healthfirst
Health Insurance for New Yorkers

Reimbursement Policy

Subject:	Urine Culture Testing for Bacteria		
Policy Number:	PO-RE-013v3		
Effective Date:	11/01/2023	**Last Approval Date:**	08/21/2023

Policy Description | Related Policies | Indications and/or Limitations of Coverage | Scientific Background | Guidelines and Recommendations | Applicable CPT/HCPCS Procedure Codes | Evidence-based Scientific References | Revision History | Disclaimer

I. Policy Description

Bacteriuria is the presence of bacteria in the urine. Urinary tract infections (UTIs) can occur in the urinary system and can be either symptomatic or asymptomatic. UTIs can include cystitis, an infection of the bladder or lower urinary tract; pyelonephritis, an infection of the upper urinary tract or kidney; urosepsis; urethritis; and male-specific conditions, such as bacterial prostatitis and epididymitis (Bonkat et al., 2023; Hooton & Gupta, 2023). Typically, in an infected person, bacteriuria, and pyuria (the presence of pus in the urine) are present and can be present in both symptomatic and asymptomatic UTIs. A urine culture can be performed to determine the presence of bacteria and to characterize the bacterial infection (Meyrier, 2023).

For guidance on pathogen panel testing from urine samples, please see AHS-G2149 Pathogen Panel Testing.

Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request. Specifications pertaining to Medicare and Medicaid can be found in the "Applicable State and Federal Regulations" section of this policy document.

1. **MEET COVERAGE CRITERIA** For pregnant individuals, urine culture testing (with isolate identification and antibiotic susceptibilities if applicable) for a urinary tract infection (UTI) **MEETS COVERAGE CRITERIA**.

2. To assess pyelonephritis, urine culture testing (with For asymptomatic individuals undergoing urological interventions which breach the mucosa, urine culture testing (with isolate identification and antibiotic susceptibilities if applicable) prior to the procedure **MEETS COVERAGE CRITERIA**.

3. For individuals exhibiting at least one sign or symptom of a possible UTI or bacteriuria (see Note 1 below), urine culture testing (with isolate identification and antibiotic susceptibilities if applicable) **MEETS COVERAGE CRITERIA**.

4. isolate identification and antibiotic susceptibilities if applicable) **MEETS COVERAGE CRITERIA**.

5. For all other instances of asymptomatic UTI or asymptomatic bacteriuria not described above, urine culture testing (with isolate identification and antibiotic susceptibilities if applicable) **DOES NOT MEET COVERAGE CRITERIA**.

6. For individuals that show evidence of clinical resolution of infection, follow-up urine culture testing for an uncomplicated UTI **DOES NOT**.

The following does not meet coverage criteria due to a lack of available published scientific literature confirming that the test(s) is/are required and beneficial for the diagnosis and treatment of an individual's illness.

7. Urine culture testing (with isolate identification and antibiotic susceptibilities if applicable) **DOES NOT MEET COVERAGE CRITERIA** in any of the following situations:

a. As a part of initial screening for asymptomatic prostatitis.
b. As a part of assessment or prognosis of prostate biopsy.

NOTES:

Note 1: Signs and symptoms of UTI/bacteriuria include (CDC, 2021)

- Fever
- Urgency to urinate
- Feeling the need to urinate despite having an empty bladder
- Increased frequency of urination
- Dysuria
- Suprapubic tenderness
- Pyuria
- Hematuria
- Cloudy urine
- Lower Back and Side (flank) pain
- Nausea
- Vomiting
- Chills
- Night sweats
- Pelvic pressure
- Change in urine smell
- Abnormal urinalysis findings

Guidelines and Recommendations

World Health Organization (WHO)

On May 16, 2018, the WHO released their first edition of the *Model List of Essential In Vitro Diagnostics* (EDL) "to advance universal health coverage, address health emergencies, and promote healthier populations." This list of in vitro diagnostics (IVD) is to be used as a reference of the essential diagnostic tools for laboratories to complement their Model List of Essential Medicines. With respect to the diagnostic tool "to detect inflammation as an indicator of various conditions," the WHO recommends CRP either in an EIA (enzyme immunoassay) or RDT (rapid diagnostic test) assay format. The specimen type can be venous whole blood, serum, or plasma.

