North Central London
Joint Formulary Committee

Shared Care Guideline
Sativex
Treatment of Multiple Sclerosis related Spasticity

Dear Primary or Secondary care clinician,

The information in the shared care guideline has been developed in consultation with Primary and Secondary Care and it has been agreed that it is suitable for shared care.

Sharing of care assumes communication between the specialist, non-specialist (primary or secondary care clinician) and patient. The intention to share care should be explained to the patient by the Consultant when treatment is initiated. It is important that patients are consulted about treatment and are in agreement with it.

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1. Introduction Target audience

This document should provide sufficient information to enable you to make an informed decision regarding the clinical and legal responsibility for prescribing this drug.

Sativex (Approved name: delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), Each 100 microlitre spray contains: 2.7 mg delta-9-tetrahydrocannabinol (THC) and 2.5 mg cannabidiol (CBD) from *Cannabis sativa L.*) is used for moderate to severe spasticity in people with Multiple Sclerosis 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. Prescribing within NCL is in line with NICE guidance (see NICE NG144 on cannabis-based medicinal products) in that it is initiated and supervised by a physician with specialist expertise in treating spasticity due to multiple sclerosis; in NCL, the tertiary service is currently provided at The National Hospital for Neurology and Neurosurgery (NHNN).

Progressing to a stable, optimal dose usually takes approximately 2-3 months. Once achieved, a shared care arrangement with you will be requested. It will clarify responsibilities between the Spasticity specialist and non-specialist clinician(GP or secondary care clinician) for managing the prescribing of Sativex such as:

- Who will prescribe;
- Who will monitor;
- Who will communicate any necessary changes in dose to the patient and the non-specialist clinician.

2. Shared Care criteria

Patients with multiple sclerosis who are stabilised on Sativex and have been monitored appropriately at baseline and after initiation of treatment with no problems identified during this period. Patient should demonstrate a 20% improvement in spasticity-related symptoms after a 4 week trial. Sativex is intended to be used in addition to the patient's current anti-spasticity medication.

3. Shared care responsibilities

3.1. Spasticity Consultant and /or Spasticity management Specialist Nurse

Send a letter to the non-specialist clinician along with shared care criteria and transfer form requesting shared care for this patient. Indication, dose and frequency to be decided by the NHNN tertiary centre spasticity team.

1) Before initiating treatment, perform baseline test to measure spasticity including Ashworth Scale and a Numerical Rating Scale (NRS) for spasticity and spasms. Ensure compatibility with other medications.
2) Discuss the benefits and side effects of treatment with the patient. Provide the patient with a Patient Information Leaflet, explain it and ensure that the patient understands the reason for the treatment, dosing regimen, potential side effects, and advise on driving.
3) If the patient is of childbearing potential, to advise on reliable contraceptive precautions for duration of therapy (and for three months after discontinuation); inform the patient to contact the spasticity specialist team if planning pregnancy.

4) Initiate treatment and prescribe until the primary or secondary care clinician formally agrees to share care (until patient is stabilised). Patients will be seen in clinic prior to consideration of shared care as outlined;

- Time =0 months; Face to face visit at NHNN and initiation of Sativex- 1 month supply given, patients also given a diary to record their NRS for Sativex.
- Time= 2 weeks; Telephone consultation from NHNN (tertiary care) to assess response and tolerability
- Time= 1 month; Face to face visit at NHNN; responders defined by a 20% reduction in their NRS will be given a 3 months' supply
- Time = 3 months; Telephone consultation from NHNN to agree dose and treatment plan for primary care

