Summary of Systematic Review for **CLINICIANS**

AMERICAN ACADEMY OF NEUROLOGY®

EFFICACY AND SAFETY OF THE THERAPEUTIC USE OF MEDICAL MARIJUANA (CANNABIS) IN SELECTED NEUROLOGIC DISORDERS

This is a summary of the American Academy of Neurology (AAN) systematic review regarding the use of medical marijuana (cannabis) for treating selected neurologic disorders.

Please refer to the full systematic review at *AAN.com/guidelines* for more information, including a definition of the classification of evidence.

Forms of Cannabis

A variety of formulations were used in the studies examined, with differing amounts of tetrahydrocannabinol (THC) and cannabidiol (CBD): Some were pills, one was a mucosal spray, and some were vaporized or smoked. See Table 1 in the published systematic review for specific formulations.

Do cannabinoids relieve spasticity in patients with multiple sclerosis (MS)?

Strong evidence	Oral cannabis extract (OCE) is established as effective for reducing patient-reported scores (**2 Class I studies**).
Moderate evidence	OCE is probably ineffective for reducing objective measures at 12 to 15 weeks (**1 Class I study**).
	THC is probably effective for reducing patient-reported scores (**1 Class I study**).
	THC is probably ineffective for reducing objective measures at 15 weeks (**1 Class I study**).
	Nabiximols is probably effective for reducing patient-reported symptoms at 6 weeks (**1 Class I study**) and probably ineffective for reducing objective measures at 6 weeks (**1 Class I study**).
Weak evidence	OCE is possibly effective for reducing objective measures at 1 year (**1 Class II study**).
	THC is possibly effective for reducing objective measures at 1 year (**1 Class II study**).
Insufficient evidence	Smoked marijuana is of uncertain efficacy (**insufficient evidence**).

Overall, 1,619 patients were treated with cannabinoids for less than 6 months. Meta-analysis of simple proportions yielded 6.9% (95% confidence interval [CI] 5.7%–8.2%) who stopped the medication because of adverse effects (AEs). Of the 1,118 who received placebo, 2.2% (95% CI 1.6%–3.5%) stopped because of AEs. Data on the symptoms that caused medication withdrawal were often incomplete.

Clinical Context

Standard medical therapy was continued in these studies, so no comment can be made as to comparative effectiveness.

Multiple methods of measuring spasticity exist. A recent study used correlations with changes on a standard Patient Global Impression of Change scale to determine that a ~ 30% change in spasticity, as measured by the patient-reported numeric rating score, best represented a clinically important difference. More improvements were seen in subjective measures than objective measures, possibly explained in part by the overall improvements in "feelings" or well-being provided by marijuana, or by pain relief allowing improved mobility.

What is the efficacy of using cannabinoids to treat central pain or painful spasms in MS?

Strong evidence	For patients with MS with central pain or painful spasms, OCE is effective for reduction of central pain (**2 Class I studies**).
Moderate evidence	THC or nabiximols (**1 Class I study each**) is probably effective for treating MS-related pain or painful spasms.
Insufficient evidence	Smoked marijuana is of unclear efficacy for reducing pain (**2 Class III studies that examined different issues**).

Do cannabinoids help treat bladder dysfunction in MS?

Moderate evidence	Nabiximols is probably effective for reducing the number of bladder voids per day at 10 weeks (**1 Class I study**).
	THC and OCE are probably ineffective for reducing bladder complaints (**1 Class I study**).
Insufficient evidence	Nabiximols is of unknown efficacy in reducing overall bladder symptoms (**contradictory Class I studies**).

Do cannabinoids help treat tremor in MS?

Moderate evidence	THC and OCE are probably ineffective for treating MS-related tremor (**1 Class I study**).
Weak evidence	Nabiximols is possibly ineffective (**1 Class II study**).

Do cannabinoids reduce symptoms in involuntary movement disorders?

Motor Symptoms in Huntington Disease

Insufficient evidence	Whereas the 2 studies identified suggest lack of benefit, both were underpowered to detect differences, and thus no reliable conclusions can be drawn (**1 Class I study, 1 Class III study**).

Levodopa-induced Dyskinesias in Parkinson Disease

Moderate evidence	OCE is probably ineffective for treating levodopa-induced dyskinesias in patients with Parkinson disease (**1 Class I study**).

