



Louisiana

Diagnosis and Management of Idiopathic Environmental Intolerance (i.e., Multiple Chemical Sensitivities)

Policy # 00367

Original Effective Date: 06/27/2013

Current Effective Date: 09/13/2021

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Intracellular Micronutrient Analysis is addressed separately in medical policy 00311.

Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers laboratory tests designed to affirm the diagnosis of idiopathic environmental intolerance to be **investigational**.*

Based on review of available data, the Company considers treatments for idiopathic environmental intolerance, including but not limited to immunoglobulin therapy (IVIg), neutralizing therapy of chemical and food extracts, avoidance therapy, elimination diets, and oral nystatin (to treat *Candida*) to be **investigational**.*

Policy Guidelines

Laboratory tests for the diagnosis of idiopathic environmental intolerance may be broadly subdivided into those intended to rule out specific diseases with well-defined presentations and diagnostic criteria and those tests designed to affirm the diagnosis of idiopathic environmental intolerance. For example, a basic diagnostic workup, including a standard panel of chemistry tests and blood workup, would be considered appropriate as an initial diagnostic step, even in patients with nonspecific symptoms, to rule out well-defined illnesses. Additional tests may be considered medically necessary in patients with more specific symptoms, suggestive, for example, of an autoimmune connective tissue disease, or infectious mononucleosis. A variety of psychiatric or psychologic assessments may be performed to assess underlying conditions. However, at the present time, no specific tests can confirm the diagnosis of idiopathic environmental intolerance, and thus, a large battery of tests performed for a patient with nonspecific symptoms must be reviewed carefully

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for medically necessity. For example, the following should be reviewed closely, particularly when ordered simultaneously: laboratory tests of immune function (i.e., lymphocyte transformation, deregulation of the 2,5A RNase L antiviral pathway), lymphocyte subsets (e.g., natural killer cells, CD4, CD8), immunoglobulin levels (e.g., IgG, IgE), levels of trace minerals in the serum or urine (e.g., selenium, manganese, mercury), antibodies for a variety of infectious agents simultaneously, allergy services (including provocation testing), positron emission tomography scans, or neuropsychologic testing and elaborate nutritional assessment, including intracellular micronutrient assays.

In addition, such treatments as IVIg therapy, provocation therapy, or counseling regarding specific avoidance environments or elimination diets would be considered investigational in the absence of specific symptoms.

Background/Overview

Idiopathic environmental intolerance is typically characterized by recurrent, nonspecific symptoms that the patient or clinician believes are provoked by low levels of exposure to chemical, biologic, or physical agents. Reported symptoms are wide-ranging, and there are not clearly established diagnostic criteria. Various tests, e.g., nutritional assessment and treatment, e.g., IVIg, have been proposed.

Idiopathic environmental intolerance has been labeled in a variety of ways over time. The original term, clinical ecology, was replaced by the term multiple chemical sensitivity (MCS). More recently, MCS has been replaced by idiopathic environmental intolerance, a term that reflects the uncertain nature of the condition and its relationship to chemical exposure. The central focus of the condition is patient reporting of recurrent, nonspecific symptoms referable to multiple organ systems that the patient believes are provoked by exposure to low levels of chemical, biologic, or physical agents. The most common environmental exposures include perfumes and scented products, pesticides, domestic and industrial solvents, new carpets, car exhaust, gasoline and diesel fumes, urban air pollution, cigarette smoke, plastics, and formaldehyde. Certain foods, food additives, drugs, electromagnetic fields (EMF), and mercury in dental fillings have also been reported as triggering events. However symptoms do not bear any relationship to established toxic effects of the specific chemical and occur at concentrations far below those expected to elicit toxicity.

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Reported symptoms are markedly variable but generally involve the central nervous system, respiratory and mucosal irritation, or gastrointestinal symptoms. Symptoms may include fatigue, difficulty in concentrating, depressed mood, memory loss, weakness, dizziness, headaches, heat intolerance, and arthralgia. In contrast to the frequently debilitating symptomatology, no specific and consistent abnormalities are noted on laboratory or other diagnostic testing. Other primarily subjectively defined disorders have symptoms that overlap with idiopathic environmental intolerance, including chronic fatigue syndrome, sick building syndrome, fibromyalgia, irritable bowel syndrome, and Gulf War syndrome. A diagnosis of intestinal dysbiosis could be considered within the category of idiopathic environmental intolerance.

The variable nature of the reported symptoms and the lack of recognized pathologic abnormalities make it extremely difficult to establish objective diagnostic criteria for the condition, which further hinders research into both the causes and appropriate treatment. Various causes for idiopathic environmental intolerances have been proposed; these have prompted different diagnostic and treatment approaches. Some believe that the condition is an unrecognized form of allergy or immunologic hypersensitivity. Advocates of this etiology may recommend a large series of immunologic tests, including a variety of provocation-neutralization tests and a panel of immunologic tests, including immune function tests (e.g., deregulation of the 2,5A RNase L antiviral pathway in peripheral mononuclear blood cells) and levels of lymphocyte subsets (i.e., natural killer cells, CD8 cells). Proposed therapies have included avoidance of exposure, either or both in the environment or in the diet. Immune globulin may be recommended for injection or sublingual drops of “neutralizing” chemical and food extracts. Others have proposed that exposure to toxic substances may have prompted the immunologic abnormality and, based on this theory, testing of levels of environmental chemicals in the blood, urine, or fat may be suggested. Detailed nutritional analyses have also been performed, including levels of trace minerals in the blood, urine, or intracellular levels. Such elaborate nutritional assessments may also be performed in asymptomatic subjects. For example, Functional Intracellular Analysis (FIA^{TM†}) is a series of laboratory tests offered by SpectraCell Labs that measure the intracellular levels of micronutrients, such as vitamins, minerals, and antioxidants in lymphocytes.

