

BLUE CROSS OF NORTHEASTERN PA "BCNEPA" MEDICAL POLICY BULLETIN	MANUAL: MEDICAL POLICY
	REFERENCE NO.: MPO-134-0003
EFFECTIVE DATE July 1, 2014	SUBJECT: Vectra® DA Blood Test for Rheumatoid Arthritis

Blue Cross of Northeastern Pennsylvania ("BCNEPA") Medical Policy

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical policy and claims payment policy are applied. Policies are provided for informational purposes only and are developed to assist in administering plan benefits and do not constitute medical advice.

Treating providers are solely responsible for medical advice and treatment. Policies are based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease.

Medical practices and information are constantly changing and BCNEPA may review and revise its medical policies periodically. Also, due to the rapid pace of changing technology and the advent of new medical procedures, BCNEPA may not have a policy to address every procedure.

In those cases, BCNEPA may review other sources of information including, but not limited to, current medical literature and other medical resources, such as Technology Evaluation Center Assessments (TEC) published by the Blue Cross Blue Shield Association. BCNEPA may also consult with health care providers possessing particular expertise in the services at issue.

DESCRIPTION:

Assessment of disease activity in rheumatoid arthritis (RA) is an important component of treatment management, as one of the main goals of treatment is to maintain low disease activity or remission. There are a variety of available instruments for measuring RA disease activity. One potential approach is the use of a multibiomarker disease activity (MBDA) score. The Vectra DA test is a commercially available MBDA blood test that uses 12 biomarkers to construct a disease activity score ranging from 0 to 100.

BENEFIT POLICY STATEMENT:

BCNEPA makes decisions on coverage based on Policy Bulletins, benefit plan documents, and the member's medical history and condition. Benefits may vary based on product line, group or contract, therefore, Member benefits must be verified. In the event of a conflict between the Member's benefit plan document and topics addressed in Medical Policy Bulletins (i.e., specific contract exclusions), the Member's benefit plan document always supersedes the information in the Medical Policy Bulletins. BCNEPA determines medical necessity only if the benefit exists and no contract exclusions are applicable.

Benefits are determined by the terms of the Member's specific benefit plan document [i.e., the Fully Insured policy, the Administrative Services Only (ASO) agreement applicable to the Self-Funded Plan Participant, or the Individual Policy] that is in effect at the time services are rendered.

BACKGROUND:

RA is a disorder characterized by chronic joint inflammation leading to painful symptoms, progressive joint destruction and loss of function. The disorder is relatively common and is associated a high burden of morbidity for affected patients.

Treatment of RA has undergone a shift from symptom management to a more proactive strategy of reducing disease activity and delaying disease progression. (1) The goal of treatment is to reduce irreversible joint damage that occurs from ongoing joint inflammation and synovitis by keeping disease activity as low as possible. The availability of an increasing number of effective disease modifying antirheumatic drugs has made achievement of remission, or sustained low disease activity, a feasible goal in a large proportion of patients with RA. This treatment strategy has been called a “tight control” approach.

The concept of “tight control” in the management of RA has gained wide acceptance as evidence from clinical trials have demonstrated that outcomes are improved with a tight control strategy. In a tight control strategy, treatment targets are used that are mainly based on measures of disease activity. In a systematic review published in 2010, Schoels et al identified 7 trials that evaluated the efficacy of tight control. (2) Four of these trials randomized patients to either a tight control using treatment targets or routine management. The treatment targets used were heterogeneous, including symptom-based measures, joint scores on exam, validated treatment activity measures, lab values, or combinations of these factors. In all 4 trials, there was a significant decrease in the Disease Activity Score (DAS) and in the likelihood of achieving remission for patients in the tight control group.

For a strategy of tight control to be successful, a reliable and valid measurement of disease activity is important. There are numerous disease activity measurements that can be used in clinical care. Composite measures include information from multiple sources, including patient self-report, physician examination and/or biomarker measurement. Composite measures are the most comprehensive but have the disadvantage of being more cumbersome and difficult to complete. Patient reported measures are intended to be simpler, and rely only on information that patients can provide expeditiously, but have the disadvantage of being more subjective. Measurements that rely only on biomarkers are objective and do not require patient input but do involve the cost and inconvenience of laboratory tests.

The most widely used and validated in clinical research is the DAS28 score. This is a composite measure that includes examination of 28 joints for swelling and tenderness, combined with a patient report of disease activity and measurement of C-reactive protein (CRP) (or erythrocyte sedimentation rate). This score has been widely validated and used for both research and clinical care and is often considered the criterion standard for measuring disease activity. However, it requires a thorough joint examination, information obtained from the patient, and laboratory testing. Therefore, there have been many attempts to create a valid disease activity measure that is simpler. Some measures include only patient self-report and thus can be completed quickly in the setting of an office visit. An example of this type of measure is the simplified disease activity index (SDAI). Another approach is to use only serum biomarkers, which only requires a blood draw. The Vectra DA is this type of biomarker-based measure. Proponents of a biomarker approach have argued that this is simpler and avoids the subjectivity of physical examination and patient report.

