



# CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

**Subject Extracorporeal  
Immunoadsorption With  
Protein A Column**

**Effective Date ..... 6/15/2011  
Next Review Date ..... 6/15/2012  
Coverage Policy Number ..... 0377**

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## Hyperlink to Related Coverage Policies

Apheresis for Familial Hypercholesterolemia  
 Photopheresis (Extracorporeal  
 Photochemotherapy)  
 Plasmapheresis

### INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2011 CIGNA

## Coverage Policy

**CIGNA covers extracorporeal immunoadsorption with protein A column as medically necessary for EITHER of the following indications:**

- diagnosis of idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP) or hemolytic uremic syndrome (HUS) when **ONE** of the following is met:
  - platelet count less than 10,000 mm<sup>3</sup> in a child or 20,000 mm<sup>3</sup> in an adult
  - platelet count less than 20,000 mm<sup>3</sup> in a child with significant mucous membrane bleeding
  - platelet count less than 50,000 mm<sup>3</sup> in an adult with EITHER significant mucous membrane bleeding or risk factors for bleeding, such as hypertension, peptic ulcer disease, or a vigorous lifestyle
- diagnosis of rheumatoid arthritis (RA) when there is failure, contraindication or intolerance of disease-modifying anti-rheumatic drugs (DMARDs), including TNF-inhibitors.

**CIGNA covers extracorporeal immunoadsorption using the Immunosorba<sup>®</sup> protein A column (i.e., Excorim<sup>®</sup> Immunoadsorption System), as medically necessary when provided in accordance with the Humanitarian Device Exemption (HDE) specifications of the U.S. Food and Drug Administration (FDA) for the treatment of an individual with hemophilia A and B who have Factor VIII or IX inhibitor titers above 10 Bethesda Units (BU)/milliliter (ml).**

**CIGNA does not cover extracorporeal immunoadsorption with protein A column for ANY other indication, including, but not limited to the following, because it is considered experimental, investigational or unproven:**

- chronic inflammatory demyelinating polyradiculoneuropathy
- dermatomyositis
- dilated cardiomyopathy
- myasthenia gravis
- paraneoplastic neurologic syndromes
- pemphigus vulgaris
- renal transplantation
- systemic lupus erythematosus

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## **General Background**

According to the American Society for Apheresis (ASFA), therapeutic plasma exchange is a therapeutic procedure in which an individual's blood is passed through a medical device which separates out plasma from other components of blood; the plasma is removed and replaced with a replacement solution such as colloid solution (e.g., albumin and/or plasma) or combination of crystalloid/colloid solution. Therapeutic apheresis is a therapeutic procedure where an individual's blood is passed through an extracorporeal medical device which separates the components of blood in order to treat disease. Therapeutic apheresis is a general term which includes all apheresis-based procedures used therapeutically (Szczepiorkowski, et al., 2007b).

Immunoadsorption is a therapeutic procedure in which plasma, after separation from the blood, is passed through a medical device which has a capacity to remove immunoglobulins by specifically binding them to the active component (e.g., Staphylococcal protein A) of the device (Szczepiorkowski, et al., 2007a).

Immunoadsorption specifically targets the substances thought to be pathogenic in a particular disease entity and removes them by the use of specific or semispecific ligands or adsorbers that bind IgG and immune complexes. Ligands bound to a column matrix may be relatively nonspecific chemical sorbents, such as charcoal or heparin, or specific ligands, such as monoclonal antibodies and recombinant protein antigens. The protein A (SPA) is a major cell wall component of *Staphylococcus aureus*. Protein A column matrix has a high affinity for the Fc portion of IgG1, IgG2, and IgG4 and for immune complexes containing these IgG subtypes.

