



COMPLEMENTARY AND ALTERNATIVE MEDICINE IN MULTIPLE SCLEROSIS

This is a summary of the American Academy of Neurology (AAN) guideline regarding complementary and alternative medicine (CAM) use in people with multiple sclerosis (MS).

Please refer to the full guideline at AAN.com/guidelines for more information, including definitions of the classifications of evidence and recommendations.

Do CAM therapies reduce specific symptoms and prevent relapses or disability in patients with MS?

Biologically-based Practices

Herbs: Oral Cannabis Extract and Synthetic Tetrahydrocannabinol

Strong evidence	Clinicians might offer oral cannabis extract (OCE) to patients with MS to reduce patient-reported symptoms of spasticity and pain (excluding central neuropathic pain) (Level A).
Moderate evidence	<p>Clinicians might offer THC to patients with MS to reduce patient-reported symptoms of spasticity and pain (excluding central neuropathic pain) (Level B).</p> <p>Clinicians should counsel patients considering OCE or THC that, although these preparations improve spasticity-related symptoms, they are probably ineffective (short-term studies [15 weeks]) for improving objective measures of spasticity (Level B).</p> <p>Clinicians should counsel patients considering OCE or THC that these preparations are probably ineffective for improving tremor (Level B).</p>
Weak evidence	<p>Clinicians might counsel patients that the symptomatic benefit of OCE for reducing spasticity symptoms and pain (excluding central neuropathic pain) is possibly maintained for 1 year (Level C).</p> <p>Clinicians might counsel patients that the symptomatic benefit of THC for reducing patient-reported symptoms of spasticity and pain (excluding central neuropathic pain) is possibly maintained for 1 year (Level C).</p>
Insufficient evidence	Data are inadequate to support or refute the use of: OCE/THC for urinary urge incontinence and overall bladder symptoms in MS (Level U) Synthetic THC (Marinol) for central neuropathic pain in MS (Level U)

Herbs: Oromucosal Cannabinoid Spray

Moderate evidence	<p>Clinicians might offer Sativex oromucosal cannabinoid spray (nabiximols), where available, to reduce symptoms of spasticity, pain, or urinary frequency (Level B).</p> <p>Clinicians should counsel patients considering Sativex oromucosal cannabinoid spray that although this preparation improves spasticity-related symptoms and urinary frequency, it is probably ineffective for improving objective measures of spasticity or the number of urinary incontinence episodes (Level B).</p>
Weak evidence	Clinicians might choose not to offer Sativex oromucosal cannabinoid spray to reduce MS-related tremor (Level C).
Insufficient evidence	<p>Data are inadequate to support or refute the use of Sativex oromucosal cannabinoid spray for overall bladder symptoms, anxiety symptoms, or sleep problems, or symptoms related to cognition, quality of life (QOL), or fatigue in MS (Level U).</p> <p>Data are inadequate to determine the abuse potential or effect on psychopathologic symptoms of Sativex oromucosal cannabinoid spray (Level U).</p>

Herbs: Smoked Cannabis

Insufficient evidence	Data are inadequate to support or refute use of smoked cannabis for spasticity, pain, balance/posture, or cognition in MS (Level U).
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Clinical Context*

The cannabinoid studies have limitations that physicians and patients must be aware of. Most studies were of short duration, 6–15 weeks. Another limitation was the potential for central side effects to unmask patients to treatment assignment—a concern with regard to all masked trials involving treatments with prominent side effects. It is also important to recognize that the Ashworth scale used for objective measurement may be insensitive to spasticity changes. These factors may contribute to the discordant effects of cannabinoids on subjective and objective spasticity measures.

Cannabinoids were generally well tolerated, although some serious adverse effects (SAEs) were reported. Few studies reported deaths in the cannabinoid-treated groups (1 due to pneumonia, 1 to seizure-related aspiration pneumonia, and 2 to cancer, presumed unrelated). Mild/moderate adverse effects (AEs) were common (approximately 50%–80% of subjects) and appeared to be equally prevalent in subjects receiving cannabinoids or placebo. No significant laboratory, hematologic, urologic, or cardiac changes, or differences in vital signs, were noted. CNS AEs (e.g., dizziness, somnolence, drowsiness, lightheadedness, memory disturbance, difficulty concentrating) were more common in subjects receiving cannabinoids vs placebo. Dizziness was most common (15%–50% of subjects). Gastrointestinal AEs, including increased appetite, nausea, vomiting, constipation, and dry/sore mouth, occurred in about 10% of subjects receiving cannabinoids and were more common in those receiving cannabinoids than placebo. Other, less-common, AEs included myalgia, increased spasticity, seizures (4/137 subjects had seizures), lower-limb weakness, hemorrhagic cystitis, dehydration, temporary psychosis (1 rated as severe), hallucinations, and oral ulceration.