In 2019, the WHO released the *Second WHO Model List of Essential In Vitro Diagnostics.* In a table titled *General IVDs for Use in Clinical Laboratories*, CRP is once again listed. The WHO now recommends CRP in an RDT, latex agglutination assay or immunoassay format (WHO, 2019).

In 2020, the WHO released *The selection and use of essential in vitro diagnostics*, which included the third WHO model list. In the section on "General IVDs for community settings and health facilities without laboratories," the WHO performed an evaluation of utilizing ESR "to aid diagnosis and monitoring of certain infections and immune diseases; and as an alternative to a C-reactive protein (CRP) test where this is not available." In their table, they recommend using the Westergren assay format with sampling from venous whole blood. The WHO ultimately concluded that despite several guidelines recommending ESR to aid in diagnosing several inflammatory diseases, "there is no strong evidence supporting ESR as an essential test" since there are also high rates of false positives and false negatives. They conclude that CRP "should remain the preferred choice of test," except in cases of systemic lupus erythematosus and low-grade bone and joint infections since "there is evidence that the condition elevates ESR without causing a raise in CRP." As of this meeting, CRP now has the purpose "to monitor response to treatment" in addition to "detect inflammation as an indicator of various response conditions," and can be assayed as RDT, latex agglutination assay, and immunoassay with sampling venous whole blood, serum, and plasma (WHO, 2020).

National Comprehensive Cancer Network (NCCN)

The NCCN guidelines concerning Hodgkin Lymphoma uses ESR as a diagnostic tool in characterizing the stage/risk classification of Classic Hodgkin Lymphoma (CHL) as well as the primary treatment of the disease. In the diagnosis/workup of Hodgkin Lymphoma in adults (age ≥18 years) (recommendation 2A), they list erythrocyte sedimentation rate (ESR) as "essential" and that ESR should be tested within 6 months of diagnosis.

In the guidelines concerning follow-up after completion of treatment up to five years, the NCCN (2022) recommends obtaining an interim history and physical "every 3-6 [months] for 1-2 [years], then every 6-12 [months] until year 3, then annually," as well as laboratory studies, which included a "[complete

blood count], platelets, ESR if elevated at time of initial diagnosis, chemistry profile, as clinically indicated" with the same timeline. ESR is also used in determining the dosage of involved-site radiation therapy (ISRT). "A dose of 20 Gy following ABVD X 2 is sufficient if the patient has non-bulky stage I-IIA disease with an ESR <50, no extralymphatic lesions, and only one or two lymph node regions involved." An ESR ≥50 is considered as an "unfavorable risk factor" for stages I and II Hodgkin Lymphoma along with B symptoms. Please note that the NCCN guidelines concerning Hodgkin Lymphoma do not contain any information concerning the use of CRP as a diagnostic or prognostic tool (NCCN, 2022).

In the NCCN guidelines concerning the B-cell lymphomas under the section concerning Castleman Disease, the NCCN recommends (category 2A) as "essential" laboratory tests "LDH, CRP, [and] ESR." Within the discussion of the text, it does not mention if all three are required or if only a minimum of one of the three tests are essential in the workup. The guidelines for B-cell lymphomas do not list either CRP or ESR for follow-up testing post-treatment.

Regarding diagnostic criteria for idiopathic MCD (Multicentric Castleman Disease), minor diagnostic criteria include elevated CRP (>10 mg/L) or ESR (>15 mm/h) where an "Evaluation of CRP is mandatory and tracking CRP levels is highly recommended, but ESR will be accepted if CRP is not available" (NCCN, 2023b).

In the NCCN guidelines concerning the T-cell lymphomas, they state that the "evaluation of serological markers such as rheumatoid factor (RF), antinuclear antibodies (ANA), and erythrocyte sedimentation rate (ESR) is useful in patients with autoimmune disease"(NCCN, 2023a). The guidelines concerning T-cell lymphomas do not mention the diagnostic or prognostic use of CRP.