### **U.S. Food and Drug Administration (FDA)**

Prosorba<sup>®</sup> column or Extracorporeal Immunoadsorption Protein A Column (Fresenius Medical Care, Lexington, MA [formerly owned by Cypress Bioscience, Inc., San Diego, CA) received Premarket Approval (PMA) in 1999 (FDA, 1999). The Prosorba column is indicated in the therapeutic removal of immunoglobulin G (IgG) and IgG-containing circulating immune complexes from plasma in patients with idiopathic thrombocytopenic purpura (ITP) having platelet counts less than 100,000 mm<sup>3</sup>. Prosorba Column is indicated for use in the therapeutic reduction of the signs and symptoms of moderate to severe rheumatoid arthritis (RA) in adult patients with long-standing disease who have failed or are intolerant to disease-modifying anti-rheumatic drugs (DMARDs) (FDA, 1999).

In 1998, the FDA granted a Humanitarian Device Exemption (HDE) to Cobe BCT, Inc., Lakewood, CO for the Excorim Immunoadsorption System (in 2000, Fresenius HemoCare acquired this system from Excorim AB). This system is FDA-approved under the HDE for the treatment of patients with hemophilia A and B who have Factor VIII or IX inhibitor titers above 10 Bethesda Units per milliliter (BU/ml). The intended purpose of treatment is to lower the inhibitor levels so that routine clotting replacement therapy can be considered. It may be used in an acute setting (to control bleeding due to an acute hemorrhage or for emergency surgery) or as a preventive measure, to prepare patients for elective surgery.

### **Indications**

The U.S. Food and Drug Administration (FDA)-approved indications include idiopathic thrombocytopenic purpura (ITP), rheumatoid arthritis and hemophilia. Off-label uses that have been proposed include thrombotic

thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS). Other proposed applications that have been studied include:

- chronic inflammatory demyelinating polyradiculoneuropathy
- dermatomyositis
- dilated cardiomyopathy
- myasthenia gravis
- paraneoplastic neurologic syndromes
- pemphigus vulgaris
- renal transplantation
- systemic lupus erythematosus

## Literature Review

**Idiopathic Thrombocytopenic Purpura (ITP), Thrombotic Thrombocytopenic Purpura (TTP), Hemolytic Uremic Syndrome (HUS):** Evidence in the peer-reviewed scientific literature supports the use of extracorporeal immunoadsorption with protein A column for ITP (Snyder, et al., 1992; Handelsman, et al., 1990); TTP (Gaddis, et al., 1997; Snyder, et al., 1993; Handelsman, et al., 1990); and HUS (Korec, et al., 1986; Handelsman, et al., 1990; Snyder, et al., 1993). For these diagnoses, other treatments such as intravenous immunoglobulin (IVIG), corticosteroids, transfusions, splenectomy, and plasmapheresis are typically attempted prior to extracorporeal immunoadsorption with protein A column. Examples of patient inclusion criteria for the studies cited included “treatment-resistant” disease, platelet counts less than 50,000/ $\mu$ L or platelet count considered “life-threatening”.

**Rheumatoid Arthritis:** Evidence in the peer-reviewed scientific literature supports the use of extracorporeal immunoadsorption with protein A column as a treatment option for rheumatoid arthritis that is refractive to DMARDs and conventional therapy (Roth, 2004; Hailey and Topfer, 2002; Gendreau, et al., 2001; Caldwell, et al., 1999; Felson, et al., 1999; Wiesenhutter, et al., 1994).

**Hemophilia:** Immunosorba is a double-column system with a nearly unlimited adsorption capacity (the capacity of ProSORBA is restricted to a maximum of 2000 ml of plasma) and is efficacious where rapid and effective antibody removal is required. For this reason, Immunosorba was approved by the FDA under the Humanitarian Device Exemption (HDE) for the treatment of individuals with hemophilia A and B who have Factor VIII or IX inhibitor titers above 10 Bethesda Units (BU)/ml (Hershko and Naparstek, et al., 2005; Watt, et al., 1992; Freiburghaus, et al., 1998; Berntorp, et al 2006).

