



Name of Policy:

Antiprothrombin Antibody

Policy #: 096

Category: Laboratory

Latest Review Date: June 2011

Policy Grade: **Active Policy but no longer scheduled for regular literature reviews and updates.**

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

- 1. The technology must have final approval from the appropriate government regulatory bodies;*
- 2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
- 3. The technology must improve the net health outcome;*
- 4. The technology must be as beneficial as any established alternatives;*
- 5. The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

- 1. In accordance with generally accepted standards of medical practice; and*
- 2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
- 3. Not primarily for the convenience of the patient, physician or other health care provider; and*
- 4. 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.*

Description of Procedure or Service:

Antiphospholipid antibodies are a heterogeneous group of immunoglobulins that bind to several anionic phospholipids, to phospholipid-protein complexes and to certain proteins in the absence of phospholipids. Several plasma proteins mostly associated with the coagulation system and characterized with strong phospholipid binding properties, have been labeled as antiphospholipid cofactors. These are thought to play an important part in the antiphospholipid syndrome (APS). The most common and extensively studied cofactors are Beta 2-Glycoprotein 1 and Prothrombin. The four clinical features common in patients with antiphospholipid syndrome are venous thrombosis, arterial thrombosis, pregnancy loss, and thrombocytopenia. Thrombosis is the most common presentation of antiphospholipid syndrome.

APS is much more common than previously appreciated. Young patients presenting with thrombosis, myocardial infarction or stroke or a woman with a history of pregnancy loss should be investigated for APS. The diagnosis depends on finding at least one of the hallmark features and a positive laboratory test. The laboratory findings include the presence of antiphospholipid antibodies (aPL). Clinically, elevated levels of these antibodies (Beta 2-Glycoprotein 1 or Prothrombin) are associated with increased risk for antiphospholipid syndrome. Recently, enzyme linked immunosorbent assay (ELISA) methods to measure antiprothrombin (aPT) antibodies have become available and many clinical laboratories are incorporating them for the serologic evaluation of APS. Protein cofactors for aPL are thought to play an important role in the pathogenesis of thrombosis in patients with APS.

Policy:

Antiprothrombin antibody does not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational**.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

Donohoe, in an editorial, states that antiprothrombin antibodies are members of the ill-defined, heterogeneous family of antiphospholipid antibodies and helps define the antiphospholipid syndrome as presented in thromboembolic complications, recurrent miscarriage, or immune thrombocytopenia. How antiphospholipid antibodies contribute to the pathophysiology of clinical complications in vivo is poorly understood.

The classic assays used for the detection of antiphospholipid antibodies measure a heterogenous mixture of antibodies, without distinguishing antigenic specificity. Antibodies to beta-2

glycoprotein-I are strongly associated with thrombosis, but their role in other clinical presentations is less clear.

Merrill states that due to the heterogeneity of autoantibodies found in patients with this syndrome, the detection of antiphospholipid antibodies by currently available tests does not predict the likelihood of thrombosis or the time at which such an event may occur. A direct pathogenic role for the antibodies is supported by the observation that high titer and IgG isotype confer an increased risk of thrombosis. Merrill also questions if there are currently available assays that can at least improve the prediction of pathogenicity and allow treatments to be initiated for some patients before a life-threatening event. His response is no, citing that the sensitivity, specificity and consistency of currently available diagnostic tests remain inadequate for this purpose. There is a need to have prospective studies and multivariate analysis to define antibody-associated risk markers remain to be performed. In the summary, Merrill states that while there is an effort to improve diagnosis and treatment of antiphospholipid syndrome (Hughes syndrome), there remain problems of lack of standardization and lack of analyses that restrict the diagnostic and predictive ability of commercially available tests.

