

Evidence Based Guideline

Therapeutic Apheresis

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Description of Procedure or Service

The terms therapeutic apheresis, plasmapheresis and plasma exchange are often used interchangeably, but actually denote different procedures.

Apheresis is a general term describing a procedure in which blood is removed from the body; a portion of the blood is separated into various components and manipulated in some way, and then returned to the patient. It is generally performed to remove harmful substances from the blood or from a component of the blood. The blood withdrawal procedure is performed by placing a catheter into the patient's vein. The catheter is connected to a machine (centrifuge) that draws the blood out and then separates it into red blood cells, white blood cells, and plasma. Plasma is the watery fluid surrounding the blood cells as they flow through the veins.

In plasmapheresis, it is the plasma that is separated from the blood and manipulated in a variety of ways. This is the most common type of apheresis procedure. However, leukapheresis or lymphocytapheresis also describes apheresis procedures in which the white blood cells are isolated and retained. As another example, peripheral stem-cell collection, done in preparation for autologous bone marrow transplant, involves an apheresis procedure in which the critical stem cells are isolated and retained.

Plasma exchange (PE) is a procedure in which the plasma is separated from the blood, discarded in total, and replaced with a substitution fluid such as albumin or with donated plasma from a healthy person. This is generally performed to remove toxins or autoantibodies that have accumulated in the plasma. Rapidly reducing the autoantibodies may sometimes lead to a rebound overproduction of the same antibodies. This rebound production of antibodies is thought to make the replicating pathogenic cells more vulnerable to cytotoxic drugs. For this reason, it is often performed to enhance the effectiveness of cytotoxic drugs.

Low density lipoprotein apheresis describes a variety of technologies used to acutely remove low density lipoprotein (LDL) from the plasma. LDL apheresis has been investigated as a technique to treat patients with familial hypercholesterolemia (FH), since they may not respond adequately to lipid-lowering drugs.

In extracorporeal immunoadsorption using protein A columns, also referred to as protein immunoadsorption therapy, plasma is collected from the patient in a pheresis procedure. Circulating immune complexes and immunoglobulin are selectively removed from the plasma. The plasma is then be returned to the patient, thus eliminating the need for plasma exchange.

Applications of therapeutic apheresis can be subdivided into 2 general categories: 1) acute self-limited diseases in which apheresis is used to acutely lower the circulating pathogenic substance; and 2) chronic diseases, in which there is ongoing production of pathogenic autoantibodies. Because apheresis does not address the underlying cause of the disease, and due to the phenomenon of rebound antibody production its use in chronic diseases has been more controversial than in acute self-limited diseases.

Policy: Therapeutic Apheresis

Evidence Based Guideline for Therapeutic Apheresis

Therapeutic Apheresis may be appropriate for use in the treatment of the following conditions:

Type of condition	Specifics
Acute self-limited conditions	
Conditions associated with hyperviscosity syndromes such as B-cell lymphocyte neoplasms such as multiple myeloma and Waldenstrom’s macroglobulinemia	Treatment is principally directed at the underlying disorder, but PE may be used to acutely lower the serum viscosity.
myasthenia gravis	As short term therapy in patients with acute exacerbations associated with severe weakness (crisis), or as part of preoperative preparation.
Guillian-Barre Syndrome	For severely ill patients with grade 3-5 disease (an ability to walk 5 meters with assistance, confinement to a bed or chairbound, or requiring assisted ventilation for at least part of the day or night) who do not initially respond to prednisone.
Thrombotic microangiopathy manifested in both Thrombotic thrombocytopenic purpura (TTP) and Hemolytic uremic syndrome (HUS)	Performed daily until a response is noted; length of treatment averages about one month with increasing intervals between PE treatments.
Idiopathic thrombocytopenic purpura (ITP) in emergency situations	Management of acute bleeding typically involves immediate platelet transfusion, occasionally in conjunction with a single infusion of IV immunoglobulin. PE is occasionally used in emergency situations.
HELLP syndrome of pregnancy	Principal form of treatment is delivery of the fetus. If fetus cannot be safely delivered, PE may be indicated, or if the maternal thrombocytopenia persists into the postnatal period, PE may be necessary.
Post-transfusion purpura	PE is the initial treatment of choice.
Progressive renal failure due to anti-basement membrane antibodies (i.e., Goodpasture syndrome)	
Acute fulminant CNS demyelination, associated with multiple sclerosis or other conditions, such as transverse myelitis	
Chronic conditions	
chronic inflammatory demyelinating polyneuropathy (CIDP)	PE reserved for those patients who do not respond to treatment with prednisone. PE may be required on a chronic basis, its frequency titrated according to the durability of the patient’s response.
Rheumatoid Arthritis	For moderate to severe rheumatoid arthritis in adult patients with long-standing disease who have failed or are intolerant to disease-modifying anti-rheumatic drugs.

