Practice Guidelines and Position Statements

Graft Versus Host Disease

Acute Graft Versus Host Disease

American Society of Blood and Marrow Transplantation

In 2012, evidence-based recommendations from the American Society of Blood and Marrow Transplantation advised that ECP cannot be considered superior to horse antithymocyte globulin for treatment of acute GVHD.[76] This conclusion was based on older studies.[43,77]

Acute Graft Versus Host Disease and Chronic Graft Versus Host Disease

National Cancer Institute

In its guideline on childhood hematopoietic cell transplantation, the National Cancer Institute listed ECP as a second-line treatment for patients with acute GVHD resistant to first-line methylprednisolone.[78] For chronic GVHD therapy, the guidelines recommended that steroids are first-line therapy, but steroid-sparing approaches, including ECP, are being developed. In this setting, ECP has shown "some efficacy in a percentage of patients."

Cutaneous T-Cell Lymphoma

National Comprehensive Cancer Network

National Comprehensive Cancer Network guidelines on primary cutaneous lymphomas (v.2.2020) lists the use of ECP as a category 2A treatment alone or in combination with other agents as first-line systemic therapy for advanced (stages III-IV) disease, as well as for patients with earlier stage mycosis fungoides with Sézary syndrome involvement. The guidelines add that ECP may be more appropriate as systemic therapy in patients with or at risk of blood involvement (B1 or B2; erythrodermic stage III disease or IVA with Sézary syndrome).[79]

Medicare National Coverage

Solid-Organ Transplants

Effective 2006, the Centers for Medicare and Medicaid Services (CMS) concluded that ECP is reasonable and necessary for persons with "acute cardiac allograft rejection whose disease is refractory to standard immunosuppressive drug treatment".[80]

Effective 2012, CMS also provided coverage for ECP for the treatment of "bronchiolitis obliterans syndrome (BOS) following lung allograft transplantation only when extracorporeal photopheresis is provided under a clinical research study" that meets certain conditions.[80]

Graft Versus Host Disease

Effective 2006, CMS provided coverage of ECP for patients with chronic GVHD "whose disease is refractory to standard immunosuppressive drug treatment."[80]

Autoimmune Disorders

There are no national coverage decisions on the use of ECP for the treatment of autoimmune disease.

Cutaneous T-Cell Lymphoma

Effective 1988, CMS provided coverage for ECP as "palliative treatment of skin manifestations of cutaneous T-cell lymphoma that has not responded to other therapy."[80]

Regulatory Status

Two photopheresis systems (Therakos; now Mallinckrodt) were approved by the U.S. Food and Drug Administration (FDA) through the premarket approval process. Both systems are approved for use in ultraviolet-A irradiation treatment, in the presence of the photoactive drug 8-methoxypsoralen, of extracorporeally circulating leukocyte-enriched blood, in the palliative treatment of skin manifestations of CTCL, in persons who have not been responsive to other forms of treatment. The two systems are:

- UVAR® XTS Photopheresis System (FDA-approved in 1987)
- CELLEX® (FDA approved in 2009)

Photoactive 8-methoxypsoralen (UVADEX®; Therakos; now Mallinckrodt) is FDA-approved for extracorporeal administration with the UVAR® XTS or CELLEX® Photopheresis System in the palliative treatment of the skin manifestations of CTCL unresponsive to other forms of treatment.

The use of either Therakos photopheresis system or UVADEX® for other conditions is off-label.

FDA product code: LNR.

