

## Vectra DA Test for Rheumatoid Arthritis

MEDICAL POLICY NUMBER: 120

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**INSTRUCTIONS FOR USE:** Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Company reserves the right to determine the application of medical policies and make revisions to medical policies at any time. The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement. Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case. In cases where medical necessity is not established by policy for specific treatment modalities, evidence not previously considered regarding the efficacy of the modality that is presented shall be given consideration to determine if the policy represents current standards of care.

**SCOPE:** Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

## PLAN PRODUCT AND BENEFIT APPLICATION

Commercial

Medicaid/OHP\*

Medicare\*\*

### \*Medicaid/OHP Members

*Oregon*: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

### \*\*Medicare Members

This *Company* policy may be applied to Medicare Plan members only when directed by a separate *Medicare* policy. Note that investigational services are considered “**not medically necessary**” for Medicare members.

## COVERAGE CRITERIA

The Vectra® DA test is considered **investigational and not covered** to guide the treatment of any condition.

Link to [Evidence Summary](#)

## POLICY CROSS REFERENCES

None

The full Company portfolio of current Medical Policies is available online and can be [accessed here](#).

## POLICY GUIDELINES

### BACKGROUND

#### Rheumatoid Arthritis (RA)

Rheumatoid arthritis (RA) is a chronic, progressive, autoimmune disease that causes stretching of tendons and ligaments, and destruction of joint cartilage and bone, with consequent disability. RA is heterogeneous in terms of disease severity and age of onset. RA is the most common autoimmune inflammatory arthritis in adults, affecting > 1.3 million people in the United States alone.<sup>1,2</sup>

## Evaluation of RA

The clinical and laboratory tests used for the initial evaluation and diagnosis of RA are also used for monitoring and management of RA. These tools may include physical and radiographic examination of joints, serological analysis for certain biomarkers, and composite scores including the Disease Activity Score (DAS), Disease Activity Score employing 28 joint counts (DAS28), Simplified Disease Activity Index (SDAI), Clinical Disease Activity Index (CDAI), Routine Assessment of Patient Index Data 3 (RAPID3), and combinations with these such as DAS28-CRP and DAS28-ESR.<sup>1</sup>

### **Serological Tests**

Serologic analysis for RA evaluation include anti-cyclic citrullinated peptide (CCP) antibodies, rheumatoid factor (RF), C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). Both CRP and ESR levels appear to be negatively correlated with disease activity. However, analysis of ESR and CRP levels can be misleading since they indicate the presence of an inflammatory state and are not specific for RA. These tests are often positive in patients who have common conditions other than RA. In addition, ESR and CRP tests can also be negative despite the presence of clinically obvious inflammation.<sup>1</sup> Therefore, accurate and sensitive assays for monitoring disease activity for RA are currently being researched. One such assay is the Vectra DA test.

#### Vectra DA test. (Crescendo Bioscience Inc.)

The Vectra DA test, by Labcorp, Inc., is a multi-biomarker serological assay designed to aid in the assessment of disease activity in RA patients when used in conjunction with standard clinical assessment.<sup>3</sup> This test is not intended or validated to diagnose RA. This test is marketed as a more complete assessment of disease activity, as it measures Vectra DA measures 12 biomarkers, including CRP, and combines them into a single composite score presumed to indicate RA disease activity.

The Vectra DA tests is proposed as a tool to be used in three clinical scenarios:

1. **Assessing disease activity:** When assessing patients with RA, the test is marketed to be used to provide an initial Vectra DA score, which provides a starting point to track RA disease activity over time. Subsequent use of the test can be used to measure subsequent interventions, with the goal of lowering disease activity.
2. **Assessing risk of joint damage:** The test is proposed as a potential tool to identify the risk for radiographic progression with Vectra DA. Patients with early RA who have high Vectra DA scores are suspected of being at higher risk of joint damage, while low to moderate scores may indicate lower risk.
3. **Assessing response to therapy:** Changes in Vectra DA scores may provide insight to help assess disease activity in response to several commonly used therapies, including methotrexate and biological therapies such as anti-TNF medications.<sup>3</sup>

## **REGULATORY STATUS**

### **U.S. FOOD AND DRUG ADMINISTRATION (FDA)**

Approval or clearance by the Food and Drug Administration (FDA) does not in itself establish medical necessity or serve as a basis for coverage. Therefore, this section is provided for informational purposes only.

## CLINICAL EVIDENCE AND LITERATURE REVIEW

### EVIDENCE REVIEW

Vectra DA test as a management tool for rheumatoid arthritis (RA). The evidence reviewed consisted of clinical studies that have reported outcomes of clinical validity (the clinical performance of the Vectra DA test) and clinical utility (how the results from the Vectra test altered management decisions and how those decisions improved outcomes including reductions in pain and swelling, improvements in functional status, and/or the reductions or prevention of joint damage). Below is a summary of the available evidence identified through April 2022.