5) Discuss the shared care arrangement with the patient.
6) Ensure the patient understands that he/she must report the warning symptoms as listed under "adverse effects"
7) Provide results of baseline assessments and recommend the dose (in sprays per day) and frequency of any monitoring to non-specialist clinician.
8) Send a letter to the non-specialist clinician after each clinic attendance ensuring current dose and how long each spray vial is expected to last is detailed.
9) Inform non-specialist clinician when to adjust the dose, stop treatment, or consult with the Spasticity management Team.
10) Periodically review the patient's condition and communicate promptly with the non-specialist clinician when treatment is changed. Counsel the patient on any dose changes that are made during clinic appointments; this will be via face-to-face or video consultation from NHNN to review dose and treatment plan for primary care (6 monthly initially but minimum of annually if stable)
11) Evaluate adverse effects reported by non-specialist clinician or patient
12) Report adverse events to the MHRA (via yellow card scheme) and non-specialist clinician
13) Inform non-specialist clinician of patients who do not attend clinic appointments
14) Ensure that clear backup arrangements exist for the primary or secondary care clinician to obtain advice and support; helpline available 020 34483439 including on call cover (as per Section 13: Contact Details).

3.2. Non-specialist primary or secondary care clinician

Complete transfer form and send back to h*ospital* confirming acceptance/ rejection of shared care for patient. If the non-specialist clinician is unable to agree to shared care, inform the Hospital team stating reasons within ***28 days*** of receipt of request (all requests will be marked URGENT). If no response is received with 28 days, the non-specialist clinician will be contacted directly to ask for a response. If no response is received by week 6, the specialist or formulary pharmacist will liaise with the patients' local medicines management team, who should be encouraged to gain a response within a 7-day turnaround time.

1) Non-specialist clinician to prescribe the drug treatment as described (but not to alter the dose unless advised to do so by the Spasticity specialist). The term "as directed" **SHOULD NOT** be used
2) Prescribe Sativex using the dose as specified by the specialist to the prescription instructions.
3) Ensure compatibility with any new concomitant medication
4) Amend the prescribed dose on the medication record as advised by the Spasticity specialist (Specialist will counsel the patient on any dose changes).

5) If the patient reports any adverse events and/or non-compliance, report this to the Spasticity specialist, where appropriate
6) Stop treatment on advice of Spasticity specialist or immediately if urgent need arises
7) Help in monitoring any changes in the patient's level of function or symptoms of stiffness and spasms and inform the hospital team of any changes to spasticity medication
8) Report adverse events to the Spasticity specialist and MHRA
9) All requests for repeat prescriptions should be reviewed individually prior to issuing

3.3. Patient responsibility

1) Attend all hospital (and, where applicable, GP) appointments, otherwise medication supply may be delayed
2) Take medicines as agreed
3) Report to the Spasticity specialist or if he/she does not have a clear understanding of the treatment
4) Inform Spasticity specialist or primary/secondary care prescriber of any other medication being taken or changes in medication, including over-the-counter products
5) Report any adverse effects or warning symptoms to primary/secondary care clinician or Spasticity specialist
6) Inform hospital and primary/secondary care clinician of any changes in address or telephone numbers

3.4. Clinical Commissioning Group

1) To provide feedback to Trusts from the standard letter, via the shared care forum.
2) To support primary care clinicians to make the decision whether or not to accept clinical responsibility for prescribing.
3) To support Trusts in the resolving issues that may arise as a result of shared care.

4. Indications

Sativex is for the treatment of adults with Multiple Sclerosis (MS) related moderate-severe spasticity refractory to other agents (e.g. baclofen, tizanidine, gabapentin). It is licensed and within NICE guidance for consideration as a treatment option (see NICE NG144 on cannabis-based medicinal products and NICE CG186 on the management of multiple sclerosis in adults).

5. Dose and Administration

Sativex is formulated as an oromucosal spray with each 100 microlitre spray containing 2.7 mg delta-9-tetrahydrocannabinol (THC) and 2.5 mg cannabidiol (CBD).

The patient self-administers Sativex by spraying it into their mouth- cheek or under the tongue. Dosage is between 1-12 sprays per day spread out according to the patient's needs. Many patients take more in the evening to help with sleep.

Each spray vial of Sativex contains 90 actuations.

6. Adverse effects

Possible adverse effects and what to do if they occur:

- Dizziness

- Psychiatric disorders
- Somnolence
- Light headedness
- Oral irritation
- Weakness or falls
- Rarely low mood can be reported

See Summary of Product Characteristics for a full list of adverse effects.