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History

Date	Comments
11/16/00	Add to Therapy Section - New Policy.
01/08/02	Replace Policy - Revised; added information on photopheresis for graft vs. host disease; considered medically necessary for chronic disease.
05/11/04	Replace Policy - Policy reviewed; literature updated; no change in policy statement.
06/14/05	Replace Policy - Policy reviewed with literature search; no change in policy statement.
06/16/06	Replace Policy - Policy updated with literature search; policy statement unchanged. Scope and Disclaimer updated.
01/08/08	Replace Policy - Policy updated with literature search; no change in policy statement. "Extracorporeal" added to the title. References and code added.
12/16/08	Minor Updates - Spelling Corrected.
06/09/09	Replace Policy - Policy updated with literature search. Three new policy statements for CTCL added (two medically necessary statements). Title changed to reflect cutaneous T-cell lymphoma (CTCL) indication. References added. Policy reviewed and recommended by Oncology Advisory Panel on May 21, 2009. OAP recommended removing chronic from first policy statement.
02/09/10	Replace Policy - Policy updated with literature search. Policy statement minor update "chronic" added to medically necessary statement, no other changes. References added.
06/10/10	Delete Policy - Policy deleted from active status.
11/09/10	Reinstate Policy - Policy reinstated. Requests are being received.
03/08/11	Replace Policy - Policy updated with literature search; reference numbers 8, 9 and 17 added; autoimmune bullous disorders added as investigational. No other changes to policy statements.
05/12/11	Reviewed by OAP - No changes recommend to the policy.
04/10/12	Replace policy. Policy updated with literature search; reference numbers 8, 9, 17 and 28 added; autoimmune bullous disorders added as investigational; no other changes to policy statements. Policy 8.01.51 (Extracorporeal Photopheresis as Treatment for and Prevention of Organ Rejection after Solid-Organ Transplant) combined with this

Date	Comments
	policy; 8.01.51 deleted as a separate policy. Title changed to reflect combined policies and coding updated.
09/10/12	Update Coding Section – ICD-10 codes are now effective 10/01/2014.
09/21/12	Update Related Policy, add 5.01.532.
02/12/13	Update Related Policies, change title on Policy 8.02.02.
04/08/13	Replace policy. Policy updated with literature search; policy statement added that ECP is investigational for any other indications; references 6, 15, 60, 61, 62 added. Title changed to "Extracorporeal Photopheresis".
03/11/14	Coding Update. Code 99.88 was removed per ICD-10 mapping project; this code is not utilized for adjudication of policy.
07/14/14	Annual Review. Policy updated with literature review through April 16, 2014; references 15, 35-36, 39, 43-45, 51-56, 65-68, 70, and 84 added; references 6, 29, 37, and 78 updated. Clinical input reviewed. New policy statement added that ECP is medically necessary in refractory acute graft-versus-host disease. For autoimmune diseases, Investigational policy statement updated to include severe atopic dermatitis and Crohn disease; no other changes to policy statements.
06/17/15	Annual Review. Policy updated with literature review through March 2, 2015; references 11, 39-40, 43, 49, 54, and 63 added. Policy statements unchanged. Benefit Application clarified. ICD-9 and ICD-10 diagnosis and procedure codes removed; these do not facilitate adjudication.
12/01/16	Annual Review, approved November 8, 2016. Policy updated with literature review. Added reference 38. No changes to policy statements.
01/01/18	Annual Review, approved December 6, 2017. Policy updated with literature review through August 2017; no references added. Policy statement unchanged.
11/01/18	Minor update, removed 8.02.02 from related policies as it was archived.
01/01/19	Annual Review, approved December 19, 2018. Policy updated with literature review through August 2018; no references added. Policy statement unchanged.
04/01/19	Minor update, added Documentation Requirements section.
01/01/20	Annual Review, approved December 10, 2019. Policy updated with literature review through August 2019; no references added. Policy statements unchanged.
04/01/20	Delete policy, approved March 10, 2020. This policy will be deleted effective July 2, 2020, and replaced with InterQual criteria for dates of service on or after July 2, 2020.
06/12/20	Correction: This policy is reinstated immediately and will no longer be deleted or replaced with InterQual criteria on July 2, 2020, as this policy was deleted in error.
01/01/21	Annual Review, approved December 1, 2020. Policy updated with literature review through September 23, 2020; reference added. 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.