**Other Indications:** Although there are some favorable results from case reports and small case series, there is insufficient evidence in the published, peer-reviewed scientific literature supporting the use of extracorporeal immunoadsorption with protein A column for any other condition including but not limited to: chronic inflammatory demyelinating polyradiculoneuropathy (Zinman, et al., 2005; Hadden, et al., 2002); dermatomyositis (Sebastiani, et al., 2009); dilated cardiomyopathy (Burgstaler, et al., 2007; Cooper, et al., 2007; Staudt, et al., 2006; Staudt, et al., 2005; Felix, et al., 2000); myasthenia gravis (Blaha, et al., 2010; Schneidewind, et al., 2001; Benny, et al., 1999); paraneoplastic neurologic syndromes (Batchelor, et al., 1998; Cher, et al., 1995); pemphigus vulgaris (Shimanovich, et al., 2008); renal transplantation (antibody mediated rejection and human leukocyte antigens desensitization) (Böhmgig, et al., 2007; Lorenz, et al., 2005; Haas, et al., 2002; Kriaa, et al., 1995; Kupin, et al., 1991); and systemic lupus erythematosus (Biesenbach, et al., 2009; Braun, et al., 2000).

## Professional Societies/Organizations

**American Society for Apheresis (ASFA):** ASFA published Guidelines on the use of Therapeutic Apheresis in Clinical Practice (Szczepiorkowski, et al., 2007a; Szczepiorkowski, et al., 2007b; Shaz, et al., 2007). The ASFA reviewed numerous modalities, including immunoadsorption. The ASFA states that “extracorporeal immunoadsorption with Staphylococcal protein A silica may be considered in patients with refractory ITP, with life-threatening bleeding or in whom splenectomy is contraindicated”. The ASFA does not address protein A immunoadsorption specifically under the diagnoses headings of TTP or HUS. Regarding rheumatoid arthritis, the ASFA notes immunoadsorption using protein A column is a therapeutic option only for patients who have failed treatment with traditional DMARDs as well as the newer biologic agents, and who have active refractory disease. Szczepiorkowski et al. (2007a) added a footnote to the guideline stating, “In December 2006 the production of Staphylococcal protein A agarose (Immunosorba1) and Staphylococcal A silica (ProSORBA1)

columns was discontinued in the United States. These devices are no longer available in the United States but may be available in other countries." There has been no update to these guidelines since 2007.

The ASFA addressed the therapeutic apheresis modality of immunoadsorption for the following disease groups/conditions:

- Hematologic - Coagulation factor inhibitors - Category III
- Hematologic - Refractory Idiopathic thrombocytopenic purpura - Category II
- Miscellaneous - Dilated cardiomyopathy - Category P
- Neurological - Paraneoplastic neurologic syndromes - Category III
- Neurological - Paraproteinemic polyneuropathies (IgG/IgA/IgM) - Category III
- Rheumatic - Rheumatoid arthritis, refractory - Category II

#### \*ASFA Categories

- Category I include diseases for which TA is standard and acceptable, either as a primary therapy or a valuable first-line adjunct therapy. (The perception of efficacy in these disorders is usually based on well designed randomized controlled trials or on a broad and non-controversial base of published experience.) Note that this designation need not imply that TA is mandatory in all cases.
- Category II denotes diseases for which TA is generally accepted but considered to be supportive or adjunctive to other, more definitive treatments, rather than a primary first-line therapy. (Randomized controlled studies are available for some of these disorders, but in others the literature contains only small series or informative case studies.)
- Category III diseases are those in which there is a suggestion of benefit for which existing evidence is insufficient, either to establish the efficacy of TA or to clarify the risk/benefit (or sometimes the cost/benefit) ratio associated with TA. Included are disorders in which controlled trials have produced conflicting results or for which anecdotal reports are too few or too variable to support an adequate consensus. Therapeutic apheresis may reasonably be used in such patients when conventional therapies do not produce an adequate response or as part of an IRB-approved research protocol.
- Category IV indicates disorders for which controlled trials have not shown benefit or anecdotal reports have been discouraging. TA for these disorders is discouraged and should be carried only in the context of an IRB-approved research protocol.
- Category P (pending) includes diseases which can be treated by therapeutic apheresis using devices that are not available in the US and/or do not have FDA clearance. This category is generally assigned to those diseases where the devices are being studied in Phase III trials in the US.

