Medicines Management Programme

Managed Access Protocol-

Delta-9-tetrahydrocannabinol/Cannabidiol (Sativex®) oromucosal spray for symptom improvement in adults, with moderate-to-severe spasticity due to multiple sclerosis.

Approved by:	Prof. Michael Barry, Clinical Lead, MMP.
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List of Abbreviations

CBD	Cannabidiol
HSE	Health Service Executive
HTH	High Tech Hub
MMP	Medicines Management Programme
MS	Multiple Sclerosis
NRS	Numeric Rating Scale
PCRS	Primary Care Reimbursement Service
SmPC	Summary of Product Characteristics
THC	Delta-9-tetrahydrocannabinol

1. Delta-9-tetrahydrocannabinol/Cannabidiol (Sativex®)

Delta-9-tetrahydrocannabinol (THC)/cannabidiol (CBD) [Sativex®] is an endocannabidoid system modulator. THC/CBD (Sativex®) is available on the High Tech Arrangement with a managed access approach.

THC/CBD (Sativex®) is an oromucosal spray in a 10 ml vial, with each single 100 microlitre spray containing 2.7 mg THC and 2.5 mg CBD from Cannabis sativa L. The 10 ml vial allows for delivery after priming of up to 90 measured sprays of 100 microlitres.

THC/CBD (Sativex®) oromucosal spray contains a substance that is listed in schedule 4, part 1 of the Misuse of Drugs Regulations 2017.

1.1 Licensed indication

THC/CBD (Sativex®) is indicated as treatment for symptom improvement in adult patients with moderate-to-severe spasticity due to multiple sclerosis (MS), who have not responded adequately to other anti-spasticity medication, and who demonstrate clinically significant improvement in spasticity-related symptoms during an initial trial of therapy (with Sativex®).

1.1.1 Trial period and dose escalation for THC/CBD (Sativex®)

THC/CBD (Sativex®) is intended to be used in addition to the patient's current anti-spasticity medication. A thorough evaluation of the severity of spasticity-related symptoms and of the response to standard anti-spasticity medication should be performed prior to initiation of treatment.

A titration period is required to reach optimum dose. The number and timings of sprays will vary between patients. Patients should gradually increase the dose from one spray in the evening on the first day, until they achieve optimum symptom relief, up to a maximum of 12 sprays per day. The median dose in clinical trials for patients with MS was eight sprays per day. The Summary of Product Characteristics (SmPC) should be consulted for further details.

Following the titration period, patients are advised to maintain the optimum dose achieved. Response to initial treatment should be reviewed after four weeks of treatment. If a clinically significant improvement in spasticity-related symptoms is not seen during this initial trial of therapy, then treatment should be discontinued. See section 3 for further information.

1.2 Reimbursement

Reimbursement of THC/CBD (Sativex®) on the High Tech Arrangement is supported only for the licensed indication as outlined in section 1.1; reimbursement is not supported for any other indications.

Prescribers are required to apply for reimbursement approval on an individual patient basis through the Health Service Executive (HSE) - Primary Care Reimbursement Service (PCRS) online application system.

If a patient is recommended for reimbursement, the High Tech prescription for THC/CBD (Sativex®) should be generated on the High Tech Hub (HTH). High Tech prescriptions which are not hub generated for THC/CBD (Sativex®) will not be eligible for reimbursement by the HSE-PCRS.

1.2.1 Reimbursement details

The reimbursement details for THC/CBD (Sativex®), available under the High Tech Arrangement from 1st October 2023, are outlined in table 1.

Table 1: Reimbursement details for THC/CBD (Sativex®)

Medicinal product (Pack size)	Reimbursement code	Reimbursement price
Sativex® Oromucosal Spray (3 x 10 ml vials)	89296	€385.56*

*As of 01/10/2023

A commercial-in-confidence arrangement is in place with the marketing authorisation holder to reduce the net acquisition cost of this medicine to the HSE.

If a patient is recommended for reimbursement, it will be supported in line with the licensed therapeutic dose. Therefore, given the maximum dose, it is anticipated that the maximum quantity required will be 17 packs annually with each pack containing 3 x 10 ml vials.

2. Reimbursement criteria – Initiation

This section outlines the criteria that must be satisfied in order for a patient to be recommended for reimbursement of THC/CBD (Sativex®) under the High Tech Arrangement.

2.1 Prescribers

The prescribing of THC/CBD (Sativex®) under the High Tech Arrangement will be confined to consultant neurologists registered with the Irish Medical Council, who have agreed to the terms of this Managed Access Protocol (MAP) and who have been approved by the HSE.

Applications for reimbursement approval will only be considered from these prescribers.

2.2 Patient clinical history

In line with the exclusion criteria for the GWSP0604 and SAVANT trials, and information contained within the SmPC, reimbursement of THC/CBD (Sativex®) will not be considered in the following circumstances:

- Patients with any known or suspected history or family history of schizophrenia, or other psychotic illness; history of severe personality disorder or other significant psychiatric disorder other than depression associated with their underlying condition.
- People who are breastfeeding (considerable levels of cannabinoids likely in maternal breast milk and the potential adverse developmental effects in infants).

2.3 Patient age

Applications for reimbursement approval will only be considered for adults aged 18 years and older at the time of application.

