

Policy #: 142

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Page: 1 of 4

Title

Anti-CCP testing for rheumatoid arthritis¹

Description

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.

When services are covered for commercial products and Medicare HMO Blue, Medicare PPO Blue, and Medicare PFFS PlusRx

We cover measurement of anti-CCP when used as part of the diagnostic workup for rheumatoid arthritis.

Current guidelines for the diagnosis of rheumatoid arthritis:

The existing guidelines for diagnosing RA were developed in 1987 and depend on a combination of clinical, laboratory, and radiographic features. Four or more of the seven criteria are required for the diagnosis of definite RA, and two or more criteria indicate possible rheumatoid arthritis.

Criteria:

1. Morning stiffness lasting at least one hour

2. Arthritis of three or more joint areas
3. Arthritis of hand joints (wrist, MCP, or PIP joint)
4. Symmetric arthritis
5. Rheumatoid nodules
6. serum rheumatoid factor
7. Radiographic changes typical of rheumatoid arthritis

When services are not covered for commercial products and Medicare HMO Blue, Medicare PPO Blue, and Medicare PFFS PlusRx

We do not cover measurement of anti-CCP when used to monitor disease activity and/or treatment response.

Individual consideration

All our medical policies are written for the majority of people with a given condition. Each policy is based on medical science. For many of our medical policies, each individual's unique clinical circumstances may be considered in light of current scientific literature. For consideration of an individual patient, physicians may send relevant clinical information to:

For services already billed

Blue Cross Blue Shield of Massachusetts
 Provider Appeals
 PO Box 986065
 Boston, MA 02298

Prior to performance of service

Blue Cross Blue Shield of Massachusetts
 Case Creation/Medical Policy
 One Enterprise Drive
 Quincy, MA 02171
 Tel: 1-800-327-6716
 Fax: 1-888-641-5330

Authorization Information

For Managed Care members:

- No authorization is required for this service; *see Managed Care Guidelines for additional requirements.*

For Indemnity and PPO members:

- No authorization is required for this service; *see Indemnity and PPO Guidelines for additional requirements.*

Managed Care Guidelines

All authorization requirements are determined by the individual's subscriber certificate, explanation of coverage, or summary plan description, however;

- **For Medicare HMO Blue members:** The service must meet the criteria for coverage noted in this policy, be medically necessary, prescribed by a plan physician and provided by a network provider.
- **For Medicare HMO Blue members:** Referrals are required for all visits to a specialist.
- For all other Managed Care plans, any specialist visit requires a referral, except for visits performed by OB/GYN specialists.
- Authorization is required for an inpatient admission.

Indemnity and PPO Guidelines

All authorization requirements are determined by the individual's subscriber certificate, explanation of coverage, or summary plan description, however;

- Authorization is required for an inpatient admission.
- Authorizations are not required for most outpatient services as determined by the individual's subscriber certificate.
- Referrals to a specialist are not required.

Coding information

Procedure codes are from current CPT, HCPCS Level II, Revenue Code, and/or ICD-9-CM manuals, as recommended by the American Medical Association, Centers for Medicare and Medicaid Services and American Hospital Associations. Blue Cross Blue Shield Association national codes may be developed when appropriate.

The following codes are included below for informational purposes. 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.

CPT codes:

- **86200**, cyclic citrullinated peptide (CCP), antibody

Policy update history

New medical policy, effective 11/01/09.

References

References for footnote 1:

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Footnotes

¹Based on BCBSA policy # 2.01.78, Anti-CCP Testing for Rheumatoid Arthritis