**American Society of Hematology (ASH):** The updated 2011 ASH Clinical Practice Guideline on the Evaluation and Management of Immune Thrombocytopenia (ITP) does not mention protein A column as a treatment modality as they did in the 1996 Practice Guideline. The authors state that, "This recommendation has major changes to the 1996 ASH guideline insofar as we have moved away from recommendations for treatment based on the platelet count. The goal of all treatment strategies for ITP in children, or in adults, is to achieve a platelet count that is associated with adequate hemostasis, rather than a "normal" platelet count." The authors state that, "The decision to treat should involve a discussion with the patient and consideration of the severity of bleeding, anticipated surgical procedures, medication side effects, and health-related quality of life" (Neunert, et al., 2011).

**American College of Rheumatology (ACR):** The ACR guidelines for the management of RA states that the use of protein A column should be considered only for patients with refractory RA in whom treatment with several DMARDs has failed (ACR, 2002). There has been no update to this guideline since 2002.

#### Summary

There are some published data to suggest that extracorporeal immunoadsorption with protein A column may be used as a safe and effective treatment for patients with idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP) or hemolytic uremic syndrome (HUS). Generally, other treatments have been tried prior to extracorporeal immunoadsorption with protein A column. Additionally, evidence supports the use of extracorporeal immunoadsorption with protein A column to treat rheumatoid arthritis when there is failure, contraindication or intolerance of disease-modifying anti-rheumatic drugs (DMARDs). The peer-reviewed literature also contains studies that support the use of the Immunosorba protein A columns (Excorim

Immunoabsorption System) for the treatment of individuals with hemophilia A and B who have Factor VIII or IX inhibitor titers above 10 Bethesda Units (BU)/milliliter (ml).

Although there are some favorable case reports and small case series; there is insufficient evidence in the published, peer-reviewed scientific literature supporting the use of extracorporeal immunoabsorption with protein A column for any other indication. The safety and efficacy of extracorporeal immunoabsorption with protein A column for other indications remains unproven. Optimal treatment protocols, duration and short- and long-term impact on health outcomes have yet to be determined.

## Coding/Billing Information

**Note:** This list of codes may not be all-inclusive.

### Covered when medically necessary:

CPT <sup>®*</sup> Codes	Description
36515	Therapeutic apheresis; with extracorporeal immunoabsorption and plasma reinfusion

ICD-9-CM Diagnosis Codes	Description
283.11	Hemolytic-uremic syndrome
286.0	Congenital factor III disorder
286.1	Congenital factor IX disorder
287.30-287.39	Primary thrombocytopenia (includes idiopathic thrombocytopenic purpura)
446.6	Thrombotic microangiopathy
714.0-714.4	Rheumatoid arthritis

### Experimental/Investigational/Unproven/Not Covered:

ICD-9-CM Diagnosis Codes	Description
272.0	Pure hypercholesterolemia
357.81	Chronic inflammatory demyelinating polyradiculoneuropathy
358.00	Myasthenia gravis without (acute) exacerbation
358.01	Myasthenia gravis with (acute) exacerbation
694.4	Pemphigus
710.0	Systemic lupus erythematosus
710.03	Dermatomyositis
V42.0	Organ or tissue replaced by transplant; kidney
	All other codes

\*Current Procedural Terminology (CPT<sup>®</sup>) © 2008 American Medical Association: Chicago, IL.

## References

1. American College of Rheumatology Subcommittee on Rheumatoid Arthritis Guidelines. Guidelines for the management of rheumatoid arthritis: 2002 Update. *Arthritis Rheum.* 2002 Feb;46(2):328-46.