American Society for Clinical Pathology (ASCP)

In the Choosing Wisely site of the ABIM Foundation, the ASCP released the recommendation to not "order an erythrocyte sedimentation rate (ESR) to look for inflammation in patients with undiagnosed conditions. Order a C-reactive protein (CRP) to detect acute phase inflammation" due to the higher sensitivity and specificity of CRP for acute phase of inflammation. "In the first 24 hours of a disease process, the CRP will be elevated, while the ESR may be normal. If the source of inflammation is removed, the CRP will return to normal within a day or so, while the ESR will remain elevated for several days until excess fibrinogen is removed from the serum" (ASCP, 2015).

European League Against Rheumatism (EULAR)

In 2009, EULAR issued their recommendations concerning the management of large vessel vasculitis. With a "Level of Evidence 3, Strength of recommendation C", they recommend "monitoring of therapy for large vessel vasculitis should be clinical and supported by measurement of inflammatory markers…. For patients with giant cell arteritis, a relapse is usually associated with a rise in ESR and CRP" (Mukhtyar et al., 2009). In this paper, no mention of the frequency of ESR and/or CRP testing is mentioned.

In 2013 in *EULAR recommendations for the use of imaging of the joints in the clinical management of rheumatoid arthritis* (Colebatch et al., 2013), they state that "baseline inflammatory disease measured by scintigraphy appears to be associated with radiographic progression. In addition, multiple regression analysis has demonstrated that progression of radiographic joint destruction was primarily predicted by ^{99m}Tc-IgG scintigraphy; joint swelling, ESR and IgM RF (Rheumatoid Factor) were not predictive. This suggests that scintigraphy may be superior to conventional clinical and laboratory measurements in the prediction of joint destruction." This set of guidelines did not include any mention concerning CRP or the frequency of ESR testing.

In 2015, EULAR and the American College of Rheumatology (ACR) issued joint recommendations concerning the management of polymyalgia rheumatica (PMR) (Dejaco et al., 2015). Within their recommendations, they list assessments that "every case of PMR should have…prior to the prescription of therapy (primary or secondary care)." They include a basic laboratory workup "to exclude mimicking conditions and establish a baseline for monitoring of therapy", and they state that this includes "rheumatoid factor and/or anti-cyclic citrullinated peptide antibodies (ACPA), C-reactive protein and/or erythrocyte sedimentation rate (ESR), blood count, glucose, creatinine, liver function tests, bone profile (including calcium, alkaline phosphatase) and dipstick urinalysis." They do not state a specific preference of either CRP or ESR nor do they state the frequency of testing.

EULAR in 2016 updated their 2007 recommendations concerning the management of early arthritis (Combe et al., 2017). The 2016 updates included the following recommendation: "Monitoring of disease activity should include tender and swollen joint counts, patient and physician global assessments, ESR and CRP, usually by applying a composite measure. Arthritis activity should be assessed at 1-month to 3-month intervals until the treatment target has been reached." The recommendation concerning including both ESR and CRP did not change between the 2016 and 2007 recommendations. Within the discussion of the recommendations, they state, "In every patient with active arthritis, closely monitoring disease activity is now considered of particular importance in the therapeutic strategy to provide a good outcome. . . Monitoring disease activity should be as frequent as the level of disease activity mandates, usually every 1-3 months, then potentially less frequently (such as every 6-12 months) once the treatment target has been achieved. Nevertheless, three changes were proposed to this item…. First, a composite measure was recommended as the method of choice to monitor disease activity; second, a specific time frame for monitoring structural damage was deliberately left out and third, patient-reported outcomes were expanded beyond functional assessments" (Combe et al., 2017).

In 2018, EULAR issued *EULAR recommendations for the use of imaging in large vessel vasculitis in clinical practice* (Dejaco et al., 2018). They make no recommendation concerning the preference of ESR or CRP nor do they state the frequency of testing; they do state "in patients with a high clinical suspicion of GCA (>50%), for example, in case of new-onset headache, visual symptoms, jaw claudication and elevated erythrocyte sedimentation rate (ESR) and C reactive protein, a positive ultrasound would result in a post-test probability of >95%."

