Extracorporeal Photopheresis

Policy # 00099
Original Effective Date: 06/05/2002
Current Effective Date: 04/10/2023

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services Are Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Organ Rejection After Solid Organ Transplant
Based on review of available data, the Company may consider extracorporeal photopheresis (ECP) to treat cardiac allograft rejection, including acute rejection, that is either recurrent or that is refractory to standard immunosuppressive drug treatment to be **eligible for coverage.****

Graft-Versus-Host Disease

Acute
Based on review of available data, the Company may consider extracorporeal photopheresis (ECP) as a technique to treat acute graft-versus-host disease (GVHD) that is refractory to medical therapy to be **eligible for coverage.****

Chronic
Based on review of available data, the Company may consider extracorporeal photopheresis (ECP) as a technique to treat chronic graft-versus-host disease (GVHD) that is refractory to medical therapy to be **eligible for coverage.****

Cutaneous T-Cell Lymphoma
Based on review of available data, the Company may consider extracorporeal photopheresis (ECP) as a technique to treat late stage (III/IV) cutaneous T-cell lymphoma (CTCL) to be **eligible for coverage.****

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Based on review of available data, the Company may consider extracorporeal photopheresis (ECP) as a technique to treat early stage (I/II) cutaneous T-cell lymphoma (CTCL) that is progressive and refractory to established nonsystemic therapies to be **eligible for coverage.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Organ Rejection After Solid Organ Transplant
Based on review of available data, the Company considers extracorporeal photopheresis (ECP) in all other situations related to treatment or prevention of rejection in solid-organ transplantation to be **investigational.***

Graft-Versus-Host Disease

Acute
Based on review of available data, the Company considers extracorporeal photopheresis (ECP) as a technique to treat acute graft-versus-host disease (GVHD) that is either previously untreated or is responding to established therapies to be **investigational.***

Chronic
Based on review of available data, the Company considers extracorporeal photopheresis (ECP) as a technique to treat chronic graft-versus-host disease (GVHD) that is either previously untreated or is responding to established therapies to be **investigational.***

Autoimmune Diseases
Based on review of available data, the Company considers extracorporeal photopheresis (ECP) as a technique to treat either the 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, or Crohn disease to be **investigational.***

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Cutaneous T-Cell Lymphoma
Based on review of available data, the Company considers extracorporeal photopheresis (ECP) as a technique to treat early stage (I/II) cutaneous T-cell lymphoma (CTCL) that is either previously untreated or is responding to established nonsystemic therapies to be **investigational.***

Other
Based on review of available data, the Company considers extracorporeal photopheresis (ECP) for all other indications to be **investigational.***

Policy Guidelines

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 2 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 2 consecutive days of ECP in month 1, followed by biweekly therapy on 2 consecutive days in months 2 and 3, then monthly on 2 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 2 consecutive days)

weekly for acute GVHD and every 2 weeks for chronic GVHD. Treatment duration is based on clinical response; 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 PG1).

Table PG1. 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.

Background/Overview

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 infections 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. Reports of the successful use of ECP in human cardiac transplant recipients were published in 1992 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. The specificity of ECP to target the immune response to the transplanted organ allows ECP to decrease organ rejection without an increased risk of infection, common with immunosuppressive drugs.

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 2 ways: (1) as an acute disease, occurring within the first 100 days after the 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 the 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 medical 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 100000 annually, but because most are low-grade malignancies with long survival, the 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.

Cutaneous T-cell lymphoma 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), or 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 of time (mean, 2 to 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 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.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

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 2 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.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to federal regulations, other plan medical policies, and accredited national guidelines.

Extracorporeal photopheresis (ECP) is a leukapheresis-based immunomodulatory procedure that involves the following 3 steps: (1) the patient's blood is collected into a centrifuge system that separates the leukocyte-rich portion (buffy coat) from the rest of the blood; (2) 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 to 2 J/cm^2; and (3) 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.

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 randomized controlled trial (RCT). Relevant outcomes are overall survival (OS), 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 that the technology results in an improvement in the net health outcome.