#### Systematic Reviews

- In 2019, Curtis and colleagues compared the MBDA score with the DAS28-CRP and CRP for predicting risk of radiographic progression in patients with rheumatoid arthritis.<sup>4</sup> Published studies of the MBDA score and radiographic progression with at least 100 patients per cohort were evaluated. In total, 5 cohorts were included for review (n=929). Radiographic progression was more frequent with increasing MBDA scores across all studies. Positive predictive value was generally similar using categories of MBDA score, DAS28-CRP or CRP, but negative predictive values were greater for MBDA score than DAS28-CRP or CRP. For patients cross-classified by MBDA score and DAS28-CRP, high vs. not-high, MBDA score significantly predicted radiographic progression independently of DAS28-CRP. While investigators concluded that MBDA score was a better predictor of radiographic progression than DAS28-CRP or CRP, the study did not validate MBDA findings with improved treatment outcomes.
- In 2018, reviewed in 2021, Hayes published a review that evaluated the Vectra DA test for management of patients with rheumatoid arthritis.<sup>1</sup> Having searched the literature through January 2018, investigators reviewed 13 studies that evaluated the clinical validity of the Vectra test and its' ability to detect or predict RA disease activity and one study that evaluated the tests' influence on clinical management. Sample sizes of included studies ranged from 78 to 646 patients and follow-up durations ranged from none to two years. The review stated that although the body of evidence for clinical validity of the Vectra test was large in size, it was low in quality, and suffered from a number of limitations, including, "retrospective analysis, lack of radiographic assessment, small number of patients with disease progression, inadequate measures for comparing the accuracy of the Vectra test with other established tests, incomplete statistical analysis, findings limited to correlations only, no evaluation of the impact of this test on patient health outcomes, and insufficient or no follow-up." This body of evidence was inconsistent and conflicting regarding the accuracy of the Vectra test relative to established methods for assessment of RA disease activity. The one included study that assessed the influence of Vectra test results on treatment plans for 101 patients with RA, reported that 38% of patients had treatment plans that were altered in response to results of the Vectra test.<sup>5</sup> However, the review stated that the study "does not provide reliable evidence of efficacy since

it did not involve any follow-up to assess the influence of these changes on health outcomes and it did not compare the Vectra test with other methods of RA disease activity assessment to determine whether they would have had similar influences on patient management.” Hayes provided a **rating of “D2”** for the use of the Vectra test for management of patients with RA, stating that additional well-designed study are needed.

Since the publication of the Hayes review, no additional studies have been identified that address the use of the Vectra DA test for any clinical scenario for RA, including but not limited to assessing disease activity, risk of joint damage or response to therapy.

- In 2018, Johnson and colleagues conducted a systematic review and meta-analysis evaluating the correlation of the multi-biomarker disease activity (MBDA) score with other rheumatoid arthritis disease activity measures.<sup>6</sup> Independent investigators systematically searched the literature through March 2017, identified eligible studies, assessed study quality, extracted data and pooled results. Correlation of the MBDA with composite RA disease activity measures were pooled with random-effects meta-analyses. In total, 8 studies were included for review (n =3,242 assays) reporting correlations of the MBDA with RA disease activity measures. Pooled analysis indicated that MBDA demonstrated modest correlations with the Disease Activity Score in 28 joints using the C-reactive protein level (DAS28-CRP) and the erythrocyte sedimentation rate. Weaker associations were reported with the Simplified Disease Activity Index and Clinical Disease Activity Index. Limitations included manufacturer funding of most studies included for review, and inconsistent reporting of sample handling. Investigators concluded that while the MBDA can complement existing RA disease activity measures, additional studies assessing clinical validity and utility are warranted.

#### Non-randomized Studies

- In 2019, Curtis and colleagues conducted a retrospective cohort study to evaluate the clinical utility of the MBDA test for the management of rheumatoid arthritis.<sup>7</sup> Using retrospective Medicare data, investigators linked RA patients to their MBDA test result, and reported initiation of a biologic or Janus kinase (JAK) inhibitor in the 6 months following MBDA testing. Authors then conducted a multivariable adjustment to evaluate the likelihood of patients adding or switching biologic/JAK inhibitor. The outcome of interest was future RA medication failure, defined by the necessity to change RA medications. Among 60,596 RA patients with MBDA testing, the proportion of patients adding or switching biologics/JAK inhibitor among those not already taking a biologic/JAK inhibitor was 9.0% for patients with low MBDA scores, 11.8% for patients with moderate MBDA scores, and 19.7% for patients with high MBDA scores. Compared to those with low disease MBDA scores, the likelihood of switching was 1.51-fold greater (95% CI 1.35–1.69) for patients with moderate MBDA scores, and 2.62 (2.26–3.05) for patients with high MBDA scores. Investigators concluded that patients with RA who had higher MBDA scores were more likely to add (or switch) biologics or JAK inhibitors compared to patients who were tested and had lower MBDA scores. Limitations include the study’s retrospective design, lack of randomization, the diversity of clinical scenarios prompting testing, and unclear clinical utility (i.e. it is unclear whether clinicians switched therapies due to the MBDA test result).