American College of Rheumatology (ACR)

In 2012, ACR released their recommendations concerning the clinical practice of using disease activity measures of rheumatoid arthritis (RA) (Anderson et al., 2012). The recommend using the Disease Activity Score with 28-joint counts (DAS28), the Clinical Disease Activity Index, the Patient Activity Scale (PAS), the PAS-II, the Simplified Disease Activity Index (SDAI), and Routine Assessment of Patient Index Data with 3 measures. The DAS28 is a composite test that can use either CRP or ESR data. The ACR states that both the CRP or ESR used in the DAS28 have been validated in RA. Of the six activity measures recommended by the ACR, only DAS28 received "excellent" recommendations for all three psychometric properties—reliability, validity, and responsiveness. Within the guidelines, the ACR also issued the scores corresponding to remission, low/minimal, moderate, and high/severe RA for all the disease activity measures, including the DAS28, as well as the mathematical formula using either CRP or ESR data to determine the DAS28. CRP is also used in the SDAI; however, the SDAI is rated as "good" for reliability because they state that "test-retest reliability for composite has not been evaluated" for the SDAI. No mention of frequency of testing is made. They do note that the "inclusion of acute-phase reactants in the DAS28 and SDAI complicates the logistics and timing using these measures in point-of-care clinical decision making. Although these measures have traditionally been used in clinical trials, academic medical centers, and large multispecialty clinics, logistical barriers have likely delayed their widespread adoption in smaller practice settings" (Anderson et al., 2012).

The ACR in 2015 (Singh et al., 2015) issued guidelines for the treatment of RA. While not specifying a preference of either CRP or ESR in diagnosing or predicting the prognosis of RA, they do state in their "Key provisos and principles" that "functional status assessment using a standardized, validated measure should be performed routinely for RA patients, at least once per year, but more frequently if disease is active." They also state that disease activity be measured using ACR-validated scales, including the DAS28 and/or SDAI. Moreover, they define RA remission as "a tender joint count, swollen joint count, C-reactive protein level (mg/dl), and patient global assessment of ≤1 each or a Simplified DAS of ≤3.3, 1 of 6 ACR-endorsed disease activity measures".

Also, in 2015 (but published in 2016), the ACR and the Spondylitis Association of America (SAA) issued their joint recommendations concerning the treatment of ankylosing spondylitis (AS) and nonradiographic axial spondyloarthritis (Ward et al., 2016). Regarding "the treatment of patients with either active or stable AS…we conditionally recommend regular-interval use and monitoring of the CRP concentrations or erythrocyte sedimentation rate (ESR) over usual care without regular CRP or ESR monitoring." This received a "very low-quality evidence; vote 100% agreement" rating. They do make note that as of the time of publication "no studies addressed the effect of routine monitoring of a disease activity measure" but that "the panel thought that monitoring would be most helpful in patients with active symptoms as a guide to treatment." Testing is not required for every clinic visit. The two organizations reaffirm the same recommendations in their 2019 update (Ward et al., 2019).

In 2019, updated recommendations by the RA disease activity measures working group were published by England et al. (2019). Recommended tests include the Clinical Disease Activity Index (CDAI), the Simplified Disease Activity Index (SDAI), the Routine Assessment of Patient Index Data 3 (RAPID3), and the 28-Joint Disease Activity Score (DAS28). As noted above, the DAS28 is a composite test that can use either CRP or ESR data. The ACR states that both the CRP or ESR used

in the DAS28 have been validated in RA. Updates to the management of rheumatoid arthritis were released by the ACR in 2022, but no mention of CRP or ESR were made (Arnold, 2022).

