



MASSACHUSETTS

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Medical Policy

Extracorporeal Photopheresis

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Policy Number: 248

BCBSA Reference Number: 8.01.36 (For Plans internal use only)

Related Policies

None

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Extracorporeal photopheresis may be considered **MEDICALLY NECESSARY** to treat the following conditions:

- Cardiac allograft rejection, including acute rejection, that is either recurrent or that is refractory to standard immunosuppressive drug treatment
- Acute graft-versus-host disease or chronic graft-versus-host disease that is refractory to medical therapy
- Late-stage (III/IV) cutaneous T-cell lymphoma, or
- Early stage (I/II) cutaneous T-cell lymphoma that is progressive and refractory to established non-systemic therapies.

Refractory rejection is defined as rejection that fails to respond adequately to a standard regimen of immunosuppressive therapy.

Extracorporeal photopheresis is considered **INVESTIGATIONAL** for the following conditions:

- Treatment or prevention of rejection in solid-organ transplantation except for rejection that is recurrent or refractory to standard immunosuppressive drug treatment
- Acute graft-versus-host disease or chronic graft-versus-host disease, that is either previously untreated or is responding to established therapies
- Cutaneous or visceral manifestations of autoimmune diseases, including but not limited to scleroderma, systemic lupus erythematosus, rheumatoid arthritis, pemphigus, psoriasis, multiple sclerosis, diabetes, or autoimmune bullous disorders, severe atopic dermatitis, or Crohn disease.
- Early stage (I/II) cutaneous T-cell lymphoma that is either previously untreated or is responding to established nonsystemic therapies.

Extracorporeal photopheresis is [INVESTIGATIONAL](#) for all other indications.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is not required .
Commercial PPO and Indemnity	Prior authorization is not required .

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

CPT Codes

CPT codes:	Code Description
36522	Photopheresis, extracorporeal

ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
C84.00	Mycosis fungoides, unspecified site
C84.01	Mycosis fungoides, lymph nodes of head, face, and neck
C84.02	Mycosis fungoides, intrathoracic lymph nodes
C84.03	Mycosis fungoides, intra-abdominal lymph nodes
C84.04	Mycosis fungoides, lymph nodes of axilla and upper limb
C84.05	Mycosis fungoides, lymph nodes of inguinal region and lower limb
C84.06	Mycosis fungoides, intrapelvic lymph nodes
C84.07	Mycosis fungoides, spleen
C84.08	Mycosis fungoides, lymph nodes of multiple sites
C84.09	Mycosis fungoides, extranodal and solid organ sites
C84.10	Sézary disease, unspecified site
C84.11	Sézary disease, lymph nodes of head, face, and neck
C84.12	Sézary disease, intrathoracic lymph nodes
C84.13	Sézary disease, intra-abdominal lymph nodes
C84.14	Sézary disease, lymph nodes of axilla and upper limb
C84.15	Sézary disease, lymph nodes of inguinal region and lower limb
C84.16	Sézary disease, intrapelvic lymph nodes
C84.17	Sézary disease, spleen
C84.18	Sézary disease, lymph nodes of multiple sites
C84.19	Sézary disease, extranodal and solid organ sites
D89.810	Acute Graft-Versus-Host Disease
D89.811	Chronic graft-versus-host disease

D89.812	Acute on chronic graft-versus-host disease
D89.813	Graft-versus-host disease, unspecified
T86.00	Unspecified complication of bone marrow transplant
T86.01	Bone marrow transplant rejection
T86.02	Bone marrow transplant failure
T86.03	Bone marrow transplant infection
T86.09	Other complications of bone marrow transplant
T86.21	Heart transplant rejection
T86.31	Heart-lung transplant rejection
T86.5	Complications of stem cell transplant

DESCRIPTION

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.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 an 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 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 evidence review, 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, 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.

Summary

Description

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/cm²; 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.

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 extracorporeal photopheresis (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 graft-versus-host disease (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.

Policy History

Date	Action
12/2023	Annual policy review. References updated. Policy statements unchanged.
12/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
12/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2021	Medicare information removed. See MP #132 Medicare Advantage Management for local coverage determination and national coverage determination reference.
12/2020	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
11/2019	Annual policy review. Description, summary, and references updated. Policy statements unchanged.