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. Relevant outcomes are OS, 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 an 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 and a prospective pilot study. Relevant outcomes are OS, change in disease status, and treatment-related mortality and morbidity. The small randomized trial is insufficient to permit conclusions on the utility of ECP. The pilot study was non-comparative and evaluated outcomes in high-risk cardiac transplant patients. Studies with more patients and longer follow-up are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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. Relevant outcomes are OS, 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 that the technology results in an improvement in the net health outcome.

For individuals who are lung transplant recipients with bronchiolitis obliterans syndrome (BOS) refractory to corticosteroids who receive ECP, the evidence includes a prospective study and numerous retrospective analyses. Relevant outcomes are OS, 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 that the technology results in an improvement in the net health outcome.

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. Relevant outcomes are OS, 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 that the technology results in an improvement in the net health outcome.

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. Relevant outcomes are OS, 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. There is a need for RCTs comparing immunosuppressive therapy with and without the use of ECP and examining histologic confirmation of treatment response. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Graft-Versus-Host Disease
For individuals who have acute or chronic GVHD refractory to medical treatment who receive ECP, the evidence includes systematic reviews, a randomized study, retrospective studies, and case series. Relevant outcomes are OS, 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 an improvement in the net health outcome.

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. Relevant outcomes are OS, 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 that the technology results in an improvement in the net health outcome.

Cutaneous T-Cell Lymphoma
For individuals who have advanced-stage (stage III or IV) cutaneous T-cell lymphoma (CTCL) who receive ECP, the evidence includes a systematic review and numerous small case series. Relevant outcomes are OS, 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 an 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. Relevant outcomes are OS, 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 an improvement in the net health outcome.

Supplemental Information

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.

2014 Input
In response to requests, input was received through 2 academic medical centers and 5 Blue Distinction Centers for Transplant when this policy was under review in 2014. Respondents agreed unanimously that extracorporeal photopheresis (ECP) should not be medically necessary for previously untreated acute graft-versus-host disease (GVHD) but should be medically necessary for acute GVHD that is refractory to medical therapy.

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Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

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 the treatment of acute GVHD. This conclusion was based on older studies.

Acute and Chronic Graft-Versus-Host Disease

National Cancer Institute
In its guidelines 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. 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 some patients."

Cutaneous T-Cell Lymphoma

National Comprehensive Cancer Network
National Comprehensive Cancer Network guidelines on primary cutaneous lymphomas (v.2.2022) list 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).

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U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage

Solid Organ Transplants
Effective 2006, the Centers for Medicare & 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".

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.

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."

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."

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
Ongoing			
GVHD			
NCT04792294	Multicenter Analysis of Efficacy and Outcomes of Extracorporeal Photopheresis as Treatment of Chronic Lung Allograft Dysfunction	800	Dec 2021 (ongoing)
NCT03112603[a]	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)	331	Dec 2022 (ongoing)
NCT03083574	A Phase II Study to Assess the Safety and the Efficacy of Extracorporeal Photopheresis Using the Theraflex ECP™‡ for Patients With Refractory Chronic Graft Versus Host Disease (cGVHD)	100	Sep 2023 (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)
CTCL			
NCT01460914	Outcomes of Cutaneous T-Cell Lymphoma and Chronic Graft-Versus-Host Disease in Patients Treated with Extracorporeal Photopheresis	100	Oct 2050 (ongoing)

Diabetes			
NCT05413005	Efficacy of Extracorporeal Photopheresis (ECP) in the Treatment of Type 1 Diabetes Mellitus (OPERA)	10	Jan 2024 (ongoing)
Multiple Sclerosis			
NCT05168384	Safety and Efficacy of Extracorporeal Photopheresis (ECP) in the Treatment of Multiple Sclerosis (PHOMS)	45	Apr 2024 (ongoing)
Systemic Sclerosis			
NCT04986605	The Effectiveness of ECP in Diffuse Cutaneous Systemic Sclerosis	15	June 2024
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			
NCT02296346[a]	Open-Label Study to Evaluate the Efficacy of ECP in Secondary Progressive Multiple Sclerosis	13/66	May 2018 (terminated)
GVHD			
NCT03204721	Prevention of Graft-versus-host Disease in Patients Treated With Allogeneic Stem Cell Transplantation: Possible Role of Extracorporeal Photopheresis	158	Dec 2021 (ongoing)

CTCL: cutaneous T-cell lymphoma; GVHD: graft-versus-host disease; NCT: national clinical trial. a Denotes industry-sponsored or cosponsored trial.