Policy: Therapeutic Apheresis

Type of condition	Specifics
IgA or IgG paraproteinemia polyneuropathy	
Familial Hypercholesterolemia 1) homozygous 2) heterozygous	As an alternative to plasma pheresis in patients who have failed a 6-month trial of diet therapy and maximum tolerated combination of drug therapy AND who meet the following FDA-approved indications (all LDL levels represent the best achievable LDL level after a program of diet and drug therapy): a) functional hypercholesterolemic heterozygotes with LDL equal to or greater than 300 mg/dL b) functional hypercholesterolemic heterozygotes with LDL equal to or greater than 200 mg/dL AND documented coronary artery disease.
Solid organ transplant	Prior to transplant for treatment of patients at high risk of antibody-mediated rejection, including highly sensitized patients and those receiving an ABO incompatible organ. And following solid organ transplant for treatment of antibody-mediated rejection.

Medical Evidence regarding Therapeutic Apheresis indicates it is not recommended in the following situations:

Plasma exchange or plasmapheresis may not be appropriate for some conditions. The use of therapeutic apheresis would be considered investigational in the treatment of the following conditions. (This is not an all inclusive list.)

- Scleroderma (systemic sclerosis)
- Systemic lupus erythematosus
- Polymyositis, dermatomyositis and inclusion body myositis
- Pemphigus
- Guillain-Barre syndrome, grades 1-2
- Chronic progressive relapsing remitting multiple sclerosis
- Amyotrophic lateral sclerosis
- Paraneoplastic syndromes including Lambert-Eaton myasthenic syndrome
- Paraproteinemic polyneuropathy including monoclonal gammopathy of undetermined significance (MGUS)
- Chronic fatigue syndrome
- Regional enteritis, (Crohn's Disease)
- Rapidly progressive glomerulonephritis, excluding those related to anti-basement membrane immunoglobulins (i.e., Goodpasture's syndrome)
- Asthma

Policy: Therapeutic Apheresis

- Stiff man syndrome
- Other autoimmune diseases
- Treatment of cancer or cancer related syndromes, other than those explicitly listed above in the "when Therapeutic Apheresis is covered" section

Benefits Application

Please refer to certificate for availability of benefit. This guideline relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore certificate language should be reviewed before applying the terms of the policy.

Billing/Coding/Physician Documentation Information

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

Applicable codes: 36511, 36512, 36513, 36514, 36515, 36516, P9034, P9035, P9036, P9037, P9050

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual - 3/96

Medical Policy Advisory Group - 12/2/99

BCBSA Medical Policy Reference Manual - 7/16/99; 8.02.04

BCBSA Medical Policy Reference Manual - 12/1/99; 8.02.03

Medical Policy Advisory Group 3/2001

BCBSA Medical Policy Reference Manual 8.02.02 5/15/02

Specialty Matched Consultant Advisory Panel - 9/2002

Specialty Matched Consultant Advisory Panel - 4/2003

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.02.02, 12/17/03.