In some instances, symptoms may appear to coincide after exposure to a viral illness (particularly common in the related condition of chronic fatigue syndrome); supporters of this theory may recommend a wide variety of tests to detect antibodies or antigens of various viruses. Some have

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also suggested that hypersensitivity to *Candida* may present with a similar array of subjective complaints and thus recommend testing for *Candida* in the stool or urine. Finally, it has also been proposed that idiopathic environmental intolerance is a manifestation of a psychiatric disease or personality disorder based in part on results of psychological/psychiatric interviews.

It should be noted that some environmentally caused illnesses can be well-characterized by their clinical presentation and laboratory tests. For example, in certain instances, “sick building” syndrome can be traced back to exposure of microorganisms related to air-handling systems. However, in contrast to idiopathic environmental intolerances, these patients experience a limited range of symptoms, and those symptoms only occur in the affected building.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

No specific U.S. FDA approval or clearance of a test for idiopathic environmental intolerance was found.

Rationale/Source

Idiopathic environmental intolerance (also known as multiple chemical sensitivities) is typically characterized by recurrent, nonspecific symptoms that the patient or clinician believes are provoked by low levels of exposure to chemical, biologic, or physical agents. Reported symptoms are wide-ranging, and there are not clearly established diagnostic criteria. Various tests (eg, nutritional assessment) and treatments (eg, immunoglobulin therapy [IVIg]) have been proposed.

There is a lack of clear diagnostic criteria for idiopathic environmental intolerance and a lack of evidence on the diagnostic accuracy of laboratory or other tests for this condition. Overall, studies using existing criteria have not found that subjects diagnosed with the condition can reliably distinguish between chemical exposure and placebo. Moreover, studies have not consistently found that low-level electromagnetic field exposure affects objective outcomes (eg, heart rate or cognitive function). In addition, there is a lack of controlled studies to evaluate treatments for idiopathic environmental intolerance. Thus, all tests and treatments for this condition are considered investigational.

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Supplemental Information

Practice Guidelines and Position Statements

A variety of organizations have presented position papers on idiopathic environmental intolerance, previously referred to as multiple chemical sensitivity or clinical ecology.

In 1999, the American Academy of Allergy, Asthma and Immunology (AAAAI) issued a position statement on idiopathic environmental intolerance. This statement is still posted on the AAAAI website, but it has been archived. The summary of the position states:

IEI [idiopathic environmental intolerances]-also called environmental illness and multiple chemical sensitivities-has been postulated to be a disease unique to modern industrial society in which certain persons are said to acquire exquisite sensitivity to numerous chemically unrelated environmental substances.... Because of the subjective nature of the illness, an objective case definition is not possible...there is an absence of scientific evidence to establish any of these mechanisms as definitive. Most studies to date, however, have found an excess of current and past psychopathology in patients with this diagnosis. The relationship of these findings to the patient's symptoms is also not apparent. Rigorously controlled studies to verify the patient's reported subjective sensitivity to specific environmental chemicals have yet to be done. Moreover, there is no evidence that these patients have any immunologic or neurologic abnormalities. In addition, no form of therapy has yet been shown to alter the patient's illness in a favorable way. A causal connection between environmental chemicals, foods, and/or drugs and the patient's symptoms continues to be speculative and cannot be based on the results of currently published scientific studies.

In 1999, the American College of Occupational and Environmental Medicine published a position statement that concluded, in part:

Although specific diagnostic tests and treatments have not yet been demonstrated to be helpful, a generalized clinical approach useful in the management of other nonspecific medical syndromes can be adopted pending further scientific findings. This approach emphasizes 1) establishing a therapeutic alliance with a goal toward functional restoration; 2) performing a medical evaluation appropriate to the presenting complaints and physical findings; 3) avoiding

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ineffective, costly, and potentially hazardous, unproven diagnostic tests or remedies that may increase a patient's distress or disease; 4) treating all diagnosable medical and psychological problems; 5) individualizing medical and behavioral coping strategies useful in managing symptoms; and 6) educating the patients about the current state of knowledge about MCS.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

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06/27/2013	Medical Policy Committee review
07/17/2013	Medical Policy Implementation Committee approval.
07/10/2014	Medical Policy Committee review
07/16/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/06/2015	Medical Policy Committee review
08/19/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/04/2016	Medical Policy Committee review
08/17/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
08/03/2017	Medical Policy Committee review
08/23/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/09/2018	Medical Policy Committee review
08/15/2018	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/01/2019	Medical Policy Committee review
08/14/2019	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/06/2020	Medical Policy Committee review
08/12/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/05/2021	Medical Policy Committee review
08/11/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.

Next Scheduled Review Date: 08/2022

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	84999, 86849
HCPCS	No codes
ICD-10 Diagnosis	All related diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into

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standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

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