2. Batchelor TT, Platten M, Hochberg FH. Immunoabsorption therapy for paraneoplastic syndromes. *J Neurooncol.* 1998 Nov;40(2):131-6.
3. Benny WB, Sutton DM, Oger J, Bril V, McAteer MJ, Rock G. Clinical evaluation of a staphylococcal protein A immunoabsorption system in the treatment of myasthenia gravis patients. *Transfusion.* 1999 Jul;39(7):682-7.
4. Berntorp E. Options for treating acute bleeds in addition to bypassing agents: extracorporeal immunoabsorption, FVIII/FIX, desmopressin and antifibrinolytics. *Haemophilia.* 2006 Dec;12 Suppl 6:62-5; discussion 65-6.
5. Biesenbach P, Schmaldienst S, Smolen JS, Hörl WH, Derfler K, Stummvoll GH. Immunoabsorption in SLE: three different high affinity columns are adequately effective in removing autoantibodies and controlling disease activity. *Atheroscler Suppl.* 2009 Dec 29;10(5):114-21.
6. Blaha M, Pit'ha J, Blaha V, Lanska M, Maly J, Filip S, Langrova H. Extracorporeal immunoglobulin elimination for the treatment of severe myasthenia gravis. *J Biomed Biotechnol.* 2010;2010:419520. Epub 2010 Mar 15.
7. Böhmig GA, Wahrmann M, Regele H, Exner M, Robl B, Derfler K, et al. Immunoabsorption in severe C4d-positive acute kidney allograft rejection: a randomized controlled trial. *Am J Transplant.* 2007 Jan;7(1):117-21.
8. Braun N, Erley C, Klein R, Kötter I, Saal J, Risler T. Immunoabsorption onto protein A induces remission in severe systemic lupus erythematosus. *Nephrol Dial Transplant.* 2000 Sep;15(9):1367-72.
9. Burgstaler EA, Cooper LT, Winters JL. Treatment of chronic dilated cardiomyopathy with immunoabsorption using the staphylococcal A-agarose column: a comparison of immunoglobulin reduction using two different techniques. *J Clin Apher.* 2007;22(4):224-32.
10. Caldwell J, Gendreau RM, Furst D, Wiesenhutter C, Quagliata F, Spindler J, et al. A pilot study using a staph protein A column (Proisorba) to treat refractory rheumatoid arthritis. *J Rheumatol.* 1999 Aug;26(8):1657-62. Erratum in: *J Rheumatol* 1999 Dec;26(12):2718.
11. Centers for Medicare and Medicaid Services. National Coverage Determination for Extracorporeal Immunoabsorption (ECI) Using Protein A Columns. NCD #20.5. Effective January 1, 2001. Accessed April 30, 2011. Available at: [http://www.cms.hhs.gov/mcd/index\\_list.asp?list\\_type=ncd#PP](http://www.cms.hhs.gov/mcd/index_list.asp?list_type=ncd#PP)
12. Cher LM, Hochberg FH, Teruya J, Nitschke M, Valenzuela RF, Schmähmann JD, et al. Therapy for paraneoplastic neurologic syndromes in six patients with protein A column immunoabsorption. *Cancer.* 1995 Apr 1;75(7):1678-83.
13. Cooper LT, Belohlavek M, Korinek J, Yoshifuku S, Sengupta PP, Burgstaler EA, et al. A pilot study to assess the use of protein a immunoabsorption for chronic dilated cardiomyopathy. *J Clin Apher.* 2007;22(4):210-4.
14. Felix SB, Staudt A, Dörffel WV, Stangl V, Merkel K, Pohl M, et al. Hemodynamic effects of immunoabsorption and subsequent immunoglobulin substitution in dilated cardiomyopathy: three-month results from a randomized study. *J Am Coll Cardiol.* 2000 May;35(6):1590-8.
15. Felson DT, LaValley MP, Baldassare AR, Block JA, Caldwell JR, Cannon GW, et al. The Proisorba column for treatment of refractory rheumatoid arthritis: a randomized, double-blind, sham-controlled trial. *Arth & Rheu.* 1999;42(10):2153-9.
16. Freiburghaus C, Berntorp E, Ekman M, Gunnarsson M, Kjellberg BM, Nilsson IM. Immunoabsorption for removal of inhibitors: update on treatments in Malmö-Lund between 1980 and 1995. *Haemophilia.* 1998 Jan;4(1):16-20.

