BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Intracellular Micronutrient Analysis

Policy #: 378
Latest Review Date: December 2021
Category: Laboratory

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*

    - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
    - *Furnished in a setting appropriate to the patient's medical needs and condition;*
    - *Ordered and furnished by qualified personnel;*
    - *One that meets, but does not exceed, the patient's medical need; and*
    - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Blue Advantage will treat **Functional Intracellular Analysis (FIA),** intracellular micronutrient panel testing, and all other live blood cell testing of intracellular nutritional status as a **non-covered** benefit and as **investigational**.

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Commercial laboratories offer panels of tests evaluating intracellular levels of micronutrients (essential vitamins and minerals). Potential uses of these tests include screening for nutritional deficiencies in healthy people or those with chronic disease and aiding in the diagnosis of disease in patients with nonspecific symptoms.

"Micronutrients" collectively refer to essential vitamins and minerals necessary in trace amounts for health. Clinical deficiency states (states occurring after prolonged consumption of a diet lacking the nutrient that is treated by adding the nutrient to the diet) have been reported for vitamins A, B1, B12, C, and D, selenium, and other micronutrients. Classic nutritional deficiency diseases are uncommon in the U. S.; most people derive sufficient nutrition from their diets alone or in combination with over-the-counter multivitamins.

Laboratory tests are available for individual micronutrients and are generally used to confirm suspected micronutrient deficiencies. Testing is performed by serum analysis using standardized values for defining normal and deficient states. Also, some commercial laboratories offer panels of vitamin and mineral testing that also use serum analysis.

Diagnostic Testing

This evidence review evaluates laboratory tests that measures the intracellular levels of micronutrients. This testing, also known as intracellular micronutrient analysis, micronutrient testing, or functional intracellular analysis, is sometimes claimed to be superior to serum testing because intracellular levels reflect more stable micronutrient levels over longer time periods compared with serum levels, because intracellular levels are not influenced by recent nutrition intake. However, the relationship between serum and intracellular levels of micronutrients is complex. The balance of intracellular and extracellular levels depend on a number of factors, including the physiology of cellular transport mechanisms and the individual cell type.

At least two commercial laboratories offer intracellular testing for micronutrients. Laboratories perform a panel of tests evaluating the intracellular level of a variety of micronutrients (e.g. minerals, vitamins, amino acids, fatty acids). The test offered by IntraCellular Diagnostics (EXA

Test®) evaluates epithelial cells from buccal swabs and assesses levels of intracellular mineral electrolyte (i.e., magnesium, calcium, potassium, phosphorus, sodium, and chloride). SpectraCell Laboratories offers a panel of tests that evaluates the intracellular status of micronutrients within lymphocytes in blood samples. The micronutrients measured by the test are as follows:

- Vitamins: Vitamins A, B1, B2, B3, B6, B12, C, D, K; biotin, folate, pantothenic acid
- Minerals: calcium, magnesium, manganese, zinc, copper
- Antioxidants: α-lipoic acid, coenzyme Q10, cysteine, glutathione, selenium, vitamin E
- Amino acids: asparagine, glutamine, serine
- Carbohydrate metabolism: chromium, fructose sensitivity, glucose-insulin metabolism
- Fatty acids: oleic acid
- Metabolites: choline, inositol, carnitine

The SpectraCell micronutrient panel also may include SPECTROX™ for evaluation of the total antioxidant function and IMMUNIDEX™ for immune response score.

KEY POINTS:

The most recent literature review was updated through October 22, 2021.

Summary of Evidence

For individuals who have chronic diseases or nonspecific generalized symptoms who receive intracellular micronutrient analysis, the evidence includes an observational study. Relevant outcomes are symptoms, and change in disease status. No studies were identified that evaluated the clinical validity or clinical utility of intracellular micronutrient testing compared with standard testing for vitamin or mineral levels. Limited data from observational studies are available on correlations between serum and intracellular micronutrient levels. No randomized controlled trials or comparative studies were identified that evaluated the direct health impact of intracellular micronutrient testing. Moreover, there are not sufficient data to construct a chain of evidence that intracellular micronutrient testing would likely lead to identifying patients whose health outcomes would be improved compared with alternative approaches to patient management. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.
No practice guidelines or position statements were identified.

U.S. Preventive Services Task Force Recommendations

Not applicable.

KEY WORDS:
Functional intracellular analysis (FIA), essential metabolic analysis, micronutrient testing, comprehensive nutritional panel, SpectraCell, IntraCellular Diagnostics, SpectraCell's micronutrient test, IntraCellular Diagnostics ExaTest, intracellular micronutrient analysis, SPECTROX®, bostonheart diagnostic®, Fatty Acid Balance test, IMMUNIDEX™

APPROVED BY GOVERNING BODIES:
Clinical laboratories may develop and validate tests in-house and market them as a laboratory service; laboratory-developed tests (LDTs) must meet the general regulatory standards of the Clinical Laboratory Improvement Amendments (CLIA). Intracellular micronutrient panel testing is offered by SpectraCell Laboratories and IntraCellular Diagnostics under the auspices of the Clinical Laboratory Improvement Amendments. Laboratories that offer LDTs must be licensed by CLIA for high-complexity testing. To date, the U.S. Food and Drug Administration has chosen not to require any regulatory review of this test.

BENEFIT APPLICATION:
Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

CURRENT CODING:
CPT Codes:
There is no specific CPT code for this panel of testing. Some of the elements of this testing might be reported with the codes below:

82310	Calcium; total
82725	Fatty acids, nonesterified
84590	Vitamin A
84591	Vitamin, not otherwise specified
84999	Unlisted chemistry procedure
86353	Lymphocyte transformation, mitogen (phytomitogen) or antigen induced blastogenesis
88348	Electron microscopy, diagnostic

REFERENCES:

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3. Haigney MC, Berger R, Schulman S et al. Tissue magnesium levels and the arrhythmic substrate in humans. J Cardiovasc Electrophysiol 1997; 8(9):980-6.
4. Haigney MC, Silver B, Tanglao E et al. Noninvasive measurement of tissue magnesium and correlation with cardiac levels. Circulation 1995; 92(8):2190-7.
5. Houston MC. The role of cellular micronutrient analysis, nutraceuticals, vitamins, antioxidants and minerals in the prevention and treatment of hypertension and cardiovascular disease. Ther Adv Cardiovasc Dis 2010; 49(3):165-83.
6. IntraCellular Diagnostics. Mitochondria: Exploration of Intracellular Space. Accessed October 22, 2021. https://www.exatest.com/
7. IOM (Institute of Medicine). 2011. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press.
8. SpectraCell Laboratories. Micronutrient Test. Accessed October 22, 2021. https://spectracell.sitewrench.com/search-tests

POLICY HISTORY:

Adopted for Blue Advantage, August 2009
Available for comment August 21-October 5, 2009
Medical Policy Group, August 2010
Medical Policy Group, August 2011
Available for comment August 11 – September 26, 2011
Medical Policy Group, September 2012
Medical Policy Group, January 2013
Medical Policy Group, September 2013
Medical Policy Group, July 2014
Medical Policy Group, July 2015
Medical Policy Group, August 2015
Medical Policy Group, March 2017
Medical Policy Group, March 2018
Medical Policy Group, December 2019
Medical Policy Group, December 2020
Medical Policy Group, December 2021

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.