In 2021, the ACR published a guideline to provide evidence-based recommendations and expert guidance for the management of giant cell arteritis (GCA). They present 22 recommendations and 2 ungraded position statements for GCA and note that all but 1 of the recommendations are conditional due to very low- to low-quality evidence. They break these recommendations down into categories, including diagnostic testing, medical management, surgical intervention, and clinical/laboratory monitoring. All diagnostic recommendations involve biopsy or imaging- they do not recommend the use of CRP or ESR for diagnosis of GCA. However, they do recommend inflammation marker monitoring as part of clinical/laboratory monitoring. They define clinical monitoring as "assessing for clinical signs and symptoms of active disease, obtaining 4 extremity blood pressures, and obtaining clinical laboratory results, including inflammation marker levels", with inflammation markers further defined as being CRP and ESR:

"Recommendation: For patients with GCA in apparent clinical remission, we strongly recommend long-term clinical monitoring over no clinical monitoring: The optimal frequency and length of monitoring are not well established and depend on factors including the duration of remission, site of involvement, risk of disease progression, whether the patient is receiving immunosuppressive therapy, and reliability of the patient to report new signs or symptoms. Clinical monitoring may include history taking, examinations, and laboratory and imaging studies. This is a strong recommendation given the minimal risks and potential catastrophic outcomes if monitoring is not performed.

Recommendation: For patients with GCA who have an increase in levels of inflammation markers alone, we conditionally recommend clinical observation and monitoring without escalation of immunosuppressive therapy. Increases in levels of inflammation markers such as erythrocyte sedimentation rate and C-reactive protein can be nonspecific (69). Therefore, increasing immunosuppressive therapy is not warranted in the setting of increased levels of inflammation markers in the absence of other signs of disease activity. However, these increased levels may warrant more frequent clinical and/or radiographic assessments for active disease" (Maz et al., 2021)

American Academy of Family Physicians (AAFP)

In 2013, the AAFP released *Recognition and Management of Polymyalgia Rheumatica and Giant Cell Arteritis*. For polymyalgia rheumatica (PMR), they note that "a normal ESR is found in 6% to 20% of persons with [PMR], although in those cases C-reactive protein level is elevated. ESR predicts relapse more reliably, but C-reactive protein is more sensitive, and is less affected by age and other factors." For giant cell arteritis (GCA), ESR is elevated in up to 89% of patients, but the sensitivity and specificity increase to 99% and 97%, respectively, if both ESR and CRP are tested. Regardless of using either ESR or CRP testing, the AAFP recommends that either ESR or CRP is tested at each clinic visit for patients with either PMR or GCA (Caylor & Perkins, 2013).

American College of Radiology (ACR)

The ACR released their updated guidelines concerning the follow-up of Hodgkin lymphoma in 2014. They state that "limited data are available on the role of routine blood work in detecting relapses." ESR is listed as one of the tests conducted as routine blood work in follow-up of Hodgkin lymphoma. They summarize their findings as the following: "In general a majority of recurrences can be detected initially by history and physical examination rather than by routine imaging studies or blood tests such as ESR, CBC, and chemistry" (Ha et al., 2014). Four of the five variants they reviewed had ESR tests conducted 1 – 2 times per year, and the ACR rated the use of ESR as a 3, 5, 5, and 7 in these four variants where a "3" indicates "usually not appropriate," a "5" is "may be appropriate", and a "7" falls in the "usually appropriate" category.

The ACR released guidelines concerning management of multi-system inflammatory syndrome in children and devised a two-tier algorithm for diagnosis. ACR recommends routine lab tests as tier 1 testing, including complete blood count with manual differential, comprehensive metabolic panel, erythrocyte sedimentation rate [ESR], CRP measurement, and testing for SARS-CoV-2 by polymerase chain reaction or serology. If tier 1 lab results include CRP ≥5 or ESR≥40 and one suggestive lab feature such as neutrophilia, lymphopenia, thrombocytopenia, hyponatremia, or hypoalbuminemia, the child should undergo tier 2 testing, which involves EKG and echocardiogram (Henderson et al., 2020; Henderson et al., 2021).

