

Policy Number	MED206.003
Policy Effective Date	05/15/2024
Policy End Date	12/31/2025

Idiopathic Environmental Intolerance (IEI) Management

Table of Contents
<u>Coverage</u>
<u>Policy Guidelines</u>
<u>Description</u>
<u>Rationale</u>
<u>Coding</u>
<u>References</u>
<u>Policy History</u>

Related Policies (if applicable)
MED206.001: Allergy Management
MED206.005: Antigen Leukocyte Antibody Test (ALCAT)
MED206.006: Sublingual Immunotherapy as a Technique of Allergen-Specific Therapy
MED207.088: Intracellular Micronutrient Analysis
MED207.118: Fecal Analysis in the Diagnosis of Intestinal Dysbiosis
THE801.008: Chelation Therapy

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

This medical policy has become inactive as of the end date above. There is no current active version and this policy is not to be used for current claims adjudication or business purposes.

All services provided for the diagnosis, treatment, and ongoing management of Idiopathic Environmental Intolerance (IEI) Management are **considered experimental, investigational and/or unproven**, including but not limited to the following services:

- Laboratory tests and other diagnostic tests designed to affirm the diagnosis of IEI; AND/OR
- Nutritional assessments or surveys, including intracellular analysis of micronutrients, in both asymptomatic persons and patients with symptoms suggestive of IEI; AND/OR
- Treatment of IEI with intravenous immunoglobulin (IVIg), neutralizing therapy of chemical and food extracts, avoidance therapy, elimination diets, and oral nystatin (to treat Candida); AND/OR

- Any aspect of the Lifestyle Eating and Performance (LEAP) program, including the Mediator Release Test (MRT), Antigen Leukocyte Cellular Antigen Test (ALCAT), or others used to identify “delayed food allergies” and treatments that include dietary manipulation with or without supplements and/or herbs; AND/OR
- Any aspect of mucosal barrier laboratory testing (of the eye, oral cavity, nasal cavity, pharyngeal cavity, tracheobronchial tree, alimentary tract, urinary tract and/or genital tract).

Policy Guidelines

Laboratory tests for the diagnosis of idiopathic environmental intolerance (IEI) may be broadly subdivided into those intended to rule out specific diseases with well-defined presentations and diagnostic criteria, and those tests that are designed to affirm the diagnosis of IEI. 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 non-specific 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. However, at the present time, no specific tests can confirm the diagnosis of IEI, and thus a large battery of tests performed for a patient with non-specific symptoms must be reviewed carefully for medical necessity. For example, the following should be reviewed closely, particularly when ordered simultaneously:

- Laboratory tests for immune function (i.e., lymphocyte transformation, deregulation of the 2,5A RNase L antiviral pathway);
- Laboratory tests for mucosal immunity function (i.e., dietary protein, yeast antibodies, aerobic and/or anaerobic antibodies, secretory antibodies, secretory IgA);
- 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);
- PET scans or other imaging studies;
- Neuropsychological testing;
- Elaborate nutritional surveys, interviews, evaluations, and/or assessments (including FIA, intracellular micronutrient assays);
- Mediator Release Test (MRT) used to identify delayed food allergies and is part of the Lifestyle Eating and Performance (LEAP) Program.

In addition, claims for treatments listed below should be carefully reviewed for medical necessity in the absence of specific symptoms. These treatments include, but are not limited to:

- IVIg therapy;
- Provocation therapy;
- Lifestyle changes;
- Avoidance therapy;

- Nutritional counseling;
- Elimination diets.

There is no specific procedure code for Lifestyle Eating and Performance (LEAP) Program or Antigen Leukocyte Cellular Antigen Test (ALCAT) testing. When non-specific/unspecified codes, including but not limited to 83516, 83520, and/or 86160, are billed for LEAP or ALCAT testing, they are considered experimental, investigational and/or unproven.

Description

Idiopathic environmental intolerance (IEI) 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, 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.

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 IEI, 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 IEI. (Intestinal dysbiosis is addressed separately in medical policy MED207.118.)