#### **CLINICAL PRACTICE GUIDELINES**

American College of Rheumatology (ACR)

In 2019, the ACR updated an evidence-based clinical practice guideline addressing the management of rheumatoid arthritis. A systematic review identified 11 measures that fulfilled a minimum standard for regular use in most clinic setting, and 5 measures were recommended: the Disease Activity Score in 28 Joints with Erythrocyte Sedimentation Rate or C-Reactive Protein Level, Clinical Disease Activity Index, Simplified Disease Activity Index, Routine Assessment of Patient Index Data 3, and Patient Activity Scale-II. Vectra DA was found to meet minimum standard.<sup>8</sup>

**EVIDENCE SUMMARY**

There is insufficient evidence of clinical validity to support the use of the Vectra DA test to guide treatment for any indication, including RA. The published data is conflicting as to whether or not the Vectra DA test performs as well as single biomarkers for assessing RA disease activity, risk of joint damage or response to therapy. There is a paucity of evidence indicating that treatment decisions can be influenced by the Vectra DA test MBDA scores and improve net health outcomes in patients with RA. The studies evaluating the clinical utility of the Vectra DA test are limited by the study design, using archived serum samples, simulated cases, or physician surveys, and did not report any health outcomes. In addition, there are no randomized controlled trials that compare use of the Vectra DA test to any currently employed methods or tools for measuring disease activity, including the commonly used DAS28 composite test. Therefore, Vectra DA tests are considered investigational.

**BILLING GUIDELINES AND CODING**

CODES*		
CPT	81490	Autoimmune (rheumatoid arthritis), analysis of 12 biomarkers using immunoassays, utilizing serum, prognostic algorithm reported as a disease activity score

**\*Coding Notes:**

- The above code list is provided as a courtesy and may not be all-inclusive. Inclusion or omission of a code from this policy neither implies nor guarantees reimbursement or coverage. Some codes may not require routine review for medical necessity, but they are subject to provider contracts, as well as member benefits, eligibility and potential utilization audit.
- All unlisted codes are reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is submitted for non-covered services addressed in this policy then it will be **denied as not covered**. If an unlisted code is submitted for potentially covered services addressed in this policy, to avoid post-service denial, **prior authorization is recommended**.
- **See the non-covered and prior authorization lists on the Company [Medical Policy, Reimbursement Policy, Pharmacy Policy and Provider Information website](#) for additional information.**
- HCPCS/CPT code(s) may be subject to National Correct Coding Initiative (NCCI) procedure-to-procedure (PTP) bundling edits and daily maximum edits known as “medically unlikely edits” (MUEs) published by the Centers for Medicare and Medicaid Services (CMS). This policy does not take precedence over NCCI edits or MUEs. Please refer to the CMS website for coding guidelines and applicable code combinations.

## REFERENCES

1. Hayes Inc. Vectra DA Test (Crescendo Bioscience Inc.) for Management of Patients with Rheumatoid Arthritis. <https://evidence.hayesinc.com/report/dir.vectrada2652>. Published 2018 (updated 2021). Accessed 5/3/2022.
2. Anderson J, Caplan L, Yazdany J, et al. Rheumatoid arthritis disease activity measures: American College of Rheumatology recommendations for use in clinical practice. *Arthritis care & research*. 2012;64(5):640-647. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4028066/>
3. Labcorp. Vectra by Labcorp. <https://www.labcorp.com/rheumatology/vectra>. Accessed 5/3/2022.
4. Curtis JR, Brahe CH, Østergaard M, et al. Predicting risk for radiographic damage in rheumatoid arthritis: comparative analysis of the multi-biomarker disease activity score and conventional measures of disease activity in multiple studies. *Current medical research and opinion*. 2019:1-11.
5. Li W, Sasso EH, Emerling D, Cavet G, Ford K. Impact of a multi-biomarker disease activity test on rheumatoid arthritis treatment decisions and therapy use. *Curr Med Res Opin*. 2013;29(1):85-92. <https://www.ncbi.nlm.nih.gov/pubmed/23176063>
6. Johnson TM, Register KA, Schmidt CM, et al. Correlation of the Multi-Biomarker Disease Activity Score with Rheumatoid Arthritis Disease Activity Measures: A Systematic Review and Meta-Analysis. *Arthritis care & research*. 2018.
7. Curtis JR, Xie F, Yang S, Danila MI, Owensby JK, Chen L. Uptake and Clinical Utility of Multibiomarker Disease Activity Testing in the United States. *The Journal of rheumatology*. 2019;46(3):237-244.
8. England BR, Tiong BK, Bergman MJ, et al. 2019 Update of the American College of Rheumatology Recommended Rheumatoid Arthritis Disease Activity Measures. *Arthritis care & research*. 2019;71(12):1540-1555. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6884664/>

## POLICY REVISION HISTORY

DATE	REVISION SUMMARY
2/2023	Converted to new policy template.