MEDICAL POLICY – 2.04.119

Vectra® DA Blood Test for Rheumatoid Arthritis

BCBSA Ref. Policy: 2.04.119

Effective Date: Sept. 1, 2017
Last Revised: Aug. 1, 2017

RELATED MEDICAL POLICIES:
None

Introduction

A biomarker is something in the body that can reflect the presence or activity of a disease. Different diseases may have different biomarkers. A blood test called Vectra DA looks at 12 different biomarkers for rheumatoid arthritis (RA) and combines the results into a single score. This single score can be followed over time to show how active the arthritis is and how it responds to therapy. Blood tests that measure many biomarkers to try to assess the RA activity level are investigational (unproven). Current medical studies do not answer whether these multi-biomarker tests are as good as or better than the standard tests.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

<table>
<thead>
<tr>
<th>Score</th>
<th>Investigational</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multi-biomarker disease</td>
<td>The use of a multi-biomarker disease activity score for</td>
</tr>
</tbody>
</table>
Score | Investigational
--- | ---
activity score | rheumatoid arthritis (RA) (eg, Vectra® DA score) is considered investigational in all situations.

Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>CPT</td>
<td></td>
</tr>
<tr>
<td>81490</td>
<td>Autoimmune (rheumatoid arthritis), analysis of 12 biomarkers using immunoassays, utilizing serum, prognostic algorithm reported as a disease activity score</td>
</tr>
</tbody>
</table>

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Related Information

N/A

Evidence Review

Description

Assessing disease activity in rheumatoid arthritis (RA) is an important part of management because a main goal of treatment is to maintain low disease activity or remission. There are a variety of available instruments for measuring RA disease activity. They use combinations of physical exam findings, radiologic results, and serum biomarkers to construct a disease activity score (DAS). A multi-biomarker disease activity (MBDA) instrument is a disease activity measure that is comprised entirely of serum biomarkers. The Vectra DA test is a commercially available MBDA blood test that uses 12 biomarkers to construct a disease activity score ranging from 1 (low disease activity) to 100 (high disease activity).
Background

*Rheumatoid Arthritis*

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 with a high burden of morbidity for affected patients.

Treatment

Treatment of RA has changed from simply managing symptoms to a more proactive approach of minimizing disease activity and the irreversible joint damage that it causes. The increased availability of effective disease-modifying antirheumatic drugs has made controlling the symptoms of RA or even achieving remission a feasible goal in many patients. This treatment strategy has been called a “tight control” approach.

The concept of “tight control” in the management of RA has gained wide acceptance because clinical trials have shown that outcomes are improved when a tight control strategy is used. In a tight control strategy, treatment targets are used that are mainly based on measures of disease activity. In a 2010 systematic review, Schoels et al. identified 7 trials that evaluated the efficacy of tight control. Four of these trials randomized patients to either tight control using treatment targets or routine management. In all four trials, patients in the tight control group had a significant decrease in their Disease Activity Score (DAS) or its 28 joint version (DAS28), and an increased likelihood of achieving remission.

Validated Assessment Tools

In order to successfully control a disease, a reliable and valid measurement of its activity is necessary. There are many disease activity measurements that can be used in clinical care. Composite measures include information from multiple sources including patient self-report, physician examination, and biomarker measurement. Composite measures are the most comprehensive tool, but are more cumbersome and difficult to complete. Patient-reported measures are simpler, and rely only on information that patients can quickly and easily provide, but they are 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 scoring system 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) and/or erythrocyte sedimentation rate (ESR). This score is often considered the criterion standard for measuring disease activity. However, it requires a thorough joint examination, patient-reported symptoms, and laboratory testing. Therefore, many attempts have been made to create a simpler, valid disease activity measure.

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 2012 systematic review of disease activity measures sponsored by the American College of Rheumatology, more than 60 measurement instruments were identified. Through a 5-stage process that included review by an expert advisory panel in RA disease activity and detailed evaluation of psychometric properties, the working group selected 6 measures that were most useful and feasible for point-of-care clinical care. These were the Clinical Disease Activity Index (CDAI), DAS28, Patient Activity Scale (PAS), Patient Activity Scale II (PAS-II), Routine Assessment of Patient Index Data 3 (RAPID3), and the Simplified Disease Activity Index (SDAI).

In another systematic review, Gaujoux-Viala et al compared 4 composite indices: the DAS, DAS28, SDAI, and CDAI. In general, the concordance between measures was good, with κ 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 κ values ranging from 0.48 to 0.63. All measures had fair-to-good correlations with an independent health status measure, the Health Assessment Questionnaire, and with radiologic examination of joint structural damage.

Salaffi et al (2012) 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 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, RAPID3, and PAS. Across all measures, there was wide variability in internal responsiveness, with the highest value obtained for the DAS28 measure. There were 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.
**Vectra DA test**

The Vectra DA test consists of 12 individual biomarkers listed below:

- 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

The Vectra DA test scores range from 1 to 100. Categories of scores were constructed to correlate with the DAS28-CRP scale:

- 45-100: high disease activity
- 30-44: moderate disease activity
- 1-29: low disease activity

**Summary of Evidence**

For individuals who have rheumatoid arthritis (RA) who are evaluated with the Vectra DA test, the evidence includes post hoc analyses of archived serum samples from 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 has correlated Vectra DA with disease
progression and other previously validated disease activity measures such as the Disease Activity Score with 28 joints (DAS28). These studies have shown that the Vectra DA score is a predictor of disease activity measures (eg, DAS28). These studies have shown that the Vectra DA score has moderate correlations with other disease activity measures (eg, DAS28). Other post hoc analyses of archived serum samples have evaluated the use of multi-biomarker disease activity (MBDA) to measure treatment response. Correlation of MBDA scores with other disease activity measures differed by the duration and type of treatment. A smaller number of studies have evaluated clinical utility by examining changes in decision-making associated with the use of Vectra DA, but these studies are limited by the design because they used archived serum samples, simulated cases, or physician surveys and did not report any health 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.

Ongoing and Unpublished Clinical Trials

There is currently an ongoing trial that might influence this review listed in Table 1.

Table 1. Summary of Key Trials

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<tr>
<td>Ongoing</td>
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<tr>
<td>NCT02832297*</td>
<td>Prospective Outcomes Study: Vectra® DA Guided Care Compared to Usual Care</td>
<td>318</td>
<td>Aug 2018</td>
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</tbody>
</table>

NCT: national clinical trial.
* Denotes industry-sponsored or cosponsored trial.

Practice Guidelines and Position Statements

In the 2015 American College of Rheumatology guidelines on the treatment of rheumatoid arthritis, ACR endorsed the following measures of disease activity: Patient Activity Scale, Routine Assessment of Patient Index Data 3, Clinical Disease Activity Index, Disease Activity Score 28, and Simplified Disease Activity Index. The guidelines indicated that other measures are available to clinicians, but that including the new measures was out of their scope.
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.

Regulatory Status

Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). The Vectra® DA test (Crescendo Bioscience, South San Francisco, CA) is available under the auspices of CLIA. Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

References


History

<table>
<thead>
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<th>Date</th>
<th>Comments</th>
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<tr>
<td>05/12/14</td>
<td>New Policy. New policy created with literature review through March 6, 2014. The Vectra DA test for measuring disease activity in rheumatoid arthritis is investigational.</td>
</tr>
<tr>
<td>06/17/15</td>
<td>Annual Review. Policy updated with literature review through March 22, 2015. References 9 and 11-12 added. No change to policy statement.</td>
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<tr>
<td>01/19/16</td>
<td>Coding update. New CPT code 81490, effective 1/1/16, added to policy.</td>
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