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 IEI 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), lifestyle eating and performance (LEAP) testing, Mediator Released Testing (MRT) for food testing, mucosal barrier testing, antigen leukocyte cellular antibody test (ALCAT), levels of lymphocyte subsets (i.e., natural killer cells, CD8 cells), serum allergy tests, multiple radioallergosorbent test (MAST), fluorescent allergosorbent test (FAST), enzyme-linked immunosorbent assay (IgG [ELISA]), serum immunoglobulins IgA and IgE (RAST), bronchial challenge testing, assays of B and T cells, complement levels and serial dilution end-point titration (SDET) or Rinkel/Rinkel method. 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™) 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.

Mucosal barrier testing is proposed as a new generation of laboratory testing. It purports to take into consideration an individual's immune system response to proteins and peptides that can challenge the immune system and produce antibodies when they enter the bloodstream. The proponents for this testing postulate that under healthy intestinal conditions this does not cause problems but may initiate onset of an autoimmune disorder in susceptible persons. Mucosal barrier testing is performed by BioHealth® Diagnostics.

The Mediator Release Test® (MRT®) involves the measurement of the aggregate release of inflammatory mediators from an individual's immunocytes after exposure to various food extracts and chemicals (e.g., food additives). A determination is made of the difference in volume of circulating immunocytes and plasma before and after an in vitro antigen challenge. For the Mediator Release Test®, a portion of an individual's blood sample is incubated with various food extracts and food additives (typically 150 different substances). The degree of reactivity is determined by the degree of mediator release from the cells. A response, change in cellular and plasma volume, is thought to indicate a hypersensitivity reaction and results are used as a basis for modifying an individual's diet. The MRT® is one component of the Lifestyle Eating and Performance (LEAP®) Program of oligo antigenic dieting. This type of testing has been promoted for individuals with, among other conditions, irritable bowel syndrome, chronic fatigue syndrome, migraine headaches, and dermatologic conditions (e.g., eczema, dermatitis).

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 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 IEI 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 IEI, these patients experience a limited range of symptoms, and those symptoms only occur in the affected building.

Regulatory Status

No specific U.S. Food and Drug Administration (FDA) approval or clearance of a test for IEI was found.

Rationale

This medical policy was created in May 1990 and has been updated regularly with searches of the PubMed database. The most recent literature review was performed through March 20, 2024.

The clinical entity of idiopathic environmental intolerance (IEI) has been controversial for decades, in part due to the lack of a set of reproducible diagnostic criteria. Absent a clear definition of the disorder, basic science research into the etiology of the disorder, appropriate laboratory tests, and identifications of effective treatment are obviously problematic. Published reviews and opinion pieces suggest controversy regarding the etiology of the condition, appropriate diagnostic criteria, and treatment strategies. (1-5)

Diagnosis

No well-designed studies were identified in the literature searches that evaluated the ability of laboratory tests, nutritional assessments, or other diagnostic tests to accurately diagnose IEI (or multiple chemical sensitivity [MCS]).

Studies to date have focused on developing reliable criteria for characterizing IEI and defining an optimal approach to diagnosing the condition. In 2006, Das-Munshi et al. published a systematic review of provocation studies in individuals with MCS. (6) The investigators identified 37 studies that included a total of 784 patients who had been diagnosed with MCS. Blinding was inadequate in most cases. In 8 of 11 studies that were described as double-blind but likely had discernible odors, individuals with MCS had positive responses to provocation. However, of the 7 studies that used chemicals at or below the threshold of detectable odors, 6 failed to show consistent responses in patients with MCS after active provocation. In the 3 studies that used olfactory-masking agents to conceal the identity of the stimulus, none found associations between provocation and response. The authors concluded that persons with MCS react to chemical challenges when they can discern differences between active and sham substances, but when stimuli are adequately masked, individuals with MCS are unable to

reliably identify active stimuli. The authors further commented that there may be psychological or behavioral factors leading individuals to have physiologic responses to stimuli when they are aware of the exposure. In reports from Europe, researchers have found that findings of psychological distress, the ability to express emotions, somatic attribution, amplification (susceptibility to sensation), and absorption (predisposition to become deeply immersed in sensory or mystical experiences) were related to the presence of IEI. (7-11)

