HEALTH PLANS
UNIVERSITY OF UTAH

Medical Policy

Vectra DA Blood Test for Rheumatoid Arthritis

Policy MP-027

Origination Date: 09/26/2018

Reviewed/Revised Date: 11/15/2023

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Current Effective Date: 11/15/2023

Disclaimer:

1. Policies are subject to change in accordance with State and Federal notice requirements.
2. Policies outline coverage determinations for U of U Health Plans Commercial, CHIP and Healthy U (Medicaid) plans. Refer to the "Policy" section for more information.
3. Services requiring prior-authorization may not be covered, if prior-authorization is not obtained.
4. This Medical Policy does not guarantee coverage or payment of the service. The service must be a benefit in the member's plan and the member must be eligible for coverage at the time of service. Additional payment guidelines may be applied that are not included in this policy.

Description:

Rheumatoid arthritis (RA) as defined by the Centers for Disease Control and Prevention (CDC), is an autoimmune and inflammatory disease, where your immune system attacks healthy cells in joints causing damage to the tissue and painful swelling. Usually attacking more than one joint at a time, RA most commonly affects the hands, wrists, feet and knees. However, RA not only causes chronic pain, it can also cause unsteadiness and deformities in your joints. On occasion RA can affect other tissues in your body and cause significant problems in organs for example the heart, lungs, and eyes. The American College of Rheumatology states that RA is the most common autoimmune inflammatory arthritis in adults.

According to their website, Vectra® DA is an advanced blood test for adults that measures 12 markers of RA disease activity. Other tests only measure one marker, such as the C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR or "sed rate"). This test has not been studied or validated for diagnosing the disease, nor has it been studied to predict which therapy would work best for the patient.

Policy Statement and Criteria

1. Commercial Plans/CHIP

U of U Health Plans does NOT cover the use of a multi-biomarker disease activity score (Vectra DA) for rheumatoid arthritis as it is considered investigational for all indications.

2. **Medicaid Plans**
   Coverage is determined by the State of Utah Medicaid program; if Utah State Medicaid has no published coverage position and InterQual criteria are not available, the U of U Health Plans Commercial criteria will apply. For the most up-to-date Medicaid policies and coverage, please visit their website at: https://medicaid.utah.gov/utah-medicaid-official-publications/ or the Utah Medicaid code Look-Up tool

   CPT/HCPCS codes covered by Utah State Medicaid may still require further evaluation to determine medical necessity for coverage.

Clinical Rationale

A 2013 study (Hirata et al) evaluated the Vectra DA test and other validated measures of disease activity, as a tool to guide management of rheumatoid arthritis (RA) patients. A total of 125 patients with rheumatoid arthritis (RA) from the Behandel Strategieën (BeSt) study, which was a multicenter RCT of 508 patients with early RA, were investigated. Clinical data and serum samples were available from 179 visits, 91 at baseline and 88 at year 1. In each serum sample, 12 biomarkers were measured by quantitative multiple immunoassays and the concentrations were used as input to a pre-specified algorithm to calculate Multi-Biomarker Disease Activity (MBDA) scores. Validated disease activity measures were DAS28, SDAI, CDAI, and the HAQ Disability Index (DI). The Vectra DA scores were significantly correlated with the DAS28 measure (Spearman correlation coefficient $\rho=0.66$, $p<0.001$), as were the changes in scores between baseline and one year (Spearman $\rho=0.55$, $p<0.001$). The Vectra scores were also significantly correlated with the SDAI, CDAI, and HAQ-DI at the $p<0.001$ level. This study was limited by the retrospective study design and small sample size. The authors noted, "Effective comparison of the Multi-biomarker disease activity score with other biomarkers will require additional studies using independent disease outcomes such as joint damage progression or functional disability."

Another study in 2014 (Marcuse et al), also used samples from the BeST trial to assess how well the Vectra score predicted the progression of radiographic joint damage and compared DAS28 with the predictive ability of Vectra DA. Radiographic progression was defined as a change of at least five points on the Sharp van der Heijde Score over a one-year period. ROC analysis was performed, with an area under the curve (AUC) for the Vectra DA test of 0.77 (95% CI 0.64 to 0.90), which was higher than the AUC for the DAS28 (0.52, 95% CI 0.39 to 0.66). Comparison of patients who had samples available from the BeST trial and those who did not revealed that the population with serum available differed from those who did not on sex (75% vs. 65% female, $p=0.04$), the median number of tender joints (11 vs. 14, $p<0.001$), and the median number of erosions seen on imaging (1.0 vs. 2.0, $p=0.005$).