11/2018	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
6/2015	Annual policy review. New references added.
10/2014	Annual policy review. New medically necessary and investigational indications described. Clarified Coding information. Effective 10/1/2014.
5/2014	Updated Coding section with ICD10 procedure and diagnosis codes. Effective 10/2015.
8/2013	Annual policy review. New investigational indications described. Title changed. Effective 8/1/2013.
2/2013	Annual policy review. No change in medical policy statement. Investigational statement clarified to apply to acute cardiac transplant rejection that is not recurrent or refractory. Effective 2/4/2013.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
4/2011	Medical Policy 248 created. No changes to policy statements from source medical policy 071: Pheresis.
11/2010	Reviewed - Medical Policy Group- Gastroenterology, Nutrition and Organ Transplantation No changes to policy statements.
9/2010	Reviewed - Medical Policy Group -Hematology and Oncology No changes to policy statements.
6/2010	Annual policy review. No changes to policy statements.
4/2010	Reviewed - Medical Policy Group -Cardiology. No changes to policy statements.
9/2009	Reviewed - Medical Policy Group -Hematology and Oncology. No changes to policy statements.
2/2008	Annual policy review. No changes to policy statements.
1/2008	Reviewed - Medical Policy Group – Neurology. No changes to policy statements.
9/2007	Reviewed - Medical Policy Group - Hematology/Oncology. No changes to policy statements.
4/2007	Reviewed - Medical Policy Group Cardiology. No changes to policy statements.
1/2007	Reviewed - Medical Policy Group Neurology. No changes to policy statements.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

[Medical Policy Terms of Use](#)

[Managed Care Guidelines](#)

[Indemnity/PPO Guidelines](#)

[Clinical Exception Process](#)

[Medical Technology Assessment Guidelines](#)

References

1. Marques MB, Tuncer HH. Photopheresis in solid organ transplant rejection. J Clin Apher. Apr 2006; 21(1): 72-7. PMID 16619230
2. Costanzo-Nordin MR, Hubbell EA, O'Sullivan EJ, et al. Photopheresis versus corticosteroids in the therapy of heart transplant rejection. Preliminary clinical report. Circulation. Nov 1992; 86(5 Suppl): II242-50. PMID 1424007
3. Rose EA, Barr ML, Xu H, et al. Photochemotherapy in human heart transplant recipients at high risk for fatal rejection. J Heart Lung Transplant. 1992; 11(4 Pt 1): 746-50. PMID 1498142
4. Hivelin M, Siemionow M, Grimbert P, et al. Extracorporeal photopheresis: from solid organs to face transplantation. Transpl Immunol. Jul 2009; 21(3): 117-28. PMID 19409991
5. Szczepiorkowski ZM, Bandarenko N, Kim HC, et al. Guidelines on the use of therapeutic apheresis in clinical practice: evidence-based approach from the Apheresis Applications Committee of the American Society for Apheresis. J Clin Apher. Jun 2007; 22(3): 106-75. PMID 17394188
6. Carlo WF, Pearce FB, George JF, et al. Single-center experience with extracorporeal photopheresis in pediatric heart transplantation. J Heart Lung Transplant. Jun 2014; 33(6): 624-8. PMID 24661684
7. Kirklin JK, Brown RN, Huang ST, et al. Rejection with hemodynamic compromise: objective evidence for efficacy of photopheresis. J Heart Lung Transplant. Mar 2006; 25(3): 283-8. PMID 16507420