In 2008, Bornschein et al. in Germany published the findings of a double-blind, placebo-controlled provocation study that included 20 patients with MCS and 17 healthy controls matched for age and gender. (12) Patients with MCS met several sets of diagnostic criteria developed in the 1990s, including criteria IEI defined by the International Program for Chemical Safety. Specific eligibility criteria included reporting symptoms that usually arise and recede within a time span of 10 minutes after the beginning of exposure and MCS symptoms that can be provoked by organic solvents. Provocations took place in a “climate chamber” (room for climatologic and chemical provocations). Participants underwent 6 consecutive 15-minute sessions, each followed by a 15-minute break. Three sessions were exposures to solvents and the other 3 were exposure to placebo (clean air), in random order; patients and staff were blinded. The solvents were a mixture of 6 hydrocarbons found in common household solvents; to avoid the need for olfactory masking, room air concentrations were set below a detectable odor threshold. Only one participant failed to complete the provocation sessions. A positive reaction to exposure was defined as: 1) the subject believed he or she had been exposed to an active agent; 2) there was an objective sign of a reaction, e.g., rash, increase in heart rate; or 3) symptom severity rose to 3 or 4 (on 4-point scale). Fifty percent of patients with MCS and 53% of matched controls showed a positive reaction in all 6 exposure sections. Eighty-two percent of controls and 50% of patients had 3 correct reactions. However, more patients than controls (30% versus 12%, respectively) reacted correctly more than 3 times. Considering only the subjective perception of exposure, 40% of patients and 35% of controls voted correctly more than 3 times. Overall, study findings suggest that patients with MCS disorders cannot reliably distinguish between solvents and placebo.

No well-designed studies were identified in the literature searches that evaluated the ability of mucosal barrier testing or the mediator release test.

Several systematic reviews of studies on the diagnosis of IEI attributed to electromagnetic fields (EMF) have been published. A 2011 systematic review by Rubin et al. identified 29 studies which were single- or double-blind, exposed participants to EMF fields, and measured objective outcomes. (13) Twenty of the 29 studies used outcomes related to the autonomic nervous system (e.g., heart rate or blood pressure). Two of 20 (10%) studies found a significant impact of EMF on function and the other 18 studies found no effect. The authors noted that findings of the 2 positive studies might have been influenced by the order of exposure e.g., including a sham exposure that was always first or second in a series of 3 or 4 consecutive exposures. None of the 4 studies measuring blood chemistry or 3 studies measuring brain physiology found a significant effect of EMF levels on outcomes. Seven studies tested cognitive function; 2 of 7 (29%) had at least one positive finding. The authors concluded that there is insufficient

evidence suggesting that individuals with idiopathic environmental intolerance attributed to EMF experience their physiological reactions as a result of exposure to EMF.

In 2012, Baliatsas et al. in the Netherlands reviewed 63 studies that included definitions or criteria for identifying individuals with idiopathic environmental intolerance related to EMF exposure. (14) The major criteria used in the studies were: 1) attribution of non-specific physical symptoms to either various or specific sources of EMF (n=13 studies); 2) self-reported idiopathic environmental intolerance attributed to EMF exposure (or similar terms) (n=14 studies); 3) experience of symptoms during or within 24 hours after perceived or actual EMF exposure (n=10 studies); and 4) high score on a symptom scale (n=6). The review found considerable variation among studies in terms of definitions and criteria; uniform diagnostic criteria have not yet been developed.

In a 2016 study by Micarelli et al., a cohort of 18 MCS patients underwent transient evoked otoacoustic emission (TEOAE) testing with and without contralateral suppression to evaluate the functionality of the medial olivocochlear (MOC) reflex involved in speech-in-noise sensitivity. (15) Results were compared with an age and gender-matched control group (n = 20) and correlation analysis with disease onset and Quick Environmental Exposure and Sensitivity Inventory (QEESI) Symptom Severity Scale (SSS) was performed. Subjects affected by MCS showed statistically significant impairment of MOC reflex, and the onset of the disease and several symptom subscales showed to be correlated to such reduction in some of the frequencies tested. These data suggest that alterations of MOC reflex could be part of the complex features of this disease although more studies are needed to further explore auditory perception disorders in environmental intolerances.

