BlueCross BlueShield Federal Employee Program.

FEP Medical Policy Manual

FEP 2.04.119 Multibiomarker Disease Activity Blood Test for Rheumatoid Arthritis

Effective Policy Date: October 1, 2023

Original Policy Date: September 2014

Related Policies:

None

Multibiomarker Disease Activity Blood Test for Rheumatoid Arthritis

Description

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Assessment of disease activity in rheumatoid arthritis (RA) is an important component of management with a goal of treatment to maintain low disease activity or achieve remission. There are a variety of instruments for measuring RA disease activity. The instruments use combinations of physical exam findings, radiologic results, and serum biomarkers to construct a disease activity score. A multibiomarker disease activity (MBDA) instrument is a disease activity measure that is comprised entirely of serum biomarkers. The Vectra test is a commercially available MBDA blood test that measures 12 biomarkers to construct a disease activity score. Concentrations of these 12 biomarkers are entered into a proprietary formula which, after adjustment by age, gender, and adiposity (i.e., leptin) levels, generates a disease activity score ("adjusted MBDA score") that ranges from 1 (low disease activity) to 100 (high disease activity).

OBJECTIVE

The objective of this evidence review is to determine whether the use of a multibiomarker disease activity (eg, Vectra) blood test as an adjunct or as a replacement of other disease activity measures improves the net health outcome in individuals with rheumatoid arthritis.

POLICY STATEMENT

The use of a multibiomarker disease activity score for rheumatoid arthritis (eg, Vectra score) is considered **investigational** in all situations.

POLICY GUIDELINES

None

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

Some Plans may have contract or benefit exclusions for genetic testing.

FDA REGULATORY STATUS

Vectra Test

The Vectra test is a commercially available multibiomarker disease activity (MBDA) test that is an approach to measuring RA disease activity that uses only serum biomarkers obtained through a laboratory blood draw. The manufacturer describes Vectra as a complement to clinical judgment.[6,] Although not explicitly stated, it appears that the test may be used as an adjunct to other disease activity measures, to potentially identify patients at high-risk of progression who would benefit from a more aggressive treatment strategy.

The Vectra test measures the serum concentrations of the following 12 biomarkers: 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), serum amyloid A (SAA), leptin, and resistin. The concentrations of these 12 biomarkers are measured in serum and, combined with age, gender, and adiposity (i.e., leptin) information, are entered in a proprietary formula to generate a score on a scale of 1 to 100 that represents the level of RA disease activity.[7,]

Categories of scores were constructed to correlate with the DAS28-CRP scale[6,8,]:

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

Prior to December 2017, the Vectra test was originally referred to as Vectra DA and the original MBDA score did not include adiposity (i.e., leptin) adjustment.[9,] However, as the current, commercially available version of the test includes the leptin-adjusted MBDA score (now called the "adjusted MBDA score"), the focus of this policy will primarily be on the leptin-adjusted Vectra test.[7,]

In the ACR working group's systematic review reported by England et al (2019),[5,] they also graded feasibility of the RA disease activity measurement tools. Any measure not commercially available or requiring advanced imaging was graded as infeasible. All other measures started with 4 points (ie, “++++”) and were downgraded by 1-point for each of the following implementation considerations: requiring a provider joint count, requiring a laboratory test, not possible to complete during a routine clinic visit, and not possible to complete on the same day as the clinic visit. The ACR Working Group downgraded the feasibility of the Vectra DA by 3 points (ie, score of “++++" decreased to “+"). This was due to its requirement of a laboratory test and because its result is not available on the same day as the clinic visit. Although the current, commercially available version of the Vectra test was not assessed in the 2019 ACR guideline, because it requires the same laboratory testing that is not available on the same days as the clinic visit, likely it would have a similar feasibility rating as the older version.