17. Gaddis TG, Guthrie TH Jr, Drew MJ, Sahud M, Howe RB, Mittelman A. Treatment of plasma refractory thrombotic thrombocytopenic purpura with protein A immunoabsorption. *Am J Hematol.* 1997 Jun;55(2):55-8.
18. Gendreau RM; ProSORBA Clinical Trial Group. A randomized double-blind sham-controlled trial of the ProSORBA column for treatment of refractory rheumatoid arthritis. *Ther Apher.* 2001 Apr;5(2):79-83.
19. George JN, Woolf SH, Raskob GE, Wasser JS, Aledort LM, Ballem PJ et al. Idiopathic thrombocytopenic purpura: a practice guideline developed by explicit methods for the American Society of Hematology. *Blood.* 1996 Jul 1;88(1):3-40.
20. Haas M, Böhmig GA, Leko-Mohr Z, Exner M, Regele H, Derfler K, et al. Peri-operative immunoabsorption in sensitized renal transplant recipients. *Nephrol Dial Transplant.* 2002 Aug;17(8):1503-8.
21. Hadden RD, Bensa S, Lunn MP, Hughes RA. Immunoabsorption inferior to plasma exchange in a patient with chronic inflammatory demyelinating polyradiculoneuropathy. *J Neurol Neurosurg Psychiatry.* 2002 May;72(5):644-6.
22. Hailey D, Topfer LA. Extracorporeal immunoabsorption treatment for rheumatoid arthritis. *Issues Emerg Health Technol.* 2002 Jan;(28):1-4.
23. Handelsman H. Protein A columns for the treatment of patients with idiopathic thrombocytopenic purpura and other indications. *Health Technol Assess Rep.* 1990;(7):1-8.
24. Hershko AY, Naparstek Y. Removal of pathogenic autoantibodies by Immunoabsorption. *Ann N.Y. Acad Sci.* 2005;1051:635-46.
25. Korec S, Schein PS, Smith FP, Neefe JR, Woolley PV, Goldberg RM, Phillips TM. Treatment of cancer-associated hemolytic uremic syndrome with staphylococcal protein A immunoperfusion. *J Clin Oncol.* 1986 Feb;4(2):210-5.
26. Kriaa F, Laurian Y, Hiesse C, Tchernia G, Charpentier B. Five years' experience at one centre with protein A immunoabsorption in patients with deleterious allo/autoantibodies (anti-HLA antibodies, autoimmune bleeding disorders) and post-transplant patients relapsing with focal glomerular sclerosis. *Nephrol Dial Transplant.* 1995;10 Suppl 6:108-10.
27. Kupin WL, Venkat KK, Hayashi H, Mozes MF, Oh HK, Watt R. Removal of lymphocytotoxic antibodies by pretransplant immunoabsorption therapy in highly sensitized renal transplant recipients. *Transplantation.* 1991 Feb;51(2):324-9.
28. Levy J, Degani N. Correcting immune imbalance: the use of ProSORBA column treatment for immune disorders. *Ther Apher Dial.* 2003 Apr;7(2):197-205.
29. Lorenz M, Regele H, Schillinger M, Kletzmayer J, Haidbauer B, Derfler K, et al. Peritransplant immunoabsorption: a strategy enabling transplantation in highly sensitized crossmatch-positive cadaveric kidney allograft recipients. *Transplantation.* 2005 Mar 27;79(6):696-701.
30. Neunert C, Lim W, Crowther M, Cohen A, Solberg L Jr, Crowther MA. The American Society of Hematology 2011 evidence-based practice guideline for immune thrombocytopenia. *Blood.* 2011 Apr 21;117(16):4190-207. Epub 2011 Feb 16. Accessed May 2, 2011. Available at URL address: <http://bloodjournal.hematologylibrary.org/content/117/16/4190.long>
31. Roth S. Effects of ProSORBA column apheresis in patients with chronic refractory rheumatoid arthritis. *J Rheumatol.* 2004 Nov;31(11):2131-5.