In order to better understand the etiology of IEI attributed to EMF, Kjellqvist et al. (2016) looked at psychological symptoms and health-related quality of life (HRQoL) in those who attribute health problems to EMF. (16) Participants with IEI-EMF (n=114) and a population-based sample of referents (n=104) were investigated with six subscales of the Symptom Checklist 90 (SCL90) to assess psychological symptoms, and with eight subscales of the Short Form (36) Health Survey (SF36) to assess HRQoL. Significantly higher scores were found on obsessive/ compulsive behavior, interpersonal hypersensitivity, hostility, phobic anxiety, paranoid thoughts in the IEI-EMF group compared to referents, whereas only a tendency of such a difference was found for psychotism. Furthermore, poorer HRQoL in the IEI-EMF group, compared to referents, were found regarding physical and social functioning, physical and emotional role limitations, general health, vitality, bodily pain, and mental health. Significant correlation with moderate to strong effect sizes were found between several of the SCL90 and SF36 subscales. The results suggest that IEI-EMF is associated with various types of psychological symptoms and with poor HRQoL. Further research is needed regarding the clinical implications of these findings.

Johnson and Colman (2017) investigated the association between MCS and major depressive disorder (MDD), generalized anxiety disorder (GAD), MDD and GAD comorbidity (MDD+GAD), severe distress, and positive mental wellbeing. (17) This cross-sectional investigation was

carried out using the 2012 Canadian Community Health Survey Mental Health Component. The study population consisted of 21,977 individuals aged 20 and older. Odds ratios were computed using multinomial logistic regression to calculate estimates of the association between MCS and mental illness. All analyses were weighted to take into account the complex survey design. Individuals with MCS had 2.37 (1.55, 3.64) times greater odds of MDD, 3.09 (1.80, 5.30) times greater odds of MDD+GAD, and 2.60 (1.67, 4.07) times greater odds of severe distress. No association between MCS and GAD was observed. A sex difference was observed with males with MCS having lower odds of positive mental wellbeing, whereas no association was observed in females. Investigators concluded that the study findings supported an association between MCS and mental illness. The causal mechanism supporting this association remains unclear.

Viziano et al. (2018) summarized evidence on MCS, with focus on indexed studies analyzing sensory pathway-related disorders. (18) Thirty-four studies met the selection criteria and were included in the analysis. Although there was moderate evidence to show that sensory pathways are somewhat altered, especially with respect to information processing in the limbic system and related cortical areas, many variables, such as different diagnostic criteria, lack of homogeneous symptom questionnaires and the general incidence of personality traits in control subjects, biased the studies. Further research is necessary to clarify whether sensory related impairments specifically affect IEI conditions as opposed to a wide spectrum of associated disorders.

In 2018, Rossi and Pitidis performed a systematic review of the literature from May 1998–December 2015 related to MCS for the purpose of detecting new diagnostic and epidemiological evidence. (19) Studies were analyzed by verifying 1) the typology of study design; 2) criteria for case definition; 3) presence of attendances in the emergency departments and hospital admissions; and 4) analysis of the risk factors. Reviewers concluded that “although over the years we have made several steps toward a better definition of this syndrome, it is still not possible to diagnose MCS with absolute certainty, as the many and diverse symptoms that patients complain following “low-dose” exposures to chemicals (not well defined in most cases) are common to various pathologies, both physical and psychic”.