8. Maccherini M, Diciolla F, Laghi Pasini F, et al. Photopheresis immunomodulation after heart transplantation. *Transplant Proc.* 2001; 33(1-2): 1591-4. PMID 11267432
9. Dall'Amico R, Montini G, Murer L, et al. Extracorporeal photochemotherapy after cardiac transplantation: a new therapeutic approach to allograft rejection. *Int J Artif Organs.* Jan 2000; 23(1): 49-54. PMID 12118837
10. Gökler J, Aliabadi-Zuckermann A, Zuckermann A, et al. Extracorporeal Photopheresis With Low-Dose Immunosuppression in High-Risk Heart Transplant Patients-A Pilot Study. *Transpl Int.* 2022; 35: 10320. PMID 35401042
11. Barr ML, Meiser BM, Eisen HJ, et al. Photopheresis for the prevention of rejection in cardiac transplantation. Photopheresis Transplantation Study Group. *N Engl J Med.* Dec 10 1998; 339(24): 1744-51. PMID 9845709
12. Villanueva J, Bhorade SM, Robinson JA, et al. Extracorporeal photopheresis for the treatment of lung allograft rejection. *Ann Transplant.* 2000; 5(3): 44-7. PMID 11233043
13. Benden C, Speich R, Hofbauer GF, et al. Extracorporeal photopheresis after lung transplantation: a 10-year single-center experience. *Transplantation.* Dec 15 2008; 86(11): 1625-7. PMID 19077900
14. Salerno CT, Park SJ, Kreykes NS, et al. Adjuvant treatment of refractory lung transplant rejection with extracorporeal photopheresis. *J Thorac Cardiovasc Surg.* Jun 1999; 117(6): 1063-9. PMID 10343253
15. Benden C, Houghton M, Leonard S, et al. Therapy options for chronic lung allograft dysfunction - bronchiolitis obliterans syndrome following first-line immunosuppressive strategies: A systematic review. *J Heart Lung Transplant.* Sep 2017; 36(9): 921-933. PMID 28662986
16. Del Fante C, Scudeller L, Oggionni T, et al. Long-Term Off-Line Extracorporeal Photochemotherapy in Patients with Chronic Lung Allograft Rejection Not Responsive to Conventional Treatment: A 10-Year Single-Centre Analysis. *Respiration.* 2015; 90(2): 118-28. PMID 26112178
17. Jaksch P, Scheed A, Keplinger M, et al. A prospective interventional study on the use of extracorporeal photopheresis in patients with bronchiolitis obliterans syndrome after lung transplantation. *J Heart Lung Transplant.* Sep 2012; 31(9): 950-7. PMID 22884382
18. Leroux J, Hirschi S, Essaydi A, et al. Initiation of extracorporeal photopheresis in lung transplant patients with mild to moderate refractory BOS: A single-center real-life experience. *Respir Med Res.* May 2022; 81: 100913. PMID 35525096
19. Greer M, Dierich M, De Wall C, et al. Phenotyping established chronic lung allograft dysfunction predicts extracorporeal photopheresis response in lung transplant patients. *Am J Transplant.* Apr 2013; 13(4): 911-918. PMID 23406373
20. Lucid CE, Savani BN, Engelhardt BG, et al. Extracorporeal photopheresis in patients with refractory bronchiolitis obliterans developing after allo-SCT. *Bone Marrow Transplant.* Mar 2011; 46(3): 426-9. PMID 20581885
21. Morrell MR, Despotis GJ, Lublin DM, et al. The efficacy of photopheresis for bronchiolitis obliterans syndrome after lung transplantation. *J Heart Lung Transplant.* Apr 2010; 29(4): 424-31. PMID 19853479
22. Urbani L, Mazzoni A, Catalano G, et al. The use of extracorporeal photopheresis for allograft rejection in liver transplant recipients. *Transplant Proc.* Dec 2004; 36(10): 3068-70. PMID 15686696
23. Urbani L, Mazzoni A, De Simone P, et al. Avoiding calcineurin inhibitors in the early post-operative course in high-risk liver transplant recipients: The role of extracorporeal photopheresis. *J Clin Apher.* 2007; 22(4): 187-94. PMID 17294458
24. Urbani L, Mazzoni A, Colombatto P, et al. Potential applications of extracorporeal photopheresis in liver transplantation. *Transplant Proc.* May 2008; 40(4): 1175-8. PMID 18555142
25. Jardine MJ, Bhandari S, Wyburn KR, et al. Photopheresis therapy for problematic renal allograft rejection. *J Clin Apher.* 2009; 24(4): 161-9. PMID 19536814
26. Kumlien G, Genberg H, Shanwell A, et al. Photopheresis for the treatment of refractory renal graft rejection. *Transplantation.* Jan 15 2005; 79(1): 123-5. PMID 15714180
27. Dall'Amico R, Murer L. Extracorporeal photochemotherapy: a new therapeutic approach for allograft rejection. *Transfus Apher Sci.* Jun 2002; 26(3): 197-204. PMID 12126206
28. Dall'Amico R, Murer L, Montini G, et al. Successful treatment of recurrent rejection in renal transplant patients with photopheresis. *J Am Soc Nephrol.* Jan 1998; 9(1): 121-7. PMID 9440096
29. Baron ED, Heeger PS, Hricik DE, et al. Immunomodulatory effect of extracorporeal photopheresis after successful treatment of resistant renal allograft rejection. *Photodermatol Photoimmunol Photomed.* Apr 2001; 17(2): 79-82. PMID 11338406