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

RATIONALE

Summary of Evidence

Vectra Test with Adjusted Multibiomarker Disease Activity Score

For individuals with rheumatoid arthritis (RA) who receive the current commercially available Vectra test ("adjusted multibiomarker disease activity [MBDA] score") as an adjunct or as a replacement of other disease activity measures, the evidence includes 2 studies that analyzed archived serum samples using combined data from RCTs and cohort studies. Relevant outcomes are test validity, other test performance measures, symptoms, change in disease status, functional outcomes, and quality of life. Analyses comparing Vectra with other previously validated disease activity measures such as the Disease Activity Score with 28 joints (DAS28) or to radiographic progression, consisted mostly of correlations. However, the positive predictive values (PPVs) that individuals with Vectra moderate to high risk disease scores had radiographic progression were low, at 4.4% and 15.8%, respectively. Additionally, due to numerous study relevance, design, and conduct limitations, the body of evidence on the Vectra test is insufficient to determine whether it is as good as or better than other disease activity measures. Given the high prevalence of discordant results across conventional measures of disease activity, the position of the Vectra test in the management pathway is unclear. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Original Vectra Disease Activity Test

For individuals with RA who receive the original Vectra DA test as an adjunct or as a replacement of other disease activity measures, the evidence includes analyses of archived serum samples from randomized controlled trials (RCTs) and prospective cohort studies. Relevant outcomes are test validity, other test performance measures, symptoms, change in disease status, functional outcomes, and quality of life. Analyses comparing Vectra DA with other previously validated disease activity measures such as the DAS28 or to radiographic progression, consisted mostly of correlations, with only 1 study providing sensitivity, specificity, PPV, and negative predictive value (NPV). The PPV from this study was 21%. Other analyses of archived serum samples evaluated the use of Vectra DA to predict treatment response. Results from those analyses were inconsistent. The 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. Additionally, there is no evidence evaluating Vectra DA as an adjunct to other disease activity measures. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American College of Rheumatology

In its 2019 guidelines on recommended rheumatoid arthritis disease activity measures, the American College of Rheumatology[5,] identified the following 11 measures of disease activity as fulfilling a minimum standard for regular use in most clinical settings: Disease Activity Score (DAS), Routine Assessment of Patient Index Data 3 (RAPID3), Routine Assessment of Patient Index Data 5 (RAPID5), Clinical Disease Activity Index (CDAI), Disease Activity Score with 28 joints (DAS28-ESR/CRP), Patient Derived DAS28, Hospital Universitario La Princesa Index (HUPI), Multibiomarker Disease Activity Score (MBDA score, Vectra DA), Rheumatoid Arthritis Disease Activity Index (RADAI), Rheumatoid Arthritis Disease Activity Index 5 (RADAI-5), Simplified Disease Activity Index (SDAI). Although the original Vectra DA test is included in this list, the current commercially available version of the test that is now called Vectra and that includes the leptin-adjusted MBDA score (now called the "adjusted MBDA score") was not addressed in the 2019 ACR guideline. This is because evidence on Vectra with the adjusted MBDA score was published subsequent to the ACR review end date.

National Institute for Health and Care Excellence

Published in 2018 and updated in 2020, the NICE guidance on the management of adult patients with rheumatoid arthritis does not include a discussion on the use of a MBDA test to monitor patients.[30,]

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There are no Medicare national coverage determinations for the Vectra test. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
September 2014	New policy	The use of a multibiomarker disease activity score for rheumatoid arthritis (eg, Vectra DA score) is considered investigational in all situations.
September 2015	Replace policy	Policy updated with literature review through March 22, 2015. References 9 and 11-12 added. No change to policy statement
September 2016	Replace policy	Policy updated with literature review through April 26, 2016; references 12-15 added. Policy statement unchanged.
September 2018	Replace policy	Policy updated with literature review through April 9, 2018; references 15-16, 18-19, 20 and 23-24 added. Policy statement unchanged. Title changed to "Multibiomarker Disease Activity Blood Test for Rheumatoid Arthritis.,
September 2019	Replace policy	Policy updated with literature review through April 23, 2019; references added. Policy statement unchanged.
September 2020	Replace policy	Policy updated with literature review through April 15, 2020; references added. Rationale section significantly revised to focus on current commercially available version of Vectra test with adjusted MBDA score rather than original Vectra DA test. Policy statement unchanged.
September 2021	Replace policy	Policy updated with literature review through May 7, 2021; reference added. Policy statement unchanged.
September 2022	Replace policy	Policy updated with literature review through May 9, 2022; references added. Policy statement unchanged.
September 2023	Replace policy	Policy updated with literature review through April 25, 2023; references added. Policy statement unchanged.