In 2021, Dantoft et al. reviewed the data from a random sample of the Danish adult population enrolled in the Danish Study of Functional Disorders (DanFunD). (20) The study population comprised a random sample of 29,088 persons drawn from the Danish Civil Registration System. A total of 9,656 (33.7%) accepted the invitation and participated in the DanFunD baseline examination conducted between 2011 and 2015. Since MCS is categorized as a functional somatic syndrome (FSS), and MCS cases often meet the criteria for other types of FSS (e.g., fibromyalgia), the primary aim was to characterize MCS regarding symptom triggers, symptoms, lifestyle and describe demographics, socioeconomics and lifestyle factors associated with MCS. A secondary aim was to examine the implication of FSS comorbidity. MCS cases (n = 188) were stratified into subgroups; MCS only (n = 109) and MCS with comorbid FSS (n = 73). Information regarding FSS comorbidities were missing for six MCS cases. MCS subgroups and controls without FSS comorbidities (n = 7,791) were compared by means of logistic regression

analyses, adjusted for age and sex. The results show that MCS was associated with female sex, not being in occupation and low social status, but not with age or education. MCS cases reported normal dietary intake and smoking habits and lower alcohol consumption. Additional associations were found between MCS and low rate of cohabitation, sedentarism, daily physically limitations, and poor quality of sleep. However, subgroup analysis revealed that these findings were primarily associated with MCS with comorbid FSS. Researchers concluded that MCS was associated with lower socioeconomic status, physically inactivity and poor quality of sleep. Subgroup analysis revealed that several associations was explained by FSS comorbidity, i.e., MCS cases with no comorbid FSS showed normal rate of cohabitation and did not report physical limitations or difficulties sleeping. Overall, researchers believe their findings emphasize the importance of screening MCS cases for FSS comorbidity both in epidemiological and clinical settings. An important strength of this study is the large random sample of the general adult population enrolled in the DanFunD study, comprising both sexes over an age span of 50 years, and the vast amount of data collected for the study. This data offers a unique opportunity within MCS research to study the epidemiology of MCS in a large and well characterized cohort, and to investigate the role of comorbid FSS. Regarding the limitations, a concern is the relatively low participation rate of the DanFunD study at 33.7%, and whether the cohort is representative of the general adult population.

Treatment

In 2012, Skovbjerg et al. in Denmark published a randomized non-blinded pilot study to evaluate mindfulness-based cognitive therapy to treat multiple chemical sensitivities. (21) Thirty-seven participants with self-reported symptoms attributed to exposure to common airborne chemicals, or with physician-diagnosed MCS were included. Participants were randomized to receive weekly group therapy for 8 weeks or usual care. At the 4-, 8- and 12-week follow-ups, no statistically significant differences were found between groups in the 2 main outcome measures, the Symptom Checklist-92 (SCL-92) and the Brief Illness Perception Questionnaire (Brief IPQ). For example, 8 weeks after the beginning of the intervention, mean scores on the somatization scale of the SCL-92 were 0.78 in the therapy group and 0.79 in the control group ($p=0.59$).

Tran et al. (2017) conducted a nationwide trial in Denmark using a randomized, parallel-group, double-blind and placebo-controlled design to evaluate the efficacy of transcranially applied pulsed electromagnetic fields (PEMF) on functional impairments and symptom severity in MCS patients. (22) A total of 39 participants were randomized to PEMF or placebo treatment. No significant difference was observed on QEESI Life Impact Scale (LIS) between groups with a mean change score of -5.9 in the PEMF group compared with -1.5 in the placebo group ($p=0.35$, effect size=-0.31). However, a significant decrease was detected on QEESI SSS within and between groups with a mean change score of -11.3 in the PEMF group compared with -3.2 in the placebo group ($p=0.03$, effect size=-0.60). Researchers concluded that PEMF treatment of 6 weeks showed no effect on functional impairments in MCS. However, a decrease in symptom severity was observed.

