



TITLE: Delta-9-tetrahydrocannabinol/Cannabidiol for Spasticity in Multiple Sclerosis: Clinical Effectiveness and Guidelines

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RESEARCH QUESTIONS

1. What is the clinical effectiveness of delta-9-tetrahydrocannabinol/cannabidiol for the treatment of spasticity in patients with Multiple Sclerosis?
2. What are the evidence-based guidelines associated with delta-9-tetrahydrocannabinol/cannabidiol for the treatment of spasticity in patients with Multiple Sclerosis?

KEY FINDINGS

Three systematic reviews, five randomized controlled trials, and two evidence-based guidelines were identified regarding delta-9-tetrahydrocannabinol/cannabidiol for the treatment of spasticity in patients with Multiple Sclerosis.

METHODS

A limited literature search was conducted on key resources including PubMed, Embase, Medline, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied to limit retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2006 and April 25, 2016. Internet links were provided, where available.

The summary of findings was prepared from the abstracts of the relevant information. Please note that data contained in abstracts may not always be an accurate reflection of the data contained within the full article.

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SELECTION CRITERIA

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Population	Patients with Multiple Sclerosis (MS) suffering from spasticity
Intervention	Sativex (delta-9-tetrahydrocannabinol/cannabidiol) buccal spray
Comparator	Standard of care (e.g., baclofen, diazepam, tizanidine, and dantrolene, clonidine, gabapentin, botulinum toxin); Placebo
Outcomes	Clinical effectiveness (including safety); Guidelines
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, evidence-based guidelines

RESULTS

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials and evidence-based guidelines.

Three systematic reviews, five randomized controlled trials, and two evidence-based guidelines were identified regarding delta-9-tetrahydrocannabinol/cannabidiol for the treatment of spasticity in patients with Multiple Sclerosis. No relevant health technology assessments were identified.

Additional references of potential interest are provided in the appendix.

OVERALL SUMMARY OF FINDINGS

Three systematic reviews were identified.¹⁻³ In one systematic review, delta-9-tetrahydrocannabinol/cannabidiol was determined as probably effective for patient-centered measures of spasticity for patient with Multiple Sclerosis (MS).¹ The authors of another systematic review reported that a significantly greater number of patients whose spasticity was treated with delta-9-tetrahydrocannabinol/cannabidiol were responders to treatment and showed more improvement than those who received placebo.² The authors of a third systematic review reported that delta-9-tetrahydrocannabinol/cannabidiol was generally well tolerated.³ Adverse events were common but were mostly reported to be of mild to moderate severity.^{2,3}

Five relevant randomized controlled trials (RCTs) were identified.⁴⁻⁸ The authors of one study confirmed the clinical benefit of delta-9-tetrahydrocannabinol/cannabidiol for MS-spasticity.⁴ Another study reported that time to treatment failure was significantly greater in the treatment group when compared to controls.⁵ One study treated patients with delta-9-tetrahydrocannabinol/cannabidiol as an add-on treatment and those patients achieving more than 20% improvement in spasticity were then enrolled into a subsequent RCT.⁶ After four weeks of treatment, 47.6% of subjects achieved a greater than 20% improvement in symptoms.⁶ In a RCT examining patients with spasticity not controlled with current treatment,⁷ the per protocol analysis found the change in the numeric rating score of spasticity and the responder analyses were both significantly greater in the treatment group when compared to placebo. The

authors reported that the drug was generally well tolerated and the adverse events reported were mild to moderate.⁷ A primary analysis of the intention-to-treat population of another RCT⁸ found that spasticity control was significantly greater with delta-9-tetrahydrocannabinol/cannabidiol.

The American Academy of Neurology recommends that clinicians may offer delta-9-tetrahydrocannabinol/cannabidiol spray to reduce the symptoms of spasticity, though it may not be effective for improving objective spasticity measures.¹⁰ The National Institute of Health and Care Excellence recommends clinicians not offer delta-9-tetrahydrocannabinol/cannabidiol spray as it is not considered to be cost-effective for the indication.⁹

REFERENCES SUMMARIZED

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

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Guidelines and Recommendations

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APPENDIX – FURTHER INFORMATION:

Previous CADTH Reports

11. Sativex for the Management of Multiple Sclerosis Symptoms [Internet]. Ottawa: CADTH; 2005 Sep. [cited 2016 May 4]. (CADTH issues in emerging health technologies; no. 72) Available from: https://www.cadth.ca/sites/default/files/pdf/310_sativex_cetap_e.pdf

Clinical Practice Guidelines – Expert Consensus

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Listing Recommendations

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