



An Independent Licensee of the Blue Cross Blue Shield Association

EVIDENCE-BASED CRITERIA
SECTION: LABORATORY

ORIGINAL EFFECTIVE DATE: 04/18/23
LAST REVIEW DATE: 04/16/24
CURRENT EFFECTIVE DATE: 04/16/24
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LABORATORY TEST FOR SYNOVASURE

Non-Discrimination Statement and Multi-Language Interpreter Services information are located at the end of this document.

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Evidence-Based Criteria must be read in its entirety to determine coverage eligibility, if any.

This Evidence-Based Criteria provides information related to coverage determinations only and does not imply that a service or treatment is clinically appropriate or inappropriate. The provider and the member are responsible for all decisions regarding the appropriateness of care. Providers should provide BCBSAZ complete medical rationale when requesting any exceptions to these guidelines.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Evidence-Based Criteria are subject to change as new information becomes available.

For purposes of this Evidence-Based Criteria, the terms "experimental" and "investigational" are considered to be interchangeable.

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LABORATORY TEST FOR SYNOVASURE

Description:

Synovasure® includes laboratory tests designed to aid in the diagnosis of periprosthetic joint infection (PJI) and several arthritis conditions. Tests offered include the Synovasure® Alpha Defensin Lateral Flow Test, the Synovasure™ Comprehensive Infection Laboratory Test Panel, and the Synovasure® Relative Inflammatory Status Classification (RISC) Panel. Synovasure® may be used in individuals with systemic inflammatory diseases, or those taking antibiotics.

Alpha defensins:

Alpha defensins are antibacterial proteins that are released from neutrophils in response to pathogens. They act to depolarize the cell membrane of the pathogen. Therefore, the presence of alpha defensins in human joints and tissues can be used as a test for diagnosing infection.

Synovasure® Alpha Defensin Lateral Flow Test:

The Synovasure® Alpha Defensin Lateral Flow Test is a qualitative, visually read immunochromatographic assay for the detection of alpha defensin in synovial fluid. It is a stand-alone device performed at the point-of-care to be used in conjunction with other clinical and diagnostic findings to aid in the diagnosis of PJI.

Synovasure® Comprehensive Infection Panel:

The Synovasure® Comprehensive Infection Panel includes several standard tests along with proprietary testing. All tests are completed on synovial fluid to aid in the diagnosis of PJI. Standard tests include fluid culture, white blood cell count with differential, C-reactive protein (CRP), and crystal analysis. Proprietary testing includes the Synovasure® Alpha Defensin ELISA, Synovasure® Microbial Identification, and Synovasure® Neutrophil Elastase tests.

Synovasure® Relative Inflammatory Status Classification (RISC™) Panel:

The Synovasure® RISC™ panel includes tests on synovial fluid to aid in the diagnosis of arthritis conditions to include native septic arthritis, osteoarthritis, rheumatoid arthritis, and crystalline arthritis. The panel includes several biomarkers for arthritis as well as Synovasure® Alpha Defensin, Synovasure® Microbial Identification, fluid culture, white blood cell count with differential, crystal analysis, and lactate.

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Criteria:

- Synovasure® testing for the diagnosis of periprosthetic joint infection (PJI) is considered **experimental or investigational** when any **ONE** or more of the following criteria are met:
 1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
 2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
 3. Insufficient evidence to support improvement of the net health outcome; or
 4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
 5. Insufficient evidence to support improvement outside the investigational setting.

- Synovasure® testing for the diagnosis of arthritis conditions is considered **experimental or investigational** when any **ONE** or more of the following criteria are met:
 1. Lack of final approval from the appropriate governmental regulatory bodies (e.g., Food and Drug Administration); or
 2. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes; or
 3. Insufficient evidence to support improvement of the net health outcome; or
 4. Insufficient evidence to support improvement of the net health outcome as much as, or more than, established alternatives; or
 5. Insufficient evidence to support improvement outside the investigational setting.