The British Society for Rheumatology (BSR) & British Health Professionals in Rheumatology (BHPR)

In 2010, BSR and BHPR issued joint guidelines concerning the management of giant cell arteritis (GCA) (Dasgupta, 2010; Dasgupta, Borg, Hassan, Alexander, et al., 2010). They recommend "early recognition and diagnosis of GCA is paramount. Particular attention should be paid to the predictive features of ischaemic neuro-ophthalmic complications." As part of this diagnostic recommendation, they specifically list laboratory tests that should be included— "full blood count, urea and electrolytes, liver function tests, CRP, ESR." They note that, although elevated ESR and CRP levels are hallmarks of GCA, "GCA can occur in the face of lower levels of inflammatory markers, if the clinical picture is typical." Another specific recommendation states, "Monitoring of therapy should be clinical and supported by the measurement of inflammatory markers (C; this is a consensus statement)" and that at each visit "full blood count, ESR/CRP, urea and electrolytes, [and] glucose" lab tests be performed.

Also, in 2010, BSR and BHPR issued joint guidelines concerning the management of polymyalgia rheumatica (PMR) (Dasgupta, Borg, Hassan, Barraclough, et al., 2010). For PMR, they recommend initial lab testing for diagnosis to include either ESR and/or CRP prior to initiating long-term steroid therapy. Also, during such therapy, they recommend monitoring either ESR or CRP every three months. This is a portion of the recommendation (B) of "vigilant monitoring of patients for response to treatment and disease activity."

The British Society for Rheumatology (BSR)

The BSR alone issued their guidelines for the management of systemic lupus erythematosus (SLE) in 2018 (Gordon et al., 2018). For the statement "CRP low or normal unless infection," the BSR gives an overall level of evidence of 2++ with a B grade of recommendation whereas they grade the statement

"ESR correlates with active lupus" a 2+ and only a C grade of recommendation. "ESR is often raised in active SLE, but can also reflect persistent polyclonal hypergammaglobulinaemia, and is not a reliable marker of disease activity…. A significantly raised CRP is more likely to indicate infection, and patients with raised CRP will need therefore to be thoroughly screened for infection, given that infection is the commonest cause of death in lupus patients. In contrast, a raised ESR does not discriminate between active lupus and infection." They recommend that CRP is tested at initial diagnosis and then every 1-3 months during active disease states. Once stabilized, then testing frequency can be every 6-12 months. They also state that CRP testing should be conducted on mothers with SLE during pregnancy, but they do not state the frequency of the testing during pregnancy. This guideline is currently in revision.

The BSR has also published guidelines on the diagnosis and treatment of giant cell arteritis (GCA). Regarding which evaluations should be performed when starting treatment, the BSR states that "When starting glucocorticoids for suspected GCA, diagnostically relevant symptoms and signs should be documented. Blood should be taken for full blood count, CRP and ESR before or immediately after commencing high-dose glucocorticoids. If GCA is strongly suspected, the first dose of glucocorticoid can be given without waiting for laboratory results" (Mackie et al., 2020). Further, the BSR provides a list of clinical assessments which should be carried out at or near a GCA diagnosis. These lists include "Measures of activity of GCA: laboratory markers of inflammation (CRP for all patients, plus either ESR or plasma viscosity) and full blood count (platelet count may be elevated in GCA)." Finally, regarding follow-up visits, "Each follow-up visit should include at least a full history, targeted physical examination and measurement of at least a full blood count, ESR and/or CRP, plus follow-up of any abnormalities relevant to the individual patient as well as drug-specific screening for toxicity" (Mackie et al., 2020). Revision for this guideline will be considered in 2024.

Canadian Rheumatology Association (CRA)

The 2012 guidelines by the CRA titled "Canadian Rheumatology Association Recommendations for Pharmacological Management of Rheumatoid Arthritis with Traditional and Biologic Disease-modifying Antirheumatic Drugs" recommends (with Level II and Strength B) "the presence of the following poor prognostic features should be assessed at baseline and considered when making treatment decisions: RF positivity, anti-CCP positivity, functional limitation, high number of swollen and tender joints, early erosions, extraarticular features, high ESR or CRP." They also recommend (with Level I and Strength A) "RA care providers should monitor disease activity as frequently as every 1 to 3 months in patients with active RA." The disease activity should be monitored by a validated method, such as DAS28 or SDAI. The most recent updated "living guidelines" for this statement does not include prognostic features or make recommendations for factors included in treatment decisions (Hazlewood et al., 2022).

