Policy Number	**MED207.088**
Policy Effective Date	**04/01/2025**

Intracellular Micronutrient Analysis

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Related Policies (if applicable)
None

Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

Intracellular micronutrient analysis, also known as functional intracellular analysis or essential metabolic analysis, **is considered experimental, investigational and/or unproven**.

Policy Guidelines

There is no specific CPT code for this panel of testing.

The specific CPT codes for each of the elements of the panel would most likely be reported (e.g., 84590 for vitamin A, 82310 for calcium, 82725 for oleic acid, etc.) along with one unit of a not otherwise specified (i.e., 84591) or unlisted (i.e., 84999) code for the balance of the panel, which does not have specific codes.

According to SpectraCell Laboratories, their total antioxidant function testing (which they call SPECTROX) is reported using CPT code 86353.

IntraCellular Diagnostics uses electron microscopy for which CPT code 88348 might be reported.

Description

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.

Background
"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, B_1, B_{12}, 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 medical policy evaluates laboratory tests that measure 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 than serum levels and because intracellular levels are not influenced by recent nutrition intake. However, the relation between serum and intracellular levels of micronutrients is complex. The balance of intracellular and extracellular levels depends on a number of factors, including the physiology of cellular transport mechanisms and the individual cell type.

At least 2 commercial laboratories offer intracellular testing for micronutrients. Laboratories perform a panel of tests evaluating the intracellular level of various 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, phosphorous, sodium, chloride). (1) SpectraCell Laboratories offers a panel of tests that evaluates the intracellular status of micronutrients within lymphocytes in blood samples. (2) The micronutrients measured by the test include:

- Vitamins: A, B_1, B_2, B_3, B_6, B_{12}, 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.

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

Rationale

Medical policies assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Medical policies assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

Intracellular Micronutrient Analysis
Clinical Context and Test Purpose
The purpose of diagnostic testing of individuals who have chronic diseases or nonspecific generalized symptoms is to identify micronutrient deficiencies, not indicated by specific signs and/or symptoms, that would inform management decisions and improve health outcomes.

The following PICO was used to select literature to inform this policy.

Populations
The relevant populations of interest are individuals with chronic diseases or with nonspecific generalized symptoms.

Interventions
The test being considered is intracellular micronutrient analysis.

Comparators
The following practices are currently being used to identify micronutrient deficiencies: serum testing for individual nutritional deficiencies or standard management without nutritional testing.

Outcomes
The general outcomes of interest are symptoms and change in disease status. The timeframe for short- and long-term symptom improvement and change in disease status vary by the chronic disease affecting the individual.

Study Selection Criteria
For the evaluation of the clinical validity of the intracellular micronutrient test panel, studies that meet the following eligibility criteria were considered:

- Reported on the accuracy of the marketed version of the technology (including any algorithms used to calculate scores);
- Included a suitable reference standard (describe the reference standard);
- Patient/sample clinical characteristics were described;
- Patient/sample selection criteria were described.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

No studies on the sensitivity and specificity of intracellular micronutrient analysis tests compared with a reference standard (e.g., serum testing) were identified.

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if patients receive correct therapy, or more effective therapy, or avoid unnecessary therapy, or avoid unnecessary testing.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for patients managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials.

No evidence from randomized controlled trials was identified supporting the use of intracellular micronutrient analysis tests.

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

An observational study by Houston (2010) provided some data relevant to a chain of evidence. (3) The study described a single center's experience with micronutrient testing in the management of hypertension. A total of 3338 patients treated over 5 years received micronutrient testing. Among the 3338 patients, 671 (20%) were considered to have hypertension (defined as blood pressure >140/90 mm Hg). The author stated that there were differences in levels of many micronutrients in the hypertensive vs nonhypertensive populations but did not report the specific micronutrients for which levels differed. Hypertensive patients identified as having micronutrient deficiencies were treated with high-dose therapy of appropriate supplements, as well as with recommendations on optimal diet, exercise, and weight management. The author reported that, after 6 months, 62% of the hypertensive population had succeeded in reaching their blood pressure goals and had tapered and discontinued hypertensive medication. The report did not provide data on micronutrient levels before or after treatment or 6-month blood pressure data for a comparison group of hypertensive patients who did not undergo micronutrient testing.

Section Summary: Clinically Useful
There is no direct evidence that intracellular micronutrient analysis improves health outcomes in patients with chronic diseases or nonspecific generalized symptoms. Moreover, there are insufficient 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.

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 evaluating the direct health impact of intracellular micronutrient testing. Moreover, there are insufficient 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
No guidelines or statements were identified.

Ongoing and Unpublished Clinical Trialsagree

A search of ClinicalTrials.gov in November 2024 did not identify any ongoing or unpublished trials that would likely influence this policy.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	82310, 82725, 84590, 84591, 84999, 86353, 88348
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

1. IntraCellular Diagnostics. Mitochondria: Exploration of Intracellular Space. Available at <https://www.exatest.com> (accessed November 25, 2024).
2. SpectraCell Laboratories. Micronutrient Test. Available at <https://spectracell.sitewrench.com> (accessed November 25, 2024).
3. 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. Jun 2010; 4(3):165-183. PMID 20400494

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does not have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been developed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision

Date	Description of Change

04/01/2025	Document updated with literature review. Coverage unchanged. No new references added.
11/15/2024	Reviewed. No changes.
12/01/2023	Document updated with literature review. Coverage unchanged. References 1 and 2 added.
07/15/2022	Reviewed. No changes.
04/01/2021	Document updated with literature review. Coverage unchanged. No new references added.
07/15/2020	Reviewed. No changes.
04/15/2019	Document updated with literature review. Coverage unchanged. No new references added.
06/15/2018	Reviewed. No changes.
10/15/2017	Document updated with literature review. Coverage unchanged.
10/01/2016	Reviewed. No changes.
07/15/2015	Document updated with literature review. No coverage changes.
12/01/2014	Reviewed. No changes.
10/15/2013	Document updated with literature review. No coverage changes. Document completely revised. Title changed from “Functional Intracellular Analysis”.
05/01/2008	Policy reviewed without literature review; new review date only. This policy is no longer scheduled for routine literature review and update.
09/01/2006	Revised/updated entire document
03/30/2004	Revised/updated entire document
05/01/1996	Revised/updated entire document
07/01/1993	New medical document