In a 2015 randomized control trial (RCT) (Hambardzumyan et al) performed a post-hoc analysis of, a total of 235 patients (48%) who had serum samples available and complete clinical and radiographic data from the Swedish Farmacotherapy (SWEFOT) clinical trial. The authors evaluated the Vectra DA score as a predictor of radiographic progression, defined as a change of at least five points on the Van der Heijde Sharp score. The Vectra DA score was a univariate predictor of radiographic progression (odds ratio [OR], 1.05 per unit increase, 95% confidence interval [CI] 1.02 to 1.08, $p<0.001$), and was an independent predictor of progression in a variety of multivariate models. For patients with a low or moderate Vectra DA score (<44), radiographic progression was uncommon, occurring in 1 in 34 (3.4%) patients during year one.

A 2016 post-hoc RCT (Reiss, et al), analyzed patients from the ACT-RAY trial in which patients who did not respond to methotrexate therapy were randomized to add-on tocilizumab therapy or placebo. Patients were included in the analysis if they had DAS28-CRP and Clinical Disease Activity Index (CDAI) scores at baseline and 24 weeks follow-up and sufficient serum for MBDA testing at the same time points. Disease activity level (low, moderate, high) agreement between DAS28-CRP and MBDA at baseline was 77%; however, the agreement between the two measures at 24 weeks of follow-up was 24%. Agreement between MBDA and CDAI followed a similar pattern: 72% agreement at baseline and 22% agreement after 24 weeks of tocilizumab therapy. DAS28-CRP and CDAI had high levels of agreement, both at baseline and 24 weeks (87% and 85%, respectively).

Another 2016 post-hoc analysis (Fleischmann et al), published results from a RTC, the Abatacept versus adaliMumab comParison in bioLogic-naivE RA (AMPLE) study, that compared different administrations of adalimumab in the treatment of patients with RA who are biologic naïve. The authors assessed the ability of an MBDA score to reflect clinical measures of disease in patients with RA. Six hundred and forty six participants were enrolled in the AMPLE study, and MBDA data on 524 of them were available. Participants MBDA score was analyzed in serum samples collected at baseline, month 3, and years 1 and 2. Cross-tabulation was used to compare the MBDA score and clinical measures of disease activity: CDAI, Simplified Disease Activity Index (SDAI), DAS28-CRP, and Routine Assessment of Patient Index Data (RAPID)-3. The authors found no association between the MBDA score and disease activity and recommended that the MBDA score not be used to guide decision-making in the management of patients with RA, although this result may be taken with caution as another group re-analyzed the same data with different results.

A 2016 RCT (Hambardzumyan et al), publicized from the SWEFOT trial of which 487 patients with two different treatment regimens, reported repeat scores at multiple time points. Of the 487 patients enrolled, 220 had baseline Vectra DA scores (45.2%), 205 had scores at three months (42.1%), and 133 had scores at one year (27.3%). Patients with low initial scores, or with a decrease in scores over time into the low range, had the lowest rate of radiographic progression at one year. Cross tabulation of Vectra DA results with the DAS28, ESR, and CRP values was presented, but no statistics that addressing the comparative accuracy of the different measures were reported.

A 2016 publication by Li et al, from the Leiden Early Arthritis Clinic Cohort (Index for Rheumatoid Arthritis Measurement, Brigham and Women's Hospital Rheumatoid Arthritis Sequential Study) used the Vectra DA score and other measures of disease activity to predict radiographic progression of disease at one year. There were 163 patients in this cohort that had complete information on Vectra DA and other disease activity measures. The proportion of patients with radiographic progression increased as Vectra DA scores increased. For patients with a score of less than 29, 2% met criteria for radiographic progression, and for patients with a score of 60 or greater, 41% met criteria for radiographic progression. Vectra DA scores and other measures of disease activity (DAS28-CRP, swollen joint count, CRP) were predictors of radiographic progression on univariate analysis. On multivariate analysis, only the Vectra DA score was a significant predictor of progression at one year ($p=0.005$).