Tic Severity in Tourette Syndrome

Insufficient evidence	For patients with Tourette syndrome, data are insufficient to support or refute efficacy of THC for reducing tic severity (**1 Class II study, 1 Class III study**).

Cervical dystonia

Insufficient evidence	For patients with cervical dystonia, data are insufficient to support or refute the efficacy of dronabinol (**1 Class III study**).

Do cannabinoids decrease seizure frequency in epilepsy?

Insufficient evidence	For patients with epilepsy, data are insufficient to support or refute the efficacy of cannabinoids for reducing seizure frequency (**no Class I–III studies**).

Clinical Context

Neither the present review, nor a Cochrane review which includes abstracts, non–peer-reviewed literature, and anecdotal reports of smoked cannabis use by patients with seizure disorders, concluded there is sufficient evidence to prescribe CBDs or recommend self-treatment with smoked marijuana.

Adverse Effects

Clinical Context

Adverse effects (AEs) are a significant concern with marijuana use. Outside the setting of treatment trials, cognitive impairment is more likely to be of concern. One study of patients with MS who smoked cannabis at least once a month showed an increase in cognitive impairment. Another article showed that patients with MS who used cannabis were twice as likely to be classified as globally cognitively impaired as those who did not use cannabis. Some patients who have neurologic conditions may have preexisting cognitive dysfunction, which may increase their susceptibility to cannabinoids' toxicities. Moreover, it is especially concerning that a medication that may have an AE of suicide may be prescribed in a population such as patients with MS who already are at increased suicide risk.

The table below shows the evidence at a glance.

Table: Evidence for Use of Cannabis to Treat Symptoms of Selected Neurologic Disorders

Evidence, by Disorder and Formulation	OCE Pill	THC Pill	Oral Spray	Smoked Cannabis
MS Symptoms				
Strong Evidence				
Established as effective for reducing patient-reported spasticity scores	X			
Effective for reduction of central pain in patients with MS with central pain or painful spasms	X			

Evidence, by Disorder and Formulation	OCE Pill	THC Pill	Oral Spray	Smoked Cannabis
MS Symptoms				
Moderate Evidence				
Probably effective for reducing patient-reported spasticity scores		X		
Probably effective for reducing patient-reported spasticity symptoms at 6 weeks			X	
Probably effective for treating MS-related pain or painful spasms		X	X	
Probably ineffective for reducing objective spasticity measures at 15 weeks		X		
Probably ineffective for reducing objective spasticity measures at 12–15 weeks	X			
Probably ineffective for reducing objective spasticity measures at 6 weeks			X	
Probably effective for reducing the number of bladder voids per day at 10 weeks			X	
Probably ineffective for reducing bladder complaints	X	X		
Probably ineffective for treating MS-related tremor	X	X		
Weak Evidence				
Possibly effective for reducing objective spasticity measures at 1 year	X	X		
Possibly ineffective for treating MS-related tremor			X	
Insufficient Evidence				
Efficacy uncertain for reducing spasticity and pain in MS				X
Efficacy unknown for reducing overall bladder symptoms			X	
PD Symptoms				
Moderate Evidence				
Probably ineffective for treating levodopa-induced dyskinesias in patients with Parkinson disease	X			
HD Symptoms				
Insufficient Evidence				
No reliable conclusions can be drawn with regard to motor symptoms in HD		X		
Tourette Syndrome				
Insufficient Evidence				
Data insufficient to support or refute efficacy for reducing tic severity		X		
Cervical Dystonia				
Insufficient Evidence				
Data insufficient to support or refute the efficacy of dronabinol		X		

OCE = oral cannabis extract (contains Δ-9-tetrahydrocannabinol and cannabidiols in varying ratio); THC = Δ-9-tetrahydrocannabinol, the main psychologically active ingredient in cannabis.

Note: Synthetic forms of OCE and THC were used in the studies. Data for seizure frequency in epilepsy not shown because no studies above Class IV available to assess.

This systematic review was endorsed by the American Autonomic Society, the American Epilepsy Society, the Consortium of Multiple Sclerosis Centers, the International Organization of Multiple Sclerosis Nurses, and the International Rett Syndrome Foundation.

American Academy of Neurology, 201 Chicago Avenue, Minneapolis, MN 55415
Copies of this summary and additional companion tools are available at *AAN.com* or through AAN Member Services at (800) 879-1960.