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この通知には重要な情報が含まれています。この通知には、Premera Blue Cross の申請または補償範囲に関する重要な情報が含まれている場合があります。この通知に記載されている可能性がある重要な日付をご確認ください。健康保険や有料サポートを維持するには、特定の期日までに行動を取らなければならない場合があります。ご希望の言語による情報とサポートが無料で提供されます。800-722-1471 (TTY: 800-842-5357)までお電話ください。

한국어 (Korean):
본 통지서에는 중요한 정보가 들어 있습니다. 즉 이 통지서는 귀하의 신청에 관하여 그리고 Premera Blue Cross 를 통한 커버리지에 관한 정보를 포함하고 있을 수 있습니다. 본 통지서에는 핵심이 되는 날짜들이 있을 수 있습니다. 귀하는 귀하의 건강 커버리지를 계속 유지하거나 비용을 절감하기 위해서 일정한 마감일까지 조치를 취해야 할 필요가 있을 수 있습니다. 귀하는 이러한 정보와 도움을 귀하의 언어로 비용 부담없이 얻을 수 있는 권리가 있습니다. 800-722-1471 (TTY: 800-842-5357) 로 전화하십시오.

ລາວ (Lao):
ແຈ້ງການນີ້ມີຂໍ້ມູນສຳຄັນ. ແຈ້ງການນີ້ອາດຈະມີຂໍ້ມູນສຳຄັນກ່ຽວກັບຄຳຮ້ອງສະໝັກ ຫຼື ຄວາມຄຸ້ມຄອງປະກັນໄພຂອງທ່ານຜ່ານ Premera Blue Cross. ອາດຈະມີວັນທີສຳຄັນໃນແຈ້ງການນີ້. ທ່ານອາດຈະຈຳເປັນຕ້ອງດຳເນີນການຕາມກຳນົດເວລາສະເພາະເພື່ອຮັກສາຄວາມຄຸ້ມຄອງປະກັນສຸຂະພາບ ຫຼື ຄວາມຊ່ວຍເຫຼືອເລື່ອງຄ່າໃຊ້ຈ່າຍຂອງທ່ານໄວ້. ທ່ານມີສິດໄດ້ຮັບຂໍ້ມູນນີ້ ແລະ ຄວາມຊ່ວຍເຫຼືອເປັນພາສາຂອງທ່ານໂດຍບໍ່ເສຍຄ່າ. ໃຫ້ໂທຫາ 800-722-1471 (TTY: 800-842-5357).

ភាសាខ្មែរ (Khmer):
សេចក្តីជូនដំណឹងនេះមានព័ត៌មានយ៉ាងសំខាន់។ សេចក្តីជូនដំណឹងនេះប្រហែលជាមានព័ត៌មានយ៉ាងសំខាន់អំពីទម្រង់បែបបទ ឬការរ៉ាប់រងរបស់អ្នកតាមរយៈ Premera Blue Cross ។ ប្រហែលជាមាន កាលបរិច្ឆេទសំខាន់នៅក្នុងសេចក្តីជូនដំណឹងនេះ។ អ្នកប្រហែលជាត្រូវការបញ្ចេញសមត្ថភាព ដល់កំណត់ថ្ងៃជាក់ច្បាស់នានា ដើម្បីនឹងរក្សាទុកការជានាវ៉ាប់រងសុខភាពរបស់អ្នក ឬប្រាក់ជំនួយចេញផ្លែ។ អ្នកមានសិទ្ធិទទួលព័ត៌មាននេះ និងជំនួយនៅក្នុងភាសារបស់អ្នកដោយមិនអស់លុយឡើយ។ សូមទូរស័ព្ទ 800-722-1471 (TTY: 800-842-5357)។