February 2007 Update

Bertolaccini et al assessed the value of testing for new antiphospholipid antibodies (aPL) specificities as an aid to identify APS in patients with systemic lupus erythematosus but repeatedly negative for conventional anti-cardiolipin (aCL) or lupus anticoagulant (LA). Laboratory diagnosis of antiphospholipid syndrome (APS) is based on a positive aCL or LA test. The aCL test is positive in about 80% of these patients, the LA is the only positive test in about 20%, and both are positive in about 60% of cases. A history of thrombosis has been reported in 7.2-12% of patients with SLE. Mortality from thrombosis in SLE has been found to be 27%. It is not unusual to find patients that are persistently negative for both tests per the authors. In some cases additional testing is required, such as beta-2 glycoprotein (GPI) or prothrombin. The authors concluded that their data suggested that tests for aCL and LA, the only antibodies closely associated with thrombosis, should be carried out for the laboratory diagnosis of APS. The inclusion of an isolated positivity for anti-Beta-2 GPI as laboratory criterion for the diagnosis of APS and in the aCL is not supported by the data. Testing for antiprothrombin antibodies (aPT) may be helpful in some areas.

February 2009 Update

A 2005 Practice Guideline from the American College of Obstetricians and Gynecologists (ACOG) continues to maintain that testing for antiprothrombin antibodies “cannot be recommended for clinical use at this time.” This position reaffirmed in 2007 by ACOG.

June 2011 Update

Oku et al (2008) stated that aCL, anti-beta2 glycoprotein I antibodies, and LA are the only laboratory tests considered within the revised criteria for the classification of the APS. Recently, antibodies against aPS/PT have been detected, and these antibodies, rather than antibodies against PT alone, are closely associated with APS and LA. The sensitivity and specificity of aPS/PT for the diagnosis of APS were assessed in a population of patients with a variety of autoimmune disorders; aCL and aPS/PT have similar diagnostic value for APS, therefore aPS/PT

should be further explored, not only for research purposes but also as a candidate for one of the laboratory criteria for the classification of the APS.

Atsumi et al (2010) stated that anticardiolipin antibodies (aCL), anti-beta(2)-glycoprotein I (beta(2)GPI) antibodies and lupus anticoagulant (LA) are the only laboratory tests considered within the revised criteria for the classification of the antiphospholipid syndrome (APS). Recently, the significance to assay the antibodies against phosphatidylserine-prothrombin complex (aPS/PT) has been discussed, and these antibodies, rather than antibodies against prothrombin alone, are closely associated with APS and LA. The sensitivity and specificity of aPS/PT for the diagnosis of APS were assessed in a population of patients with a variety of autoimmune disorders. The aCL and aPS/PT have similar diagnostic value for APS, and most of APS patients with aPS/PT had positive LA. Therefore, aPS/PT should be further explored, not only for research purposes, but also as a candidate for one of the enzyme-linked immunosorbent assay (ELISA)-based confirmatory test for APS associated LA.

Key Words:

Prothrombin, antiprothrombin antibody, antiphospholipid antibody, APL, antiphospholipid syndrome, APS, Hughes syndrome, beta-2 glycoprotein I, thrombosis, pregnancy loss, thrombocytopenia

Approved by Governing Bodies:

Not applicable

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Covered if covered by the Participating Home Plan

FEP contracts: FEP does not consider investigational if FDA approved. Will be reviewed for medical necessity.

Pre-certification/Pre-determination requirements: Not required

Current Coding:

CPT coding:

86849 Unlisted Immunology procedure (Effective January 1, 2013)

Previous Coding:

**0030T Antiprothrombin (phospholipid cofactor) antibody, each Ig class
(Deleted effective January 1, 2013)**

References:

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3. Aziz, Douglas C. *Antiphospholipid syndrome*, Tiwary Clinical Lab online, <http://www.tclonline.com/reference/antiphospho.htm>.
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Policy History:

Medical Policy Group, February 2003, (1)

Medical Policy Administration Committee, February 2003

Available for comment February 19-April 7, 2003

Medical Policy Group, February 2005 (1)

Medical Policy Group, February 2007 (1)

Medical Policy Group, February 2009 (1)

Medical Policy Group, June 2011 (1) Update to Key Points and References

Medical Policy Group, September 2012 (3): **Active Policy but no longer scheduled for regular literature reviews and updates.**

Medical Policy Group, November 2012: 2013 Coding Update – added Code 86849

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.