Resources:

Literature reviewed 04/16/24. We do not include marketing materials, poster boards and non-published literature in our review.

1. Baddour LM, Chen A. Prosthetic Joint Infection: Epidemiology, microbiology, clinical manifestations, and diagnosis. In: Spelman D, ed. *UpToDate*. UpToDate; 2023. Accessed April 9, 2024. <https://www.uptodate.com/contents/prosthetic-joint-infection-epidemiology-microbiology-clinical-manifestations-and-diagnosis>
2. Balato G, Franceschini V, Ascione T, et al. High performance of alpha-defensin lateral flow assay (Synovasure) in the diagnosis of chronic knee prosthetic infections. *Knee surgery, sports traumatology, arthroscopy : official journal of the ESSKA*. Jun 2018;26(6):1717-1722. doi:10.1007/s00167-017-4745-x
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6. CD Diagnostics Inc. Synovasure Alpha Defensin Lateral Flow Test. Accessed April 9, 2024. <https://www.zimmerbiomet.com/en/products-and-solutions/specialties/diagnostics/synovasure-alpha-defensin-lateral-flow-test.html>
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9. Cooper KB, Siegel ER, Stambough JB, Bumpass DB, Mears SC. The Alpha-Defensin Prosthetic Joint Infection Test Has Poor Validity for Native Knee Joint Infection. *J Arthroplasty*. Aug 2021;36(8):2957-2961. doi:10.1016/j.arth.2021.03.020
10. de Saint Vincent B, Martinot P, Pascal A, et al. Does the alpha-defensin lateral flow test conserve its diagnostic properties in a larger population of chronic complex periprosthetic infections? Enlargement to 112 tests, from 42 tests in a preliminary study, in a reference center. *Orthop Traumatol Surg Res*. Jun 2021;107(4):102912. doi:10.1016/j.otsr.2021.102912
11. Ding BT, Tan KG, Kau CY, Chan HYH, Mohd Fadil MFB. Accuracy of the α -defensin lateral flow assay for diagnosing periprosthetic joint infection in Asians. *J Orthop Surg (Hong Kong)*. Jan-Apr 2019;27(1):2309499019828459. doi:10.1177/2309499019828459
12. Eriksson HK, Nordstrom J, Gabrysch K, Hailer NP, Lazarinis S. Does the Alpha-defensin Immunoassay or the Lateral Flow Test Have Better Diagnostic Value for Periprosthetic Joint Infection? A Systematic Review. *Clinical orthopaedics and related research*. May 2018;476(5):1065-1072. doi:10.1007/s11999.0000000000000244
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15. Kleeman-Forsthuber LT, Dennis DA, Brady AC, Pollet AK, Johnson RM, Jennings JM. Alpha-Defensin Is Not Superior to Traditional Diagnostic Methods for Detection of Periprosthetic Joint Infection in Total Hip Arthroplasty and Total Knee Arthroplasty Patients. *J Arthroplasty*. Jan 21 2021;doi:10.1016/j.arth.2021.01.036
16. Li H, Li R, Erlong N, et al. It can be unnecessary to combine common synovial fluid analysis and alpha-defensin tests for periprosthetic joint infection diagnosis. *BMC Musculoskelet Disord*. Jun 29 2023;24(1):529. doi:10.1186/s12891-023-06594-5
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22. Petrucca A, Santino I, Gentile G, et al. Detection of α -defensin in synovial fluids by matrix-assisted laser desorption/ionization time-of-flight mass spectrometry as an innovative and cost-effective assay for improved definition of periprosthetic joint infections. *Rapid Commun Mass Spectrom*. Jun 15 2020;34(11):e8791. doi:10.1002/rcm.8791
23. Plate A, Stadler L, Sutter R, et al. Inflammatory disorders mimicking periprosthetic joint infections may result in false positive alpha-defensin. *Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases*. Feb 26 2018;doi:10.1016/j.cmi.2018.02.019