ਪੰਜਾਬੀ (Punjabi):
ਇਸ ਨੋਟਿਸ ਵਿਚ ਖਾਸ ਜਾਣਕਾਰੀ ਹੈ. ਇਸ ਨੋਟਿਸ ਵਿਚ Premera Blue Cross ਵਲੋਂ ਤੁਹਾਡੀ ਕਵਰੇਜ ਅਤੇ ਅਰਜੀ ਬਾਰੇ ਮਹੱਤਵਪੂਰਨ ਜਾਣਕਾਰੀ ਹੋ ਸਕਦੀ ਹੈ . ਇਸ ਨੋਜਿਸ ਜਵਚ ਖਾਸ ਤਾਰੀਖਾ ਹੋ ਸਕਦੀਆਂ ਹਨ. ਜੇਕਰ ਤੁਸੀ ਜਸਹਤ ਕਵਰੇਜ ਰਿੱਖਣੀ ਹੋਵੇ ਜਾ ਓਸ ਦੀ ਲਾਗਤ ਜਵਿੱਚ ਮਦਦ ਦੇ ਇਛੁੱਕ ਹੋ ਤਾਂ ਤੁਹਾਨੂੰ ਅੰਤਮ ਤਾਰੀਖ਼ ਤੋਂ ਪਹਿਲਾਂ ਕੁੱਝ ਖਾਸ ਕਦਮ ਚੁੱਕਣ ਦੀ ਲੋੜ ਹੋ ਸਕਦੀ ਹੈ ,ਤੁਹਾਨੂੰ ਮੁਫ਼ਤ ਵਿੱਚ ਤੇ ਆਪਣੀ ਭਾਸ਼ਾ ਵਿੱਚ ਜਾਣਕਾਰੀ ਅਤੇ ਮਦਦ ਪ੍ਰਾਪਤ ਕਰਨ ਦਾ ਅਧਿਕਾਰ ਹੈ ,ਕਾਲ 800-722-1471 (TTY: 800-842-5357).

فارسی (Farsi):
این اعلامیه حاوی اطلاعات مهم میباشد .این اعلامیه ممکن است حاوی اطلاعات مهم درباره فرم تقاضا و یا پوشش بیمه ای شما از طریق Premera Blue Cross باشد. به تاریخ های مهم در این اعلامیه توجه نمایید .شما ممکن است برای حفظ پوشش بیمه تان یا کمک در پرداخت هزینه های درمانی تان، به تاریخ های مشخصی برای انجام کارهای خاصی احتیاج داشته باشید .شما حق این را دارید که این اطلاعات و کمک را به زبان خود به طور رایگان دریافت نمایید. برای کسب اطلاعات با شماره 800-722-1471 (کاربران TTY تماس باشماره 800-842-5357) تماس برقرار نمایید.

Polskie (Polish):
To ogłoszenie może zawierać ważne informacje. To ogłoszenie może zawierać ważne informacje odnośnie Państwa wniosku lub zakresu świadczeń poprzez Premera Blue Cross. Prosimy zwrócic uwagę na kluczowe daty, które mogą być zawarte w tym ogłoszeniu aby nie przekroczyć terminów w przypadku utrzymania polisy ubezpieczeniowej lub pomocy związanej z kosztami. Macie Państwo prawo do bezpłatnej informacji we własnym języku. Zadzwońcie pod 800-722-1471 (TTY: 800-842-5357).

Português (Portuguese):
Este aviso contém informações importantes. Este aviso poderá conter informações importantes a respeito de sua aplicação ou cobertura por meio do Premera Blue Cross. Poderão existir datas importantes neste aviso. Talvez seja necessário que você tome providências dentro de determinados prazos para manter sua cobertura de saúde ou ajuda de custos. Você tem o direito de obter esta informação e ajuda em seu idioma e sem custos. Ligue para 800-722-1471 (TTY: 800-842-5357).

Română (Romanian):
Prezenta notificare conține informații importante. Această notificare poate conține informații importante privind cererea sau acoperirea asigurării dumneavoastre de sănătate prin Premera Blue Cross. Pot exista date cheie în această notificare. Este posibil să fie nevoie să acționați până la anumite termene limită pentru a vă menține acoperirea asigurării de sănătate sau asistența privitoare la costuri. Aveți dreptul de a obține gratuit aceste informații și ajutor în limba dumneavoastră. Sunați la 800-722-1471 (TTY: 800-842-5357).