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.02.04, 3/7/06.

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.02.02, 4/25/06.

BCBSA Medical Policy Reference Manual [Electronic Version]. 8.02.03, 4/25/06.

Centers for Medicare & Medicaid Services. National Coverage Determination, Manual Section Number 20.5. Retrieved 9/8/06 from http://www.cms.hhs.gov/mcd/viewncd.asp?ncd_id=20.5

Canadian Coordinating Office for Health Technology Assessment (CCOHTA). Extracorporeal Immunoadsorption Treatment for Rheumatoid Arthritis. January 2002.

U.S. Food and Drug Administration. Premarket Approval PROSORBA COLUMN, 4/14/04. Retrieved 9/11/06 from <http://www.accessdata.fda.gov/scripts/cdrh/devicesatfda/index.cfm?db=PMA&id=6509>

ECRI Custom Hotline Response-Protein A Columns (PROSORBA) for Rheumatoid Arthritis (8/30/05) retrieved 9/11/06 from http://www.ta.ecri.org/Hotline/Prod/summary/archive.aspx?doc_id=7709

Policy: Therapeutic Apheresis

Policy Implementation/Update Information

- 5/81 Original Policy
- 4/82 Reaffirmed
- 3/83 Reaffirmed
- 6/85 Revised: systemic Lupus erythematosus
- 5/87 Evaluated: Guillain-Barre Syndrome
- 7/96 Revised: National Association reviewed 3/96. Added numbers 11 through 18 under those conditions covered and added numbers 4 and 5 under investigational.
- 7/97 Reaffirmed: Added PCP and MedPoint to Product Indicators.
- 9/99 Reformatted, Description of Procedure or Service changed, Medical Term Definitions added.
- 12/99 Reaffirmed, Medical Policy Advisory Group
- 12/00 Revised. Removed diagnosis for Rheumatoid Arthritis from investigational status to a covered indication. Added other investigational indications. 2001 HCPCS codes added; P9034, P9035, P9036, P9037. System coding changes.
- 3/01 Revised to include low density lipid apheresis criteria. Medical Policy Advisory Group approved.
- 10/02 Revised policy to include both covered and noncovered criteria. Added code P9050. Specialty Matched Consultant Advisory Panel review. System coding changes.
- 1/03 Codes 36511, 36512, 36513, 36514, 36515, 36516 added to the policy. Deleted codes 36520 and 36521 from the Billing/Coding section. System coding changes.
- 5/03 Specialty Matched Consultant Advisory Panel review. No change to policy. Reaffirm.
- 4/7/05 Specialty Matched Consultant Advisory Panel [MPAG] review on 3/10/2005. No changes made to policy criteria. Reference added.
- 4/21/05 Benefit and Billing/Coding sections updated for consistent policy language. Sentence referring to code deletions removed in Billing/Coding section.
- 9/18/06 Description section revised for clarity. Added the following to the When Appropriate section: as part of preoperative preparation in myasthenia gravis and prior to solid organ transplant for treatment of antibody-mediated rejection including highly sensitized patients and those receiving an ABO incompatible organ and following solid organ transplant for treatment of anti-mediated rejection. Rheumatoid arthritis added to the list of Not Recommended conditions and renal transplant recipients deleted. Medical Policy changed to Evidence Based Guideline.
- 10/16/06 Added information regarding extracorporeal immunoabsorption therapy to Description section. "Rheumatoid arthritis" deleted from the Not Recommended section. References updated.
- 4/9/07 Routine biennial review. Specialty Matched Consultant Advisory Panel review 3/15/07. No changes to policy coverage criteria. (adn)
- 4/27/09 Routine biennial review. Specialty Matched Consultant Advisory Panel review 3/15/07. No changes to policy coverage criteria. (adn)

Policy: Therapeutic Apheresis

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