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Policy History

Original Effective Date: 06/05/2002
Current Effective Date: 04/10/2023

05/14/2002	Medical Director review
05/16/2002	Medical Policy Committee review
06/05/2002	Managed Care Advisory Council approval
06/24/2002	Format revision. No substance change to policy
06/01/2004	Medical Director review
06/15/2004	Medical Policy Committee review. Format revision. No substance change to policy
06/28/2004	Managed Care Advisory Council approval
07/12/2006	Medical Director review
07/19/2006	Medical Policy Committee review. Format revision. No change to policy guidelines.
11/07/2007	Medical Director review
11/15/2007	Medical Policy Committee approval. No change to coverage eligibility.
11/05/2008	Medical Director review
11/18/2008	Medical Policy Committee approval. No change to coverage eligibility.
12/04/2009	Medical Policy Committee approval.

12/16/2009	Medical Policy Implementation Committee approval. Policy title revised to reflect cutaneous T-cell lymphoma (CTCL) indication. Three new policy statements for CTCL added.
12/01/2010	Medical Policy Committee approval.
12/15/2010	Medical Policy Implementation Committee approval. No change to coverage.
12/08/2011	Medical Policy Committee review
12/21/2011	Medical Policy Implementation Committee approval. Changed title from "Extracorporeal Photopheresis after Solid-Organ Transplant and for Graft-versus-Host Disease, Autoimmune Disease, and Cutaneous T-Cell Lymphoma" to "Extracorporeal Photopheresis after Solid-Organ Transplant and for Graft-versus-Host Disease, Autoimmune Disease, and Cutaneous T-Cell Lymphoma". Added coverage statement for extracorporeal photopheresis to treat cardiac allograft rejection, including acute rejection, that is either recurrent or that is refractory to standard immunosuppressive drug treatment. Extracorporeal photopheresis in all other situations related to treatment or prevention of rejection in solid-organ transplantation added as investigational. Autoimmune bullous disorders added as investigational. Updated coverage guidelines, Background/Overview, Rationale, and References.
12/06/2012	Medical Policy Committee review
12/19/2012	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
12/12/1013	Medical Policy Committee review
12/18/2013	Medical Policy Implementation Committee approval. Title changed from "Extracorporeal Photopheresis after Solid-Organ Transplant and for Graft-versus-Host Disease, Autoimmune Disease, and Cutaneous T-Cell Lymphoma" to "Extracorporeal Photopheresis". Statement added that extracorporeal photopheresis is investigational for any other indications.
03/05/2015	Medical Policy Committee review
03/20/2015	Medical Policy Implementation Committee approval. Coverage eligibility updated, added coverage of acute GVHD. Rationale and references updated.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.
03/03/2016	Medical Policy Committee review
03/16/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
10/01/2016	Coding update
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes

03/02/2017 Medical Policy Committee review
03/15/2017 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/01/2018 Medical Policy Committee review
03/21/2018 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/07/2019 Medical Policy Committee review
03/20/2019 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/05/2020 Medical Policy Committee review
03/11/2020 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/10/2020 Coding update
03/04/2021 Medical Policy Committee review
03/10/2021 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
09/30/2021 Coding update
03/03/2022 Medical Policy Committee review
03/09/2022 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
03/02/2023 Medical Policy Committee review
03/08/2023 Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
Next Scheduled Review Date: 03/2024

Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2022 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	36522
HCPCS	No codes
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

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**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.