In 2017, Hambardzumyan et al analyzed subset of data from the SWEFOT trial to examine the use of MBDA as a predictor of optimal treatment in patients with early RA who did not respond to methotrexate (MTX) therapy. As defined earlier, patients (n=157) in the SWEFOT trial were randomized into two groups: triple therapy (MTX plus sulfasalazine plus hydroxychloroquine) and MTX plus infliximab. MBDA categories were defined as: <30 = low disease activity, 30 to 44 = moderate disease activity, and >44 = high disease activity. Responders after a 1 year follow-up were defined as patients with DAS28 less than 3.2. The analysists compared MBDA scores at 3 months with DAS28-ESR measures

at 1 year to determine if MBDA scores at 3 months could accurately predict the patients' response to therapy at the 1 year follow-up. Among patients with low MBDA scores at 3 months, 88% (7 of 8) subsequently had a clinical response to triple therapy, and 18% (2 of 11) had a clinical response to MTX plus infliximab. Among patients with high MBDA scores at 3 months, 35% (15 of 43) subsequently responded to triple therapy, and 58% (26 of 46) responded to MTX plus infliximab. The three-month low and high MBDA scores were better predictors of clinical response to therapy than clinical and inflammatory markers. In conclusion, the 3 month MBDA scores have the potential to inform the decision on which type of therapy to recommend to patients who do not respond to initial methotrexate therapy.

A 2018 study (Curtis et al) reviewed the influence of obesity, age, and other comorbidities on the MBDA test in rheumatoid arthritis. The study included 357 patients who were classified at having low (<30), moderate (30-44), and high (>44) MBDA scores. The study found that MBDA scores were significantly associated with body mass index, age, clinical disease activity index, and swollen joint count. The data suggest that older age and obesity can have independent, potentially confounding effects of MBDA testing. Because of this, the authors propose adjusting MBDA scores to account for the effects of age and body mass index.

In 2020, a publication by Ma et al, reported on a study of MBDA scores looking at patients who were already in clinical remission or had a low disease activity state. There were 148 patients enrolled in the Remission in Rheumatoid Arthritis (REMIRA) cohort. The data shows that MBDA scores, including biomarkers IL-6, leptin, SAA, and CRP were able to differentiate remission versus low disease activity at baseline and predicted remission outcomes at 1 year. However, the study did not address using MBDA testing for patients with moderate to severely active disease and only concludes that it is important to follow patients frequently to assess their disease activity.

Another 2020 study (Luedders et al) evaluated whether MBDA scores predict response to first line treatment with methotrexate. Out of the 130 patients enrolled in the study only 95 of these patients had follow-up on MBDA scores. This study was a 16 week open-label trial that monitored MBDA scores, disease activity, and DAS28-ESR. Baseline MBDA scores did not predict ACR response to methotrexate or achievement of low disease activity at 16 weeks. The MBDA scores had weak-to-very weak correlations to patient global and function. However, the DAS28-ESR was significantly associated with ACR20 response if elevated at baseline and demonstrated much greater responsiveness following treatment with methotrexate compared to MBDA.

A 2021 article published by Fleishmann et al demonstrated that MBDA scores are not sufficiently responsive for assessing RA disease activity after repository corticotrophin injection therapy, which is consistent with what has been seen in clinical trials with other RA drugs. The conclusion of this study was that MBDA should not be a preferred disease activity measure in clinical practice.

Also in 2021, a cohort analysis (Curtis, et al) investigated the prognostic ability of the MBDA score to predict radiographic analysis. This cohort analysis demonstrated that the MBDA score was a stronger predictor of radiographic progression than DAS28- CRP, CRP, SJC, and CDAI, and its prognostic ability was not improved by any of these other measures, including when it was discordant with them. However, it is important to remember that this is radiographic progression and not the measurement of disease activity.

The 2015 American College of Rheumatology (ACR) guidelines for the treatment of RA endorse 6 measurements of rheumatoid arthritis disease activity:

1. Patient Activity Scale (PAS) or

2. Patient Activity Scale-II (PASII)
3. Routine Assessment of Patient Index Data 3 (RAPID3)
4. Clinical Disease Activity Index (CDAI)
5. Disease Activity Score (DAS) 28 – Erythrocyte Sedimentation Rate (ESR)
6. Simplified Disease Activity Index (SDAI)

As of 2019, the ACR updated their recommendations to 5 measurements of rheumatoid arthritis disease activity instead of 6 as follows:

1. Routine Assessment of Patient Index Data 3 (RAPID3)
2. Clinical Disease Activity Index (CDAI)
3. Disease Activity Score (DAS) 28 – Erythrocyte Sedimentation Rate (ESR) or C-Reactive Protein Level (CRP)
4. Simplified Disease Activity Index (SDAI)
5. Patient Activity Scale-II (PAS-II),

These guidelines list MBDA as "inconclusive" and do not definitively recommend this testing for measuring rheumatoid arthritis disease activity. This is because a majority of the voters did not recommend MBDA testing for monitoring rheumatoid arthritis disease activity. A 2021 review of literature found that the ACR had not changed these 2019 recommendations.

The ACR recognizes that there are other measures available to clinicians, however, because of the scope of this review they were not included in this guideline.

Applicable Coding

CPT Codes

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

HCPCS Codes

No applicable codes found

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