Vectra® DA Blood Test for Rheumatoid Arthritis

**Description of Procedure or Service**

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 multi-biomarker 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 0-100. It is one of numerous disease activity measures that are available for rheumatoid arthritis.

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 rheumatoid arthritis has undergone a shift from symptom management to a more proactive strategy of minimizing 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 anti-rheumatic drugs (DMARDs) 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 four 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.

In order for a strategy of tight control to be successful, a reliable and valid measurement of disease activity is necessary. 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 CRP (or ESR). This score has been widely validated and used for both research and clinical care, and is often considered the gold standard for measuring disease activity. However, it requires a thorough joint examination, patient reported symptoms, 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 requires only 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 five-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), the 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 four composite indices, the disease activity score (DAS), the disease activity score with 28 joints (DAS28), the simplified disease activity index (SDAI), and the clinical disease activity index (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 0.48-0.63. 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. The composite indices evaluated were the disease activity score–28 joints (DAS28), the simplified disease activity index (SDAI), the clinical disease activity index (CDAI), and the mean overall index for RA (MOI-RA). The patient reported measures evaluated were the clinical arthritis activity (PRO-CLARA) index, the rheumatoid disease activity index (RDAI), the routine assessment of patient index data (RAPID3), and the patient activity score (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 not difference in internal or external responsiveness.

**Vectra DA test**

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

- 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)
- C-reactive protein (CRP)
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- Serum amyloid A (SAA)
- Leptin
- Resistin

**Regulatory Status**

There are no FDA-approved multi-biomarker disease activity (MBDA) tests for measuring disease activity in RA. Commercially available tests are laboratory-developed tests that are not subject to U.S. Food and Drug Administration (FDA) approval. Clinical laboratories may develop and validate tests in-house (“home-brew”) and market them as a laboratory service; such tests must meet the general regulatory standards of the Clinical Laboratory Improvement Act (CLIA).

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

**Policy**

Vectra DA Blood Test for Rheumatoid Arthritis is considered investigational for all applications. BCBSNC does not provide coverage for investigational services or procedures.

**Benefits Application**

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

**When Vectra DA Blood Test for Rheumatoid Arthritis is covered**

Not applicable

**When Vectra DA Blood Test for Rheumatoid Arthritis is not covered**

The use of a multi-biomarker disease activity score for rheumatoid arthritis is considered investigational in all situations.

**Policy Guidelines**

For individuals who have rheumatoid arthritis (RA) who are evaluated with the Vectra DA test, the evidence includes post hoc analyses of randomized controlled trials and prospective cohort studies. Relevant outcomes are test accuracy and validity, other test performance measures, symptoms, change in disease status, functional outcomes, and quality of life. Evidence from the available studies correlates Vectra DA with disease progression, response to therapy, and/or other previously validated disease activity measures such as the Disease Activity Score with 28 joints (DAS28). These studies have established that the Vectra DA score is a predictor of disease progression and that decreases in the score correlate with disease response. They have also shown moderate correlations between Vectra and the DAS28. A smaller number of studies have evaluated clinical utility by examining changes in decision making associated with use of Vectra, but these studies are limited by the design because they used simulated cases or physician surveys and did not report any outcomes data. This body of evidence on the Vectra DA test is insufficient to determine whether it is as good as or better than other disease activity measures, and it is uncertain whether it is as accurate as the DAS28. The evidence is insufficient to determine the effects of the technology on health outcomes.

**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. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 81490

The following codes may be submitted: 84999, 83520, 86140

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources


Medical Director review 5/2014

Specialty Matched Consultant Advisory Panel 2/2015


Policy Implementation/Update Information

5/27/14 New policy developed. The Vectra DA blood test to predict rheumatoid arthritis is considered investigational. Medical director review 5/2014. (lpr)

3/10/15 Specialty matched consultant advisory panel review meeting 2/25/2015. No change to policy statement. (lpr)

5/26/15 Reference added. No change to policy statement. (lpr)

12/30/15 Added CPT code 81490 to Billing/Coding section for effective date 1/1/2016. (lpr)

4/1/16 Specialty Matched Consultant Advisory Panel review 2/24/2016. No change to policy. (an)

3/31/17 Updated Policy Guidelines section. Specialty Matched Consultant Advisory Panel review 2/22/2017. No change to policy statement. (an)

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.