2.4 Confirmed diagnosis of moderate-to-severe spasticity due to multiple sclerosis

Clinicians will be required to confirm a diagnosis of MS at the time of application. When reviewing applications, the HSE-Medicines Management Programme (MMP) may request additional evidence to confirm a diagnosis of MS.

Clinicians will be required to confirm a diagnosis of moderate-to-severe spasticity due to MS at the time of application. Moderate-to-severe spasticity is defined as a score of ≥ 4 on a 0 to 10 point

numeric rating scale (NRS), on which patients indicate the average level of their spasticity-related symptoms over the last 24 hours, where 0 is no spasticity and 10 is the worst possible spasticity.

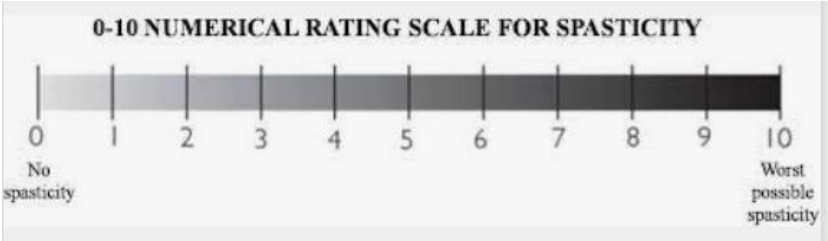

Figure 1: 0-10 Numeric Rating Scale for Spasticity

2.5 Pharmacological interventions

THC/CBD (Sativex®) is intended to be used in adult patients with moderate-to-severe spasticity due to MS, **as an add-on to current anti-spasticity medication, in patients who have not responded adequately to other anti-spasticity medication**.

2.5.1 Previous anti-spasticity medications

Reimbursement will be supported for patients who have had an inadequate response to at least two anti-spasticity medications at the maximum tolerated dose, at least one of which the patient must currently remain on treatment with.

For the purpose of reimbursement approval, an adequate trial of an anti-spasticity medication is defined as a period of at least three consecutive months.

Anti-spasticity medications such as:

- Antispasmodic drugs e.g. baclofen, tizanidine, dantrolene
- Benzodiazepines e.g. diazepam
- Anti-epileptic drugs e.g. gabapentin
- Botulinum Toxin Type A (Botox®)

Not all of these medications are licensed for the treatment of muscle spasticity. Please refer to individual SmPCs for further information.

When reviewing applications, the MMP may request additional evidence to demonstrate that the patient has had an inadequate response to the specified medication for a period of at least three months.

2.5.2 Anti-spasticity medication is not tolerated

In cases where a patient did not tolerate a medication and experienced a clinically significant adverse reaction, which led to discontinuation of treatment prior to completion of an adequate trial or following a period of treatment at the maximum tolerated dose, information in relation to the duration of treatment and the adverse reaction experienced should be provided in the application.

2.5.3 Anti-spasticity medication is contraindicated

For patients in whom treatment with an anti-spasticity medication is contraindicated, details of the contraindication, including supporting evidence, must be provided at the time of application for reimbursement approval.

3. Reimbursement criteria - Continuation

In line with the SmPC, the patient's response to THC/CBD (Sativex®) should be reviewed after four weeks of treatment. If a clinically significant improvement in spasticity related symptoms is not demonstrated during this initial trial of therapy, then treatment should be discontinued.

From clinical trials and for the purposes of continued reimbursement support, a clinically significant improvement is defined as at least a 20% improvement in spasticity-related symptoms on a 0-10 point NRS. The NRS score should be recorded at baseline (prior to treatment initiation) where the patient indicates the average level of their spasticity related symptoms over the previous 24 hours. The NRS score should be re-assessed after four weeks of treatment with THC/CBD (Sativex®), with the patient indicating the average level of their spasticity-related symptoms over the previous 24 hours.

Patients not demonstrating at least a 20% improvement in spasticity-related symptoms (on NRS) after four weeks of treatment, would be considered to have not demonstrated a clinically significant improvement, and treatment should be discontinued.

Therefore, following approval of a patient for reimbursement of THC/CBD (Sativex®) under the High-Tech Arrangement, the prescribing clinician is required to submit, upon request by the MMP, the following outcome data:

- Information on spasticity-related symptoms on a 0-10 point NRS, on which the patient indicated the average level of their spasticity-related symptoms over the previous 24 hours, after four weeks of treatment with THC/CBD (Sativex®).

Follow-up data may be requested by the HSE/MMP for audit purposes and provision of same is a condition of ongoing reimbursement.

4. Prescribing of Sativex®

Prescriptions must be generated through the HTH (details outlined separately) and only approved prescriber(s) will have access to prescribe THC/CBD (Sativex®).

The following confirmations are required when prescribing THC/CBD (Sativex®) on the HTH:

- Confirmation that THC/CBD (Sativex®) is being prescribed for a MMP approved patient in accordance with the MAP established in line with the terms of reimbursement approval given by the HSE
- Confirmation that the prescriber will assist the HSE/MMP in their conduct of audits* through provision of information as requested, to provide assurance that the product is being prescribed in line with HSE reimbursement approval and the MAP
- Confirmation that the patient is aware that the application for reimbursement approval is being made on their behalf and that audits may occur during which their personal data will be reviewed.

*Follow-up data may be requested by the HSE/MMP for audit purposes and provision of same is a condition of ongoing reimbursement.

Prescribers should refer to the SmPC for THC/CBD (Sativex®) for full prescribing information including monitoring and patient counselling requirements.