Русский (Russian):
Настоящее уведомление содержит важную информацию. Это уведомление может содержать важную информацию о вашем заявлении или страховом покрытии через Premera Blue Cross. В настоящем уведомлении могут быть указаны ключевые даты. Вам, возможно, потребуется принять меры к определенным предельным срокам для сохранения страхового покрытия или помощи с расходами. Вы имеете право на бесплатное получение этой информации и помощь на вашем языке. Звоните по телефону 800-722-1471 (TTY: 800-842-5357).

Fa'asamoa (Samoan):
Atonu ua iai i lenei fa'asilasilaga ni fa'amatalaga e sili ona taua e tatau ona e malamalama i ai. O lenei fa'asilasilaga o se fesoasoani e fa'amatala atili i ai i le tulaga o le polokalame, Premera Blue Cross, ua e tau fia maua atu i ai. Fa'amolemole, ia e iloilo fa'alelei i aso fa'apitoa olo'o iai i lenei fa'asilasilaga taua. Masalo o le'a iai ni feau e tatau ona e faia ao le'i aulia le aso ua ta'ua i lenei fa'asilasilaga ina ia e iai pea ma maua fesoasoani mai ai i le polokalame a le Malo olo'o e iai i ai. Olo'o iai iate oe le aia tatau e maua atu i lenei fa'asilasilaga ma lenei fa'amatalaga i legagana e te malamalama i ai aunoa ma se togiga tupe. Vili atu i le telefoni 800-722-1471 (TTY: 800-842-5357).

Español (Spanish):
Este Aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de Premera Blue Cross. Es posible que haya fechas clave en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).

Tagalog (Tagalog):
Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon. Ang paunawa na ito ay maaaring naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa pamamagitan ng Premera Blue Cross. Maaaring may mga mahalagang petsa dito sa paunawa. Maaring mangailangan ka na magsagawa ng hakbang sa ilang mga itinakdang panahon upang mapanatili ang iyong pagsakop sa kalusugan o tulong na walang gastos. May karapatan ka na makakuha ng ganitong impormasyon at tulong sa iyong wika ng walang gastos. Tumawag sa 800-722-1471 (TTY: 800-842-5357).

ไทย (Thai):
ประกาศนี้มีข้อมูลสำคัญ ประกาศนี้อาจมีข้อมูลที่สำคัญเกี่ยวกับการการสมัครหรือขอบเขตประกันสุขภาพของคุณผ่าน Premera Blue Cross และอาจมีกำหนดการในประกาศนี้ คุณอาจจะต้องดำเนินการภายในกำหนดระยะเวลาที่แน่นอนเพื่อจะรักษาการประกันสุขภาพของคุณหรือการช่วยเหลือที่มีค่าใช้จ่าย คุณมีสิทธิที่จะได้รับข้อมูลและความช่วยเหลือนี้ในภาษาของคุณโดยไม่มีค่าใช้จ่าย โทร 800-722-1471 (TTY: 800-842-5357)

Український (Ukrainian):
Це повідомлення містить важливу інформацію. Це повідомлення може містити важливу інформацію про Ваше звернення щодо страхувального покриття через Premera Blue Cross. Зверніть увагу на ключові дати, які можуть бути вказані у цьому повідомленні. Існує імовірність того, що Вам треба буде здійснити певні кроки у конкретні кінцеві строки для того, щоб зберегти Ваше медичне страхування або отримати фінансову допомогу. У Вас є право на отримання цієї інформації та допомоги безкоштовно на Вашій рідній мові. Дзвоніть за номером телефону 800-722-1471 (TTY: 800-842-5357).

Tiếng Việt (Vietnamese):
Thông báo này cung cấp thông tin quan trọng. Thông báo này có thông tin quan trọng về đơn xin tham gia hoặc hợp đồng bảo hiểm của quý vị qua chương trình Premera Blue Cross. Xin xem ngày quan trọng trong thông báo này. Quý vị có thể phải thực hiện theo thông báo đúng trong thời hạn để duy trì bảo hiểm sức khỏe hoặc được trợ giúp thêm về chi phí. Quý vị có quyền được biết thông tin này và được trợ giúp bằng ngôn ngữ của mình miễn phí. Xin gọi số 800-722-1471 (TTY: 800-842-5357).