UpToDate

A 2023 UpToDate article on idiopathic environmental intolerance states “Idiopathic environmental intolerance (IEI), formerly called multiple chemical sensitivity, is a subjective illness marked by recurrent, nonspecific symptoms attributed to low levels of chemical, biologic, or physical agents. These symptoms occur in the absence of consistent objective diagnostic physical findings or laboratory tests that define an illness. Many experiments and observational studies consistently identify psychopathology in patients with IEI and implicate behavioral or psychiatric causes for this illness. This indicates that the underlying illness in many cases of IEI is actually a psychiatric disorder, such as a somatoform, depressive, or anxiety disorder.” The article goes on to say “Prominent medical societies view IEI with marked skepticism. As an example, the American Medical Association concluded that, ‘Until such accurate, reproducible, and well-controlled studies are available, the American Medical Association Council on Scientific Affairs believes that multiple chemical sensitivity should not be considered a recognizable syndrome’.” (23)

Summary of Evidence

There is a lack of clear diagnostic criteria for idiopathic environmental intolerance (IEI) (also known as multiple chemical sensitivities [MCS]) 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 (e.g., 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 experimental, investigational and/or unproven.

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.

American Academy of Allergy, Asthma and Immunology (AAAAI)

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. (24) 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."

American College of Occupational and Environmental Medicine (ACOEM)

In 1999, ACOEM published a position statement (25) that concluded, in part:

"Although specific diagnostic test and treatment 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 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 [multiple chemical sensitivity]."

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	83516, 86160
HCPCS Codes	None

*Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.

References

1. Aaron LA, Buchwald D. A review of the evidence for overlap among unexplained clinical conditions. *Ann Intern Med.* 2001; 134(9 pt 2):868-881. PMID 11346323
2. Barsky AJ, Borus JF. Functional somatic syndromes. *Ann Intern Med.* 1999; 130(11):910-921. PMID 10375340
3. Graveling RA, Pilkington A, George JP, et al. A review of multiple chemical sensitivity. *Occup Environ Med.* 1999; 56(2):73-85. PMID 10448311

4. Lacour M, Zunder T, Huber R, et al. The pathogenetic significance of intestinal Candida colonization--a systematic review from an interdisciplinary and environmental medical point of view. *Int J Hyg Environ Health*. 2002; 205(4):257-268. PMID 12068745
5. Winder C. Mechanisms of multiple chemical sensitivity. *Toxicol Lett*. 2002; 128(3-Jan):85-97. PMID 11869820
6. Das-Munshi J, Rubin GJ, Wessely S. Multiple chemical sensitivities: a systematic review of provocation studies. *J Allergy Clin Immunol*. 2006; 118(6):1257-1264. PMID 17137865
7. Bailer J, Witthoft M, Rist F. Psychological predictors of short- and medium term outcome in individuals with idiopathic environmental intolerance (IEI) and individuals with somatoform disorders. *J Toxicol Environ Health A*. 2008; 71(11-12):766-775. PMID 18569575
8. Witthoft M, Rist F, Bailer J. Evidence for a specific link between the personality trait of absorption and idiopathic environmental intolerance. *J Toxicol Environ Health A*. 2008; 71(11-12):795-802. PMID 18569578
9. Skovbjerg S, Zachariae R, Rasmussen A, et al. Attention to bodily sensations and symptom perception in individuals with idiopathic environmental intolerance. *Environ Health Prev Med*. 2010; 15(3):141-150. PMID 19953345
10. Skovberg S, Zachariae R, Rasumussen R, et al. Regressive coping and alexithymia in idiopathic environmental intolerance. *Environ Health Prev Med*. 2010; 15(5):299-310. PMID 21432559
11. Skovbjerg S, Rasmussen A, Zachariae R, et al. The association between idiopathic environmental intolerance and psychological distress, and the influence of social support and recent major life events. *Environ Health Prev Med*. 2012; 17(1):2-9. PMID 21431806
12. Bornschein S, Hausteiner C, Rommelt H, et al. Double-blind placebo-controlled provocation study in patients with subjective Multiple Chemical Sensitivity (MCS) and matched control subjects. *Clin Toxicology*. 2008; 46(5):443-449. PMID 18568800
13. Rubin GJ, Hillert L, Nieto-Hernandez R, et al. Do people with idiopathic environmental intolerance attributed to electromagnetic fields display physiological effects when exposed to electromagnetic fields? A systematic review of provocation studies. *Bioelectromagnetics*. 2011; 32(8):593-609. PMID 21769898
14. Baliatsas C, Van Kamp I, Lebret E, et al. Idiopathic environmental intolerance attributed to electromagnetic fields (IEI-EMF): a systematic review of identifying criteria. *BMC Public Health*. 2012; 12:643. PMID 22883305
15. Micarelli A, Viziano A, Genovesi G, et al. Lack of contralateral suppression in transient-evoked otoacoustic emissions in multiple chemical sensitivity: a clinical correlation study. *Noise Health*. 2016; 18(82):143-149. PMID 27157687
16. Kjellqvist A, Palmquist E, Nordin S. Psychological symptoms and health-related quality of life in idiopathic environmental intolerance attributed to electromagnetic fields. *J Psychosom Res*. 2016; 84:8-12. PMID 27095153
17. Johnson D, Colman I. The association between multiple chemical sensitivity and mental illness: Evidence from a nationally representative sample of Canadians. *J Psychosom Res*. 2017; 99:40-44. PMID 28712429
18. Viziano A, Micarelli A, Pasquantonio G, et al. Perspectives on multisensory perception disruption in idiopathic environmental intolerance: a systematic review. *Int Arch Occup Environ Health*. 2018; 91(8):923-935. PMID 30088144

