

## Evidence Based Guideline

# Anti-CCP Testing for Rheumatoid Arthritis

**File Name:** anti-ccp\_testing\_for\_rheumatoid\_arthritis  
**Guideline Number:** EBG.MED1039  
**Origination:** 4/2009  
**Last Review:** 5/2009  
**Next Review:** 12/2009

### Description of Procedure or Service

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Autoantibodies directed against cyclic citrullinated proteins (anti-CCP) are found in many patients with rheumatoid arthritis (RA). Citrullination refers to the post-translational modification of the amino acid arginine to citrulline by the enzyme peptidylarginine deiminase (PAD). The physiologic role of citrullination is unclear; however it has been shown to occur during apoptosis, and is thought to play a role in the degradation of intracellular proteins by unfolding protein molecules and thereby exposing them to degradation enzymes. PAD enzymes can be found in monocytes and macrophages associated with inflammation, including in the synovial fluid of patients with active RA. In patients with RA and active joint inflammation, levels of anti-CCP are higher in the synovial fluid than in the peripheral circulation. Anti-CCP found in the serum is thought to be a result of diffusion of these antibodies from the synovial fluid into the general circulation.

Autoantibodies against CCP have been recognized and measured for several decades, by means of the anti-perinuclear factor (APF) and the anti-keratin antibody (AKA). However, these older tests were performed by a cumbersome immunofluorescence assay and were not commonly used in routine clinical practice. Following the recognition that APF and AKA activity were entirely dependent upon citrullination, attention turned toward measuring anti-CCP antibodies. Serum Anti-CCP levels are currently measured using an ELISA assay. The first generation of anti-CCP testing (CCP1) used citrullinated proteins derived from human filaggrin. This method of testing was expensive and difficult to standardize, since it required purification of sufficient quantities of the human antigen. The second generation of anti-CCP testing (CCP2) uses a synthetic peptide antigen, thus making the test cheaper and easy to standardize. CCP2 is currently the only commercially available method for testing for anti-CCP antibodies.

The INOVA Diagnostics QUANTA Lite™ CCP IgG ELISA and the Axis-Shield Diagnostics Diastat™ anti-CCP ELISA test received 510(k) marketing clearance from the U.S. Food and Drug Administration (FDA) in 2002 for use as an aid in the diagnosis of rheumatoid arthritis. According to the FDA statement for the Diastat, “autoantibody levels represent one parameter in a multi-criterion diagnostic process, encompassing both clinical and laboratory-based assessments.” Additional anti-CCP tests have received 510(k) marketing clearance since 2002.

\*\*\*Note: The Evidence Based Guideline on Anti-CCP Testing for Rheumatoid Arthritis is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

## Policy: Anti-CCP Testing for Rheumatoid Arthritis

### Evidence Based Guideline for Anti-CCP Testing for Rheumatoid Arthritis.

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Measurement of anti-CCP may be appropriate when used as part of the diagnostic workup for rheumatoid arthritis.

### Medical Evidence regarding Anti-CCP Testing for Rheumatoid Arthritis indicates it is not recommended in the following situations:

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Measurement of anti-CCP is not recommended when used to monitor disease activity and/or treatment response.

The standard methods for diagnosing RA have limited sensitivity for patients with early inflammatory arthritis. Confirming the diagnosis of RA early in the course of inflammatory arthritis may be important, given that early initiation of treatment with DMARDs can minimize joint damage and improve functional outcomes. Anti-CCP has high specificity and moderate sensitivity in diagnosing RA. In addition, multivariate predictive models have demonstrated the potential utility of anti-CCP testing in combination with other known clinical, laboratory and radiologic parameters. However, there are currently no prospectively validated prediction models that demonstrate the additional predictive value of anti-CCP for this purpose.

### Benefits Application

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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

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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](http://www.bcbsnc.com). They are listed in the Category Search on the Medical Policy search page.

*Applicable codes: 86200*

### Scientific Background and Reference Sources

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BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.78, 2/12/09.

Senior Medical Director - 4/2009

### Policy Implementation/Update Information

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5/11/09 Evidence based guideline adopted from the BCBS Association. Reviewed with the Senior Medical Director 4/6/2009. "Measurement of anti-CCP may be appropriate when used as part of the diagnostic workup for rheumatoid arthritis." "Measurement of anti-CCP is not recommended when used to monitor disease activity and/or treatment response." (btw)

## **Policy: Anti-CCP Testing for Rheumatoid Arthritis**

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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.