There is a fairly large body of evidence comparing the performance of different disease activity measures in clinical care, including a number of systematic reviews. In a systematic review of disease activity measures sponsored by the American College of Rheumatology in 2012, more than 60 measurement instruments were identified. (3) Through a 5-stage process that included review by an expert advisory panel in RA disease activity and detailed evaluation of psychometric properties, the workgroup selected 6 that were most useful and feasible for point-of-care clinical care. These were the Clinical Disease Activity Index (CDAI), Disease Activity Score with 28 joints (DAS28), Patient Activity Scale (PAS), Patient Activity

Scale II (PAS-II), Routine Assessment of Patient Index data with 3 measures (RAPI), and the Simplified Disease Activity Index (SDAI).

In another systematic review, Gaujoux-Viala et al compared 4 composite indices, DAS, DAS28, SDAI, and CDAI. (4) In general, the concordance between measures was good, with kappa values in the range of 0.7. An exception to this level of concordance was in the definition of remission, for which the DAS28 had lower levels of concordance with other measures, with kappa values ranging from 0.48 to 0.63. All of the measures had fair-to-good correlations with an independent health status measure, the Health Assessment Questionnaire (HAQ) and with radiologic examination of joint structural damage.

Salaffi et al compared the responsiveness of numerous disease activity measures, including patient self-report measures and composite indices, over a 6-month period of treatment with disease modifying drugs. (5) The composite indices evaluated were DAS28, SDAI, CDAI, and the Mean Overall Index for RA. The patient-reported measures evaluated were the Clinical Arthritis index, the Rheumatoid Disease Activity Index, the Routine Assessment of Patient Index Data (RAPID3), and PAS. Across all measures, there was wide variability in internal responsiveness, with the highest value obtained for the DAS28 measure. There were some differences in responsiveness between the measures, but all were considered suitable for use in clinical care. When comparing the patient-reported measures with the composite measures, there was no difference in internal or external responsiveness.

MEDICAL POLICY STATEMENT:

BCNEPA will not provide coverage for the use of a multi-biomarker disease activity score for rheumatoid arthritis (RA) (eg, Vectra DA score) as this is considered investigational in all situations.

GUIDELINES:

The Vectra DA test (Crescendo Bioscience, South San Francisco, CA) consists of 12 individual biomarkers. These are (6):

- Interleukin-6 (IL-6)
- Tumor necrosis factor receptor type I (TNFRI)
- Vascular cell adhesion molecule 1 (VCAM-1)
- Epidermal growth factor (EGF)
- Vascular endothelial growth factor A (VEGF-A)
- YKL-40
- Matrix metalloproteinase 1 (MMP-1)
- Matrix metalloproteinase 3 (MMP-3)
- CRP
- Serum amyloid A (SAA)
- Leptin
- Resistin

There are no U.S. Food and Drug Administration (FDA)-approved MBDA tests for measuring disease activity in RA.

RATIONALE:

The Vectra DA is a biomarker-based measurement of disease activity in rheumatoid arthritis (RA) that uses results of 12 serum biomarkers to construct a score ranging from 0 to 100. It is one of numerous disease activity measures that are available for use in clinical care, and there are other disease activity

scores (eg, Disease Activity Score with 28 joints, DAS28) that have been more extensively validated. Evidence of validity for the measure consists of several studies that correlate Vectra DA with other previously validated measures such as the DAS28. These studies show moderate correlations of Vectra with the DAS28. A small number of studies evaluate clinical utility by examining changes in decision making associated with use of Vectra, but these are limited by the design of using simulated cases or physician surveys and do not report any outcome data. This limited body of evidence on the Vectra DA test is not sufficient to determine whether it is as good as or better than other disease activity measures, and it is possible that it is not as accurate as the DAS28. As a result, the Vectra DA test is considered investigational for use as a measure of disease activity in the patients with RA.

Medicare National Coverage

There are no Medicare National Coverage Determinations for the Vectra DA test. In July 2013, Palmetto GBA, the Medicare contractor in California, issued a positive coverage decision for the Vectra DA test. Because all Vectra DA tests are processed out of the Crescendo Bioscience laboratory in California, the test will be covered for Medicare patients in the United States.

DEFINITIONS:

N/A

CODING:

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 - Covered procedure codes are dependent upon meeting criteria of the policy and appropriate diagnosis code.
 - The following list of codes may not be all-inclusive, and are subject to change at any time.
 - Benefits are determined by the terms of the Member's specific benefit plan document [i.e., the Fully Insured policy, the Administrative Services Only (ASO) agreement applicable to the Self-Funded Plan Participant, or the Individual Policy] that is in effect at the time services are rendered.
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PROCEDURE CODES

84999

SOURCES:

1. Upchurch KS, Kay J. Evolution of treatment for rheumatoid arthritis. *Rheumatology (Oxford)* 2012; 51 Suppl 6:vi28-36.
2. Schoels M, Knevel R, Aletaha D et al. Evidence for treating rheumatoid arthritis to target: results of a systematic literature search. *Ann Rheum Dis* 2010; 69(4):638-43.
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8. Centola M, Cavet G, Shen Y et al. Development of a multi-biomarker disease activity test for rheumatoid arthritis. *PLoS One* 2013; 8(4):e60635.
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APPROVALS:

Approved by Vice President, Clinical Operations & Chief Medical Officer:

Signature: 
(Nina M. Taggart, MA, MD, MBA)

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HISTORY:

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Policy developed by: Medical Policy Department