19. Rossi S, Pitidis A. Multiple chemical sensitivity: Review of the state of the art in epidemiology, diagnosis, and future perspectives. *J Occup Environ Med.* 2018; 60(2):138-146. PMID 29111991
20. Dantoft T, Nordin S, Andersson L, et al. Multiple chemical sensitivity described in the Danish general population: Cohort characteristics and the importance of screening for functional somatic syndrome comorbidity—The DanFunD study. *PLoS One.* 2021; 16(2):e0246461. PMID 33626058
21. Skovbjerg S, Hauge CR, Rasmussen A, et al. Mindfulness-based cognitive therapy to treat multiple chemical sensitivities: a randomized pilot trial. *Scand J Psychol.* Jun 2012; 53(3):233-238. PMID 22530938
22. Tran MTD, Skovbjerg S, Arendt-Nielsen L, et al. A randomised, placebo-controlled trial of transcranial pulsed electromagnetic fields in patients with multiple chemical sensitivity. *Acta Neuropsychiatr.* 2017; 29(5):267-277 PMID 27919300
23. Black DW, Temple S. Overview of idiopathic environmental intolerance (multiple chemical sensitivity). In UpToDate, Dimsdale J (Ed), UpToDate, Waltham, MA. Available at: <<https://www.uptodate.com>> (accessed March 18, 2024).
24. American Academy of Allergy Asthma and Immunology Position Statement on Idiopathic Environmental Intolerances (1999). Available at: <<https://www.aaaai.org>> (accessed March 20, 2024).
25. American College of Occupational Environmental Medicine Position Statement. Multiple chemical sensitivities: idiopathic environmental intolerance. *J Occup Environ Med.* 1999; 41(11):940-942.

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 <<http://www.cms.hhs.gov>>.

Policy History/Revision

Date	Description of Change
12/31/2025	Document became inactive.
05/15/2024	Document updated with literature review. Coverage unchanged. Reference 20 added.
03/15/2023	Reviewed. No changes.
10/01/2022	Document updated with literature review. Coverage unchanged. One reference removed.

01/01/2022	Document reviewed. Coverage unchanged. No new references added.
10/15/2020	Reviewed. No changes.
01/15/2020	Document updated with literature review. Coverage unchanged. The following references were added: 15-19 and 21.
09/01/2017	Reviewed. No changes.
01/01/2017	Document updated with literature review. Coverage unchanged.
07/15/2015	Reviewed. No changes.
02/15/2014	Document updated with literature review. Coverage unchanged.
01/01/2011	Document updated with literature search. New indication added. Mucosal barrier test as experimental, investigational and unproven. Rationale revised. CPT codes added.
02/15/2008	Coverage Revised
01/15/2008	Revised/Updated Entire Document
05/01/2006	Revised/Updated Entire Document
11/01/2000	Revised/Updated Entire Document
04/01/1993	Revised/Updated Entire Document
05/01/1990	New Medical Document