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23. Zeng YQ, Deng S, Zhu XY, et al. Diagnostic Accuracy of the Synovial Fluid α -Defensin Lateral Flow Test in Periprosthetic Joint Infection: A Meta-analysis. *Orthop Surg*. Mar 14 2021;doi:10.1111/os.12966



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Coding:

CPT: 83516, 83605, 84311, 86140, 87070, 87071, 87073, 89051, 89060

History:

Date:

Activity:

Medical Policy Panel	04/16/24	Review with revisions
Medical Policy Panel	04/18/23	Approved guideline
Medical Director (Dr. Deering, Dr. Raja)	04/05/23	Review with revisions

Policy Revisions:

04/16/24 Updated: Resources section



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Non-Discrimination Statement:

Blue Cross Blue Shield of Arizona (BCBSAZ) complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability or sex. BCBSAZ provides appropriate free aids and services, such as qualified interpreters and written information in other formats, to people with disabilities to communicate effectively with us. BCBSAZ also provides free language services to people whose primary language is not English, such as qualified interpreters and information written in other languages. If you need these services, call (602) 864-4884 for Spanish and (877) 475-4799 for all other languages and other aids and services.

If you believe that BCBSAZ has failed to provide these services or discriminated in another way on the basis of race, color, national origin, age, disability or sex, you can file a grievance with: BCBSAZ's Civil Rights Coordinator, Attn: Civil Rights Coordinator, Blue Cross Blue Shield of Arizona, P.O. Box 13466, Phoenix, AZ 85002-3466, (602) 864-2288, TTY/TDD (602) 864-4823, crc@azblue.com. You can file a grievance in person or by mail or email. If you need help filing a grievance BCBSAZ's Civil Rights Coordinator is available to help you. You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights electronically through the Office for Civil Rights Complaint Portal, available at <https://ocrportal.hhs.gov/ocr/portal/lobby.jsf>, or by mail or phone at: U.S. Department of Health and Human Services, 200 Independence Avenue SW., Room 509F, HHH Building, Washington, DC 20201, 1-800-368-1019, 800-537-7697 (TDD). Complaint forms are available at <http://www.hhs.gov/ocr/office/file/index.html>

Multi-Language Interpreter Services:

Spanish: Si usted, o alguien a quien usted está ayudando, tiene preguntas acerca de Blue Cross Blue Shield of Arizona, tiene derecho a obtener ayuda e información en su idioma sin costo alguno. Para hablar con un intérprete, llame al 602-864-4884.

Navajo: Díí kwe'é atah nilínigíí Blue Cross Blue Shield of Arizona haada yit'éego bína'idííkidgo éí doodago Háida bíjá anilyeedígíí t'áadoo le'é yína'idííkidgo beehaz'áanii hólp díí t'áa hazaadk'ehjí háká a'doowołgo bee haz'ą doo baqah ilínígóó. Ata' halne'ígíí kojí' bich'í' hodíilnih 877-475-4799.

Chinese: 如果您，或是您正在協助的對象，有關於插入項目的名稱 Blue Cross Blue Shield of Arizona 方面的問題，您有權利免費以您的母語得到幫助和訊息。洽詢一位翻譯員，請撥電話 在此插入數字 877-475-4799。

Vietnamese: Nếu quý vị, hay người mà quý vị đang giúp đỡ, có câu hỏi về Blue Cross Blue Shield of Arizona quý vị sẽ có quyền được giúp và có thêm thông tin bằng ngôn ngữ của mình miễn phí. Để nói chuyện với một thông dịch viên, xin gọi 877-475-4799.

Arabic:

إن كان لديك أو لدى شخص تساعد أسئلة بخصوص Blue Cross Blue Shield of Arizona، فلديك الحق في الحصول على المساعدة والمعلومات الضرورية بلغتك من دون أية تكلفة. للتحدث مع مترجم اتصل بـ 877-475-4799.