In 2018, CRA released guidelines on assessment and monitoring of Systemic Lupus Erythematosus. Regarding diagnosis, CRA recommends that best clinical practice includes a complete history and physical examination at baseline with laboratory monitoring which could possibly include (but is not limited to) the following tests: "complete blood count (CBC), liver enzymes, creatine kinase, creatinine and estimated glomerular filtration rate (eGFR), urine routine/microscopic (urinalysis), urine protein-creatinine ratio, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), complements (C3,

C4), anti-dsDNA, antinuclear antibodies, antibodies to extractable nuclear antigens, antiphospholipid antibodies (aPL), lupus anticoagulant (LAC), anticardiolipin (aCL), anti-β2-glycoprotein I (anti-β2-GPI), and lipid profile. Follow up laboratory monitoring will depend on the patient's clinical status and may include CBC, eGFR, urinalysis, urine protein-creatinine ratio, CRP, and/or ESR, C3, C4, and anti-dsDNA antibodies" (Keeling et al., 2018).

Joint Task Force on Practice Parameters (JTFPP) of the Academy of Allergy, Asthma & Immunology (AAAAI); the American College of Allergy, Asthma & Immunology (ACAAI); and the Joint Council of Allergy, Asthma & Immunology

The JTFPP within their guidelines concerning the diagnosis and management of acute and chronic urticaria state, "Targeted laboratory testing based on history or physical examination findings is appropriate, and limited laboratory testing can be obtained. Limited laboratory testing includes a CBC with differential, sedimentation rate, and/or C-reactive protein, liver enzyme, and thyroid-stimulating hormone (TSH) measurement… Targeted laboratory testing based on history and/or physical examination (eg, obtaining TSH in a patient with weight gain, heat/cold intolerance, and thyromegaly) is recommended" (Bernstein et al., 2014).

National Institute for Health and Care Excellence (NICE)

The NICE first issued the guidelines concerning irritable bowel syndrome (IBS) in 2008 with updates in 2015 and 2017. In individuals who meet the IBS diagnostic criteria, they recommend ESR and CRP along with full blood count and antibody testing for celiac disease or tissue transglutaminase to exclude other possible diagnoses. They do not state anything concerning follow-up testing of either ESR or CRP (NICE, 2017).

In 2020, NICE issues guidelines concerning management of rheumatoid arthritis (RA). In adults with active RA, they recommend measuring CRP and disease activity monthly in specialist care until remission or low disease activity is achieved (NICE, 2020).

American Academy of Orthopaedic Surgeons (AAOS)

The AAOS notes that "Strong evidence supports the use of [ESR and CRP] to aid in the preoperative diagnosis of prosthetic joint infection (PJI)." However, the AAOS remarks that neither biomarker is perfectly accurate for PJI diagnosis and should not be used as sole tests for diagnosis. Critically, neither marker informs clinicians of the microbiology of the PJI.

These guidelines were endorsed by IDSA, the American College of Radiology, and the Society of Nuclear Medicine and Molecular Imaging (AAOS, 2019).

Pediatric Infectious Diseases Society and the Infectious Diseases Society of America

In 2021, a guideline was released on the diagnosis and management of Acute Hematogenous Osteomyelitis (AHO) in pediatrics. In children with suspected AHO, they recommend performing a serum C-reactive protein (CRP) on initial evaluation. "Serum CRP has a low accuracy to establish the

diagnosis of AHO, but in situations where AHO is confirmed, the serum CRP performed on initial evaluation can serve as the baseline value for sequential monitoring." They recommend against using serum PCT. In terms of ESR, they comment that the ESR is no longer used routinely to diagnose AHO in children. "ESR combined with CRP may slightly improve sensitivity and negative predictive value for the diagnosis of AHO, but specific thresholds and the overall clinical utility of using both CRP and ESR for diagnostic purposes remain uncertain" (Woods et al., 2021).

"There are no data to support a particular frequency of CRP monitoring during the course of AHO in children. Measurement every 2 to 3 days during the early therapeutic course, rather than daily, followed by weekly or other periodic measurement until normalization (or a clear trend toward normalization is evident) is an acceptable approach" (Woods et al., 2021).