30. Sunder-Plassman G, Druml W, Steininger R, et al. Renal allograft rejection controlled by photopheresis. *Lancet*. Aug 19 1995; 346(8973): 506. PMID 7637500
31. Abu-Dalle I, Reljic T, Nishihori T, et al. Extracorporeal photopheresis in steroid-refractory acute or chronic graft-versus-host disease: results of a systematic review of prospective studies. *Biol Blood Marrow Transplant*. Nov 2014; 20(11): 1677-86. PMID 24867779
32. Flowers ME, Apperley JF, van Besien K, et al. A multicenter prospective phase 2 randomized study of extracorporeal photopheresis for treatment of chronic graft-versus-host disease. *Blood*. Oct 01 2008; 112(7): 2667-74. PMID 18621929
33. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Extracorporeal photopheresis for graft-versus-host disease. *TEC Assessments*. 2001;Volume 16:Tab 9.
34. Hautmann AH, Wolff D, Hahn J, et al. Extracorporeal photopheresis in 62 patients with acute and chronic GVHD: results of treatment with the COBE Spectra System. *Bone Marrow Transplant*. Mar 2013; 48(3): 439-45. PMID 22922407
35. Ussowicz M, Musiał J, Mielcarek M, et al. Steroid-sparing effect of extracorporeal photopheresis in the therapy of graft-versus-host disease after allogeneic hematopoietic stem cell transplantation. *Transplant Proc*. Nov 2013; 45(9): 3375-80. PMID 24182819
36. Weitz M, Strahm B, Meerpohl JJ, et al. Extracorporeal photopheresis versus standard treatment for acute graft-versus-host disease after haematopoietic stem cell transplantation in paediatric patients. *Cochrane Database Syst Rev*. Feb 25 2014; (2): CD009759. PMID 24569960
37. Weitz M, Strahm B, Meerpohl JJ, et al. Extracorporeal photopheresis versus alternative treatment for chronic graft-versus-host disease after haematopoietic stem cell transplantation in paediatric patients. *Cochrane Database Syst Rev*. Feb 25 2014; (2): CD009898. PMID 24569961
38. Buder K, Zirngibl M, Bapistella S, et al. Extracorporeal photopheresis versus alternative treatment for chronic graft-versus-host disease after haematopoietic stem cell transplantation in children and adolescents. *Cochrane Database Syst Rev*. Jun 09 2022; 6(6): CD009898. PMID 35679154
39. Kitko CL, Abdel-Azim H, Carpenter PA, et al. A Prospective, Multicenter Study of Closed-System Extracorporeal Photopheresis for Children with Steroid-Refractory Acute Graft-versus-Host Disease. *Transplant Cell Ther*. May 2022; 28(5): 261.e1-261.e7. PMID 35124293
40. Perotti C, Del Fante C, Tinelli C, et al. Extracorporeal photochemotherapy in graft-versus-host disease: a longitudinal study on factors influencing the response and survival in pediatric patients. *Transfusion*. Jun 2010; 50(6): 1359-69. PMID 20113452
41. Halle P, Paillard C, D'Incan M, et al. Successful extracorporeal photochemotherapy for chronic graft-versus-host disease in pediatric patients. *J Hematother Stem Cell Res*. Jun 2002; 11(3): 501-12. PMID 12183835
42. Salvaneschi L, Perotti C, Zecca M, et al. Extracorporeal photochemotherapy for treatment of acute and chronic GVHD in childhood. *Transfusion*. Oct 2001; 41(10): 1299-305. PMID 11606832
43. Berger M, Pessolano R, Albiani R, et al. Extracorporeal photopheresis for steroid resistant graft versus host disease in pediatric patients: a pilot single institution report. *J Pediatr Hematol Oncol*. Oct 2007; 29(10): 678-87. PMID 17921848
44. Kozlov A, Estrina M, Paina O, et al. Extracorporeal Photopheresis in Children with Chronic Graft-Versus-Host Disease. *Pharmaceuticals (Basel)*. Aug 17 2021; 14(8). PMID 34451905
45. Zhang H, Chen R, Cheng J, et al. Systematic review and meta-analysis of prospective studies for ECP treatment in patients with steroid-refractory acute GVHD. *Patient Prefer Adherence*. 2015; 9: 105-11. PMID 25653504
46. Mehta RS, Bassett R, Rondon G, et al. Randomized phase II trial of extracorporeal phototherapy and steroids vs. steroids alone for newly diagnosed acute GVHD. *Bone Marrow Transplant*. Jun 2021; 56(6): 1316-1324. PMID 33398094
47. Solh MM, Farnham C, Solomon SR, et al. Extracorporeal photopheresis (ECP) improves overall survival in the treatment of steroid refractory acute graft-versus-host disease (SR aGvHD). *Bone Marrow Transplant*. Feb 2023; 58(2): 168-174. PMID 36352015
48. Greinix HT, Knobler RM, Worel N, et al. The effect of intensified extracorporeal photochemotherapy on long-term survival in patients with severe acute graft-versus-host disease. *Haematologica*. Mar 2006; 91(3): 405-8. PMID 16531267
49. Batgi H, Dal MS, Erkurt MA, et al. Extracorporeal photopheresis in the treatment of acute graft-versus-host disease: A multicenter experience. *Transfus Apher Sci*. Oct 2021; 60(5): 103242. PMID 34420882