Because cannabinoids have known psychoactive properties, their potential for psychopathological and neurocognitive AEs is a concern especially in a patient population that may be vulnerable due to underlying disorders. Clinicians should therefore counsel patients about the potential for psychopathologic/cognitive AEs as well as other AEs associated with cannabinoids. Sativex oromucosal cannabinoid spray is not US Food and Drug Administration (FDA) approved and is not available in the United States. In the United States, caution should be exercised with regard to the extrapolation of the results of trials of standardized OCEs (which are not commercially available) to other, nonstandardized and nonregulated, cannabis extracts (which may be commercially available in states with medical marijuana laws).

Herbs: Ginkgo Biloba

Strong evidence	Clinicians might counsel patients with MS that ginkgo biloba (GB) is established as ineffective for improving cognitive function in MS (Level A).
Weak evidence	Clinicians might counsel patients with MS that GB is possibly effective for reducing fatigue in MS (Level C).

Dietary Supplementation

Moderate evidence	Clinicians might counsel patients that a low-fat diet with fish oil (omega-3 fatty acids) supplementation is probably ineffective for reducing relapses, disability, or MRI lesions, or for improving fatigue or QOL symptoms in MS (Level B).
Weak evidence	Clinicians might counsel patients with MS that lofepramine plus L-phenylalanine with vitamin B ₁₂ (Cari Loder regimen) is possibly ineffective for treating MS-related disability, symptoms, depression, or fatigue (Level C).

Clinical Context

GB and other supplements are not FDA regulated. Their quality control may play a role in their effectiveness and AE risk. Moreover, interactions of supplements with other medications, especially disease-modifying therapies for MS, are a clinical concern.

Other Biologically-based Practices

Weak evidence	Clinicians might counsel patients with MS that bee sting therapy is possibly ineffective for reducing MS-related relapses, disability, fatigue, total MRI lesion burden, new gadolinium-enhancing lesion volume, or health-related QOL (Level C).
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Clinical Context

Bee stings can be associated with anaphylactic reaction and possible death.

Energy Medicine and Manipulative Body-based Practices

Moderate evidence	Clinicians might counsel patients with MS that magnetic therapy is probably effective for reducing fatigue (Level B) and probably ineffective for reducing depression (Level B).
Weak evidence	Clinicians might counsel patients with MS that reflexology is possibly effective for reducing MS-associated paresthesia (Level C).

Can CAM use worsen MS, cause SAEs, or interfere with MS disease-modifying therapies?

Insufficient evidence	Clinicians should counsel patients with MS that the safety and efficacy of other reviewed CAM, or the interaction of CAM with disease-modifying therapies for MS, are unknown (Level U).** Further research is warranted.
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Clinical Context

CAM therapies are not regulated by the FDA. The quality control of these supplements may play a role both in their effectiveness and in their AE risk. Interactions of CAM therapies with other medications, especially disease-modifying therapies for MS, are a clinical concern. Given the popularity of CAM therapies both in patients with MS and in patients with other neurologic disorders (e.g., Alzheimer disease, Parkinson disease), it may be useful for neurologists to routinely ask patients about their CAM use.

Information resources for health professionals include:

- National Multiple Sclerosis Society – nmss.org
- National Institutes of Health (NIH) – nih.gov
- NIH division of the National Center for Complementary and Alternative Medicines – nccam.nih.gov

Patients should be counseled regarding applicable quality control, safety, lack of FDA regulation of CAM, potential out-of-pocket expenses (these may not be covered by insurers), and potential drug interactions with other symptomatic and disease-modifying therapies in MS.

*Clinical context content slightly abridged. See the full guideline for complete text.

**See complete guideline for list of CAM therapies for which no studies were available or for which the available studies were insufficient for making evidence-based recommendations.

This guideline was endorsed by the Consortium of Multiple Sclerosis Centers and the International Organization of Multiple Sclerosis Nurses.

This statement is provided as an educational service of the American Academy of Neurology. It is designed to provide members with evidence-based guideline recommendations to assist the decision making in patient care. It is based on an assessment of current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, and are based on all of the circumstances involved. Physicians are encouraged to carefully review the full AAN guidelines so they understand all recommendations associated with care of these patients.

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