Corporate Medical Policy

Intracellular Micronutrient Analysis AHS – G2099

Description of Procedure or Service

Micronutrients are dietary components, often referred to as vitamins and minerals, which although only required by the body in small amounts, are vital to development, disease prevention, and wellbeing. Micronutrients are not produced in the body and must be derived from the diet (CDC, 2015; Life, 2012). Micronutrients include essential trace elements (inorganic components), and essential vitamins (organic) (Gidden & Shenkin, 2000).

Related Policies
Diagnosis of Idiopathic Environmental Intolerance AHS – G2056

***Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.

Policy

Reimbursement for Intracellular Micronutrient Analysis is not allowed

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Intracellular Micronutrient Analysis is covered

Not applicable.

When Intracellular Micronutrient Analysis is not covered

Reimbursement is not allowed for Intracellular micronutrient panel testing, including but not limited to SpectraCell and ExaTest, for all applications.

Policy Guidelines

Background
Micronutrients, such as zinc, selenium, and copper are involved in metabolic processes, either as catalysts or facilitating various enzymatic functions. Micronutrient deficiency can result from general malnutrition, a current illness, or side effects of treatments or procedures. Severe conditions or treatments may get worse with nutritional loss as the inflammatory response draws...
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micronutrients to the damaged organs. This increased oxidative stress causes normal defenses and maintenance to fail (Preiser et al., 2015). For example, a copper deficiency may cause muscle weakness and edema; an iodine deficiency may cause metabolic problems. (Pazirandeh, 2018).

Measurement of serum levels of several vitamins is widely available via several commercial testing companies. However, blood concentrations of many nutrients, especially those involved in regulatory mechanisms such as calcium and zinc, are maintained within narrow ranges regardless of body stores. Changes in blood concentrations of these nutrients only occur during severe deficiency. Other nutrients such as carotenoids vary depending on recent intake or half-life length. Infections or stress can also influence serum concentrations of some nutrients. Concentrations in other tissues, such as cell membranes or bone, fluctuate less but are more difficult to obtain (Elmadfa & Meyer, 2014). Vitamin testing is promoted to the public as a screening for nutrient deficiency and to personalize supplements to an individual, but tests are usually unwarranted. There is not enough information about the optimal blood levels of vitamins. Moreover, there is a lack of evidence that vitamin supplements prevent disease in healthy adults with low blood levels of vitamins, apart from those with specific diets or conditions. Vitamin deficiencies typically occur in special populations such as the elderly or those with gastric bypass surgery, not the general public (Fairfield, 2017).

Another possible method of measuring vitamin deficiency is to assess the intracellular concentration (as opposed to the typical serum measurement). Intracellular micronutrient lymphocyte analysis was developed based on the premise that a peripheral blood lymphocyte reflects the genetic and biochemical state of the person at the time it was formed (Shive et al., 1986). A study was performed to validate the measurement of lymphocytes as an indicator of an individual’s nutrient state. Lymphocytes were hypothesized to provide a superior history of nutrition status rather than a “snapshot” from typical serum testing as proclaimed by the authors. Lymphocytes were grown in various chemically defined serum-free media, and their growth responses were measured. This lymphocyte growth response was used as an indicator of nutritional status. The authors concluded that lymphocytes provide an accurate method of determining nutrient needs, requirements, or deficiencies (Bucci, 1993, 1994).

Lymphocytes measurement is the basis of SpectraCell’s micronutrient testing procedure. Lymphocytes are isolated from the blood sample and placed in a culture medium containing the optimal levels of nutrients for sustained growth. A given micronutrient is removed, and then growth is measured and compared against the 100% level of growth. For example, Vitamin B6 may be removed from the medium. The growth rate of the cell is theoretically only dependent on vitamin B6 as all other micronutrients are at optimal levels; therefore, any deficiency in cell growth would be caused by issues with intracellular Vitamin B6. This is done for all 33 micronutrients in the panel and results are reported. The micronutrients included in SpectraCell’s panels are as follows: Vitamins A, B1, B2, B3, B6, B12, C, D, E, and K, as well as biotin, folate, pantothenate, calcium, magnesium, manganese, zinc, copper, asparagine, glutamine, serine, oleic acid, alpha-lipoic acid, coenzyme Q10, cysteine, glutathione, selenium, chromium, choline, inositol, and carnitine. SpectraCell also provides an assessment of “Total Antioxidant Function”, an “Immune Response Score”, and measures of fructose sensitivity and glucose-insulin metabolism (SpectraCell, 2014).