50. Jagasia M, Greinix H, Robin M, et al. Extracorporeal photopheresis versus anticytokine therapy as a second-line treatment for steroid-refractory acute GVHD: a multicenter comparative analysis. *Biol Blood Marrow Transplant.* Jul 2013; 19(7): 1129-33. PMID 23623892
51. Rubegni P, Feci L, Poggiali S, et al. Extracorporeal photopheresis: a useful therapy for patients with steroid-refractory acute graft-versus-host disease but not for the prevention of the chronic form. *Br J Dermatol.* Aug 2013; 169(2): 450-7. PMID 23534380
52. Shaughnessy PJ, Bolwell BJ, van Besien K, et al. Extracorporeal photopheresis for the prevention of acute GVHD in patients undergoing standard myeloablative conditioning and allogeneic hematopoietic stem cell transplantation. *Bone Marrow Transplant.* Jun 2010; 45(6): 1068-76. PMID 19915634
53. Perfetti P, Carlier P, Strada P, et al. Extracorporeal photopheresis for the treatment of steroid refractory acute GVHD. *Bone Marrow Transplant.* Nov 2008; 42(9): 609-17. PMID 18660840
54. Malik MI, Litzow M, Hogan W, et al. Extracorporeal photopheresis for chronic graft-versus-host disease: a systematic review and meta-analysis. *Blood Res.* Jun 2014; 49(2): 100-6. PMID 25025011
55. Ontario Health Technology Advisory Committee. OHTAC Recommendation: Extracorporeal Photopheresis. 2006; http://www.hqontario.ca/english/providers/program/ohtac/tech/recommend/rec_ecp_032806.pdf. Accessed September 6, 2023.
56. Foss FM, DiVenuti GM, Chin K, et al. Prospective study of extracorporeal photopheresis in steroid-refractory or steroid-resistant extensive chronic graft-versus-host disease: analysis of response and survival incorporating prognostic factors. *Bone Marrow Transplant.* Jun 2005; 35(12): 1187-93. PMID 15852025
57. Dignan FL, Aguilar S, Scarisbrick JJ, et al. Impact of extracorporeal photopheresis on skin scores and quality of life in patients with steroid-refractory chronic GVHD. *Bone Marrow Transplant.* May 2014; 49(5): 704-8. PMID 24566709
58. Kansu E, Ward D, Sanchez AP, et al. Extracorporeal photopheresis for the treatment of chronic graft versus host disease. *Hematology.* Dec 2022; 27(1): 785-794. PMID 35802815
59. Dal MS, Batgi H, Erkurt MA, et al. Extracorporeal photopheresis in steroid-refractory chronic graft-versus-host disease: A retrospective multicenter study. *Transfus Apher Sci.* Oct 2021; 60(5): 103243. PMID 34420879
60. Greinix HT, Volc-Platzer B, Knobler R. Criteria for assessing chronic GVHD. *Bone Marrow Transplant.* Mar 2000; 25(5): 575. PMID 10713639
61. Rubegni P, Cuccia A, Sbano P, et al. Role of extracorporeal photochemotherapy in patients with refractory chronic graft-versus-host disease. *Br J Haematol.* Jul 2005; 130(2): 271-5. PMID 16029456
62. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Extracorporeal photopheresis for autoimmune disease. *TEC Assessments.* 2001;Volume 16:Tab 10.
63. Rook AH, Freundlich B, Jegasothy BV, et al. Treatment of systemic sclerosis with extracorporeal photochemotherapy. Results of a multicenter trial. *Arch Dermatol.* Mar 1992; 128(3): 337-46. PMID 1550365
64. Fries JF, Seibold JR, Medsger TA. Photopheresis for scleroderma? No!. *J Rheumatol.* Jul 1992; 19(7): 1011-3. PMID 1512753
65. Melski JW. Price of technology. A blind spot. *JAMA.* Mar 18 1992; 267(11): 1516-8. PMID 1538542
66. Trentham DE. Photochemotherapy in systemic sclerosis. The stage is set. *Arch Dermatol.* Mar 1992; 128(3): 389-90. PMID 1550373
67. Papp G, Horvath IF, Barath S, et al. Immunomodulatory effects of extracorporeal photochemotherapy in systemic sclerosis. *Clin Immunol.* Feb 2012; 142(2): 150-9. PMID 22036269
68. Cavaletti G, Perseghin P, Dassi M, et al. Extracorporeal photochemotherapy: a safety and tolerability pilot study with preliminary efficacy results in refractory relapsing-remitting multiple sclerosis. *Neurol Sci.* Apr 2006; 27(1): 24-32. PMID 16688596
69. Ludvigsson J, Samuelsson U, Ernerudh J, et al. Photopheresis at onset of type 1 diabetes: a randomised, double blind, placebo controlled trial. *Arch Dis Child.* Aug 2001; 85(2): 149-54. PMID 11466190
70. Sanli H, Akay BN, Ayyildiz E, et al. Remission of severe autoimmune bullous disorders induced by long-term extracorporeal photochemotherapy. *Transfus Apher Sci.* Dec 2010; 43(3): 353-359. PMID 21035398