Food and Drug Administration

Testing of serum acute phase reactants and ESR is performed in laboratories meeting Clinical Laboratory Improvement Act (CLIA) quality standards. The FDA has approved multiple tests for human CRP, including assays for conventional CRP, high-sensitivity CRP (hsCRP), and cardiac CRP (cCRP). On September 22, 2005, the FDA issued guidelines concerning the assessment of CRP (FDA, 2005). A search of the FDA Medical Devices database (FDA, 2018) on April 20, 2021, shows that the FDA has approved ESR systems from multiple companies, including the ESR Control -M Hematology Erythrocyte Sedimentation system (K972172) and the ESR Control -HC Hematology Erythrocyte Sedimentation system (K972170) by R & D Systems, the Seditainer Erythrocyte Sedimentation Rate System (K953994) from Becton Dickinson Vacutainer Systems, the Westergren Dispette for ESR (K831195) by Ulster Scientific, and the Dade ESR Kit (K823368) from American Dade.

Many labs have developed specific tests that they must validate and perform in house. These laboratory-developed tests (LDTs) are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA '88). LDTs are not approved or cleared by the U. S. Food and Drug Administration; however, FDA clearance or approval is not currently required for clinical use.

Applicable Codes

Code	Description	Comment
82746	Folic acid; serum	
82747	Folic acid; RBC	
0399U	Neurology (cerebral folate deficiency), serum, detection of anti-human folate receptor IgG-binding antibody and blocking autoantibodies by enzyme-linked immunoassay (ELISA),	

	qualitative, and blocking autoantibodies, using a functional blocking assay for IgG or IgM, quantitative, reported as positive or not detected Proprietary test: FRAT® (Folate Receptor Antibody Test) Lab/Manufacturer: Religen Inc	

Definitions

Term	Meaning

II. Related Policies

Policy Number	Policy Description

Procedure codes appearing in Reimbursement Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

III. Reference Materials

BCSH. (2021). *Guidelines for the Investigation and Management of Vitamin B12 and Folate Deficiency*. https://www.hey.nhs.uk/wp/wp-content/uploads/2016/03/vitaminB12FolateDeficiency.pdf
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IV. Revision History

Revision Date	Summary of Changes
05/31/2023	Reviewed and Updated: Updated background, guidelines, and evidence-based scientific references. Literature review necessitated the following changes in coverage criteria: CC1 reorganized from having subcriteria into being a single, main CC. Now reads: "1) For individuals diagnosed with megaloblastic or macrocytic anemia and for whom the megaloblastic anemia and/or macrocytosis does not resolve after folic acid treatment, measurement of serum folate concentration MEETS COVERAGE CRITERIA." All CC edited for clarity and consistency. Addition of new CC4: "4) For all situations, folate receptor autoantibody testing DOES NOT MEET COVERAGE CRITERIA." Added PLA code 0399U.

Disclaimer

Healthfirst's claim edits follow national industry standards aligned with CMS standards that include, but are not limited to, the National Correct Coding Initiative (NCCI), the National and Local Coverage Determination (NCD/LCD) policies, appropriate modifier usage, global surgery and multiple procedure reduction rules, medically unlikely edits, duplicates, etc. In addition, Healthfirst's coding edits incorporate industry-accepted AMA and CMS CPT, HCPCS and ICD-10 coding principles, National Uniform Billing Editor's revenue coding guidelines, CPT Assistant guidelines, New York State-specific coding, billing, and payment policies, as well as national physician specialty academy guidelines (coding and clinical). Failure to follow proper coding, billing, and/or reimbursement policy guidelines could result in the denial and/or recoupment of the claim payment.

This policy is intended to serve as a resource for providers to use in understanding reimbursement guidelines for professional and institutional claims. This information is accurate and current as of the date of publication. It provides information from industry sources about proper coding practice. However, this document does not represent or guarantee that Healthfirst will cover and/or pay for services outlined. Reimbursement decisions are based on the terms of the applicable evidence of coverage, state and federal requirements or mandates, and the provider's participation agreement. This includes the determination of any amounts that Healthfirst or the member owes the provider.