32. Schneidewind JM, Zettl UK, Winkler RE, Ramlow W, Tiess M, Michelsen A, et al. The outcome in myasthenia gravis patients--an eight-year follow-up after finishing immunoabsorption therapy. *Transfus Apher Sci.* 2001 Feb;24(1):95-8.
33. Shaz BH, Linenberger ML, Bandarenko N, Winters JL, Kim HC, Marques MB, et al. Category IV indications for therapeutic apheresis: ASFA fourth special issue. *J Clin Apher.* 2007 Jun;22(3):176-80.
34. Shimanovich I, Nitschke M, Rose C, Grabbe J, Zillikens D. Treatment of severe pemphigus with protein A immunoabsorption, rituximab and intravenous immunoglobulins. *Br J Dermatol.* 2008 Feb;158(2):382-8.
35. Snyder HW, Cochran SK, Balint JP, Bertram JH, Mittelman A, Guthrie TH and Jones FR. Experience with protein A-Immunoabsorption in treatment-resistant adult immune thrombocytopenic purpura. *Blood.* 1992;79(9):2237-45
36. Snyder HW Jr, Mittelman A, Oral A, Messerschmidt GL, Henry DH, Korec S, et al. Treatment of cancer chemotherapy-associated thrombotic thrombocytopenic purpura/hemolytic uremic syndrome by protein A immunoabsorption of plasma. *Cancer.* 1993 Mar 1;71(5):1882-92.
37. Staudt A, Dörr M, Staudt Y, Böhm M, Probst M, Empen K, et al. Role of immunoglobulin G3 subclass in dilated cardiomyopathy: results from protein A immunoabsorption. *Am Heart J.* 2005 Oct;150(4):729-36.
38. Staudt A, Hummel A, Ruppert J, Dörr M, Trimpert C, Birkenmeier K, et al. Immunoabsorption in dilated cardiomyopathy: 6-month results from a randomized study. *Am Heart J.* 2006 Oct;152(4):712.e1-6.
39. Szczepiorkowski ZM, Bandarenko N, Kim HC, Linenberger ML, American Society for Apheresis, Apheresis Applications Committee of the American Society for Apheresis. 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.* 2007a Jun;22(3):106-75.
40. Szczepiorkowski ZM, Shaz BH, Bandarenko N, Winters JL. The new approach to assignment of ASFA categories--introduction to the fourth special issue: clinical applications of therapeutic apheresis. *J Clin Apher.* 2007b Jun;22(3):96-105. Review.
41. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health. Excorim® Immunoabsorption System. Page last updated March 28, 2011. (H970004) Accessed April 30, 2011. Available at URL address: <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/HDEApprovals/ucm161827.htm>
42. U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health. ProSORBA® column. P850020. March 15, 1999. Accessed April 30, 2011. Available at URL address: [http://www.accessdata.fda.gov/cdrh\\_docs/pdf/P850020S011b.pdf](http://www.accessdata.fda.gov/cdrh_docs/pdf/P850020S011b.pdf)
43. Watt RM, Bunitsky K, Faulkner EB, Hart CM, Horan J, Ramstack JM, et al. Treatment of congenital and acquired hemophilia patients by extracorporeal removal of antibodies to coagulation factors: a review of US clinical studies 1987-1990. Hemophilia Study Group. *Transfus Sci.* 1992 Apr;13(2):233-53.
44. Wiesenhutter CW, Irish BL, Bertram JH. Treatment of patients with refractory rheumatoid arthritis with extracorporeal protein A immunoabsorption columns: a pilot trial. *J Rheumatol.* 1994 May;21(5):804-12.
45. Zinman LH, Sutton D, Ng E, Nwe P, Ngo M, Brill V. A pilot study to compare the use of the Excorim staphylococcal protein immunoabsorption system and IVIG in chronic inflammatory demyelinating polyneuropathy. *Transfus Apher Sci.* 2005 Nov;33(3):317-24.

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## Policy History

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<u>Pre-Merger Organizations</u>	<u>Last Review Date</u>	<u>Policy Number</u>	<u>Title</u>
CIGNA HealthCare	8/15/2008	0377	Extracorporeal Immunoabsorption With Protein A Column

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