Another test analyzing intracellular concentration is ExaTest by IntraCellular Diagnostics. From their laboratory website, this test uses “rapidly metabolizing sublingual epithelial cells under Analytical Scanning Electron Microscopy, (ASEM) an Energy Dispersive X-Ray Analysis, (EXA) to reflect fast tissue changes of vital mineral electrolytes”. This test is primarily for aid with the management of heart disease and provides tissue evaluations of magnesium, sodium, calcium, phosphorus, potassium, and chloride. ExaTest proclaims its ability to follow a patient’s metabolic status and assess electrolyte imbalance easily. First, the buccal, epithelial cells are swabbed from the patient. Then the sample is analyzed by the proprietary energy dispersive x-ray analysis and bombarded with X-Rays. Energy is released by wavelengths (unique to each element), and the element composition is analyzed and reported. ExaTest states that the serum or urine of some
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minerals do not correlate with intracellular levels and that these deficiencies are common in patients with various health issues, particularly heart disease. Buccal cells are used as they are easily accessible and have an easily analyzed structure for electrolytes (Exatest, 2014).

Vibrant America has also developed a test that gives both extracellular and intracellular information on approximately 40 vitamins, minerals, amino acids, fatty acids and antioxidants in the body (Vibrant, 2017). Vibrant America states that the benefits of intracellular testing include the identification of potential functional deficiencies in the cellular nutrient absorption process (which may increase the risk of certain diseases), and the identification of an individual’s nutritional status in the previous four to six months (Vibrant, 2017).

While limited research has been completed regarding intracellular micronutrient lymphocyte analysis, Yamada, Yamada, Waki, and Umegaki (2004) did complete a study with 41 type 2 diabetes patients and 50 healthy controls. No participants were taking vitamin supplements at the time of the study. Blood samples were taken from all participants during a fasting state; the researchers determined that the lymphocyte vitamin C level was significantly lower in the type 2 diabetes patients than in controls (Yamada et al., 2004). This study may support the above theory that lymphocytes can be used as an indicator of an individual’s nutrient state.

Houston (2010) published a small study stating that treating the intracellular micronutrient deficiencies in combination with optimal diet, exercise and other weight management resulted in reaching blood pressure goals for 62% of a hypertensive population (Houston, 2010). Another small study of 10 patients found that both genders showed overall improvement in their vitamin and mineral cellular storage balance after being tested with SpectraCell’s assessment (Frye, 2010). However, the authors of each of the aforementioned studies (Houston, Bucci, Frye, and Shive) are associated with SpectraCell Laboratories. SpectraCell has listed several studies on their website discussing serum versus intracellular deficiencies; from discussing the effect of the inflammatory response on serum micronutrient levels to Vitamin B12’s difficult serum profile to micronutrient deficiencies in special populations (SpectraCell, 2018). However, none of these studies reported use SpectraCell’s actual method as of 2018, nor did the studies cover the healthy population for which the test is marketed. Most of these studies listed used other methods such as HPLC to measure micronutrient levels instead of the proprietary method provided by SpectraCell. Few other studies listed on SpectraCell’s website used lymphocytes as the analyte as well.

Applicable Federal Regulations

Intracellular micronutrient testing is offered by companies SpectraCell and IntraCellular Diagnostics, which have Clinical Laboratories Improvement Amendments (CLIA) accredited laboratories. SpectraCell’s micronutrient panel test and the IntraCellular Diagnostics ExaTest have not been through the FDA approval process. Additionally, 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). As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.

Guidelines and Recommendations

No studies evaluating the accuracy or clinical utility of intracellular micronutrient testing compared to standard testing for vitamin or mineral levels were identified. In addition, no controlled studies that evaluated changes to patient management or health impact of intracellular micronutrient testing were identified. Limited data are available on correlations between serum and intracellular micronutrient levels. Intracellular micronutrient analysis was not included in recent reviews on micronutrient analysis (Elmadfa & Meyer, 2014; Raghavan, Ashour, & Bailey, 2016).
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No recommendations or practice guidelines recommending intracellular micronutrient testing were identified in a literature search.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina website at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable service codes: 82128, 82136, 82180, 82310, 82379, 82495, 82525, 82607, 82652, 82725, 82746, 82978, 83735, 83785, 84207, 84252, 84255, 84425, 84446, 84590, 84591, 84597, 84630, 84999 86353, 88348

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources


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**Policy Implementation/Update Information**

1/1/2019 BCBSNC will not provide coverage for intracellular micronutrient panel testing because it is considered investigational for all applications. BCBSNC does not provide coverage for investigational services or procedures. Medical Director review 1/1/2019. Policy noticed 1/1/2019 for effective date 4/1/2019. (jd)

5/14/19 Reviewed by Avalon 1st Quarter 2019 CAB. Minor revisions to Description section. Policy guidelines and references updated. Medical Director review 5/2019. (jd)

10/29/19 Wording in the Policy, When Covered, and/or Not Covered section(s) changed from Medical Necessity to Reimbursement language, where needed. (gm)


5/12/20 Reviewed by Avalon 1st Quarter 2020 CAB. Added the Related Policies section, to include Diagnosis of Idiopathic Environmental Intolerance AHS – G2056. Under the When Not Covered section, added “SpectraCell and ExaTest”. References updated. Medical Director review. (jd)
Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.