71. Rubegni P, Poggiali S, Cevenini G, et al. Long term follow-up results on severe recalcitrant atopic dermatitis treated with extracorporeal photochemotherapy. *J Eur Acad Dermatol Venereol.* Apr 2013; 27(4): 523-6. PMID 22540319
72. Wolf P, Georgas D, Tomi NS, et al. Extracorporeal photochemotherapy as systemic monotherapy of severe, refractory atopic dermatitis: results from a prospective trial. *Photochem Photobiol Sci.* Jan 2013; 12(1): 174-81. PMID 22948099
73. Reinisch W, Knobler R, Rutgeerts PJ, et al. Extracorporeal photopheresis (ECP) in patients with steroid-dependent Crohn's disease: an open-label, multicenter, prospective trial. *Inflamm Bowel Dis.* Feb 2013; 19(2): 293-300. PMID 22573600
74. Edelson R, Berger C, Gasparro F, et al. Treatment of cutaneous T-cell lymphoma by extracorporeal photochemotherapy. Preliminary results. *N Engl J Med.* Feb 05 1987; 316(6): 297-303. PMID 3543674
75. Knobler R, Duvic M, Querfeld C, et al. Long-term follow-up and survival of cutaneous T-cell lymphoma patients treated with extracorporeal photopheresis. *Photodermatol Photoimmunol Photomed.* Oct 2012; 28(5): 250-7. PMID 22971190
76. Freiman A, Sasseville D. Treatment of mycosis fungoides: overview. *J Cutan Med Surg.* 2006; 10(5): 228-33. PMID 17234106
77. Keehn CA, Belongie IP, Shistik G, et al. The diagnosis, staging, and treatment options for mycosis fungoides. *Cancer Control.* Apr 2007; 14(2): 102-11. PMID 17387295
78. Knobler E. Current management strategies for cutaneous T-cell lymphoma. *Clin Dermatol.* 2004; 22(3): 197-208. PMID 15262305
79. Scarisbrick JJ. Staging and management of cutaneous T-cell lymphoma. *Clin Exp Dermatol.* Mar 2006; 31(2): 181-6. PMID 16487086
80. Whittaker SJ, Foss FM. Efficacy and tolerability of currently available therapies for the mycosis fungoides and Sezary syndrome variants of cutaneous T-cell lymphoma. *Cancer Treat Rev.* Apr 2007; 33(2): 146-60. PMID 17275192
81. Gao C, McCormack C, van der Weyden C, et al. Prolonged survival with the early use of a novel extracorporeal photopheresis regimen in patients with Sézary syndrome. *Blood.* Oct 17 2019; 134(16): 1346-1350. PMID 31467061
82. Scarisbrick JJ, Taylor P, Holtick U, et al. U.K. consensus statement on the use of extracorporeal photopheresis for treatment of cutaneous T-cell lymphoma and chronic graft-versus-host disease. *Br J Dermatol.* Apr 2008; 158(4): 659-78. PMID 18241274
83. Trautinger F, Knobler R, Willemze R, et al. EORTC consensus recommendations for the treatment of mycosis fungoides/Sézary syndrome. *Eur J Cancer.* May 2006; 42(8): 1014-30. PMID 16574401
84. Whittaker SJ, Marsden JR, Spittle M, et al. Joint British Association of Dermatologists and U.K. Cutaneous Lymphoma Group guidelines for the management of primary cutaneous T-cell lymphomas. *Br J Dermatol.* Dec 2003; 149(6): 1095-1107. PMID 14696593
85. National Cancer Institute. Mycosis Fungoides (Including Sezary Syndrome) Treatment (PDQ) Health Professional Version. June 27, 2023; <https://www.cancer.gov/types/lymphoma/hp/mycosis-fungoides-treatment-pdq> Accessed September 6, 2023.
86. Miller JD, Kirkland EB, Domingo DS, et al. Review of extracorporeal photopheresis in early-stage (IA, IB, and IIA) cutaneous T-cell lymphoma. *Photodermatol Photoimmunol Photomed.* Oct 2007; 23(5): 163-71. PMID 17803594
87. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood.* May 15 2005; 105(10): 3768-85. PMID 15692063
88. Verleden GM, Glanville AR, Lease ED, et al. Chronic lung allograft dysfunction: Definition, diagnostic criteria, and approaches to treatment-A consensus report from the Pulmonary Council of the ISHLT. *J Heart Lung Transplant.* May 2019; 38(5): 493-503. PMID 30962148
89. Martin PJ, Rizzo JD, Wingard JR, et al. First- and second-line systemic treatment of acute graft-versus-host disease: recommendations of the American Society of Blood and Marrow Transplantation. *Biol Blood Marrow Transplant.* Aug 2012; 18(8): 1150-63. PMID 22510384
90. Messina C, Locatelli F, Lanino E, et al. Extracorporeal photochemotherapy for paediatric patients with graft-versus-host disease after haematopoietic stem cell transplantation. *Br J Haematol.* Jul 2003; 122(1): 118-27. PMID 12823353

91. National Cancer Institute. Childhood Hematopoietic Cell Transplantation (PDQ) Health Professional Version. February 4, 2022; https://www.cancer.gov/types/childhood-cancers/hp-stem-cell-transplant#_5 Accessed September 6, 2023.
92. National Comprehensive Cancer Network (NCCN). NCCN Clinical practice Guidelines in Oncology: Primary Cutaneous Lymphomas. Version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf. Accessed September 6, 2023.
93. Center for Medicare & Medicaid Services (CMS). National Coverage Determination (NCD) for Extracorporeal Photopheresis (110.4). 2012; <https://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=113>. Accessed September 6, 2023.