If side effects occur the dose should be lowered by 1-2 sprays/day, in the case of oral irritation the patient should be advised to vary the site of the spray around the mouth and avoid any ulcers or irritated areas. If the primary or secondary care clinician has any concern regarding dose changes, they may wish to contact the Spasticity Team for advice (See Section 13)

Serious suspected reactions (even if well recognised or causal link uncertain) should be reported to the CHM.

7. Cautions

- Moderate to severe hepatic impairment
- Moderate to severe renal impairment
- Severe depression
- Women who are breast feeding
- Sativex may reduce effectiveness of systemically acting hormonal contraceptives, therefore women using systemically acting hormonal contraception for example the oral contraceptive pill or contraceptive implant should use an additional method of contraception for the duration of therapy and for three months after discontinuation.
- Sativex is a controlled drug and its legal status varies between countries. Information on travelling abroad with Sativex is available at www.gov.uk/travelling-controlled-drugs
- Sativex should not be used in pregnancy unless benefit of treatment outweighs risk to the foetus
- Until further information is available, caution should be taken when treating patients with a history of epilepsy or recurrent seizures.

For a full list of cautions, refer to the Summary of Product Characteristics.

8. Clinical Monitoring

No blood monitoring is required. During routine review, consider reviewing the patient for potential adverse effects (see Section 6), the patient's impression of efficacy and their mood. Adverse effects or change in mood that cannot be managed in Primary care or a loss of efficacy should be reported to the Spasticity Specialist.

The Spasticity specialist may conduct additional investigations as required e.g. physical assessment and recording of the Ashworth Scale. The results will be sent to the primary/secondary care clinician.

Sativex may produce undesirable effects such as dizziness and somnolence which may impair judgement and performance of skilled tasks. Patients should not drive, operate machinery or engage in any hazardous activity if they are experiencing any significant CNS effects such as dizziness or somnolence. Patients are informed of this on initiation. For more information, please see the summary of product characteristics.

9. Contraindications

- With hypersensitivity to cannabinoids or to any of the excipients.

- 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.
- Who are breast feeding

For a full list of contraindications, refer to the Summary of Product Characteristics.

10. Drug Interactions

There is a theoretical risk that there may be an additive effect with other muscle-relaxing agents such as baclofen and benzodiazepines, thereby increasing the risk of somnolence, weakness and falls.

Sativex is metabolised by the Cytochrome P-450 enzyme system, therefore enzyme inducers or inhibitors may decrease or increase the concentration of Sativex in the circulation. Seek specialist advice if necessary.

Sativex may reduce effectiveness of systemically acting hormonal contraceptives, therefore women using systemically acting hormonal contraception for example the oral contraceptive pill or contraceptive implant should use an additional method of contraception for the duration of therapy and for three months after discontinuation.

Care should be taken with hypnotics, sedatives alcohol due to the additive side effects.

For a full list of drug interactions, refer to the Summary of Product Characteristics.

11. References

Drugs and Driving: The Law. https://www.gov.uk/drug-driving-law Accessed 28/08/2020

NICE guidance: Cannabis-based medicinal products. https://www.nice.org.uk/guidance/NG144 Accessed 28/08/2020

NICE guidance: Multiple sclerosis in adults: Management. https://www.nice.org.uk/guidance/cg186/ Accessed 28/08/2020

Sativex Oromucosal Spray, GW Pharma Ltd.. Last updated 27/05/20, hyperlink https://www.medicines.org.uk/emc/product/602/smpc Accessed 28/08/20

12. Associated documents

Patient information on Sativex – Patient information Leaflet - https://www.medicines.org.uk/emc/files/pil.602.pdf

Driving Advice for Sativex Users - https://www.mstrust.org.uk/sites/default/files/DfT-New%20Drug%20Driving%20Rules-Sativex-A5.pdf

Drugs and Driving: The Law - https://www.gov.uk/drug-driving-law

13. Contact Details

The National Hospital for Neurology and Neurosurgery: Multiple Sclerosis related spasticity service

Consultant: Val Stevenson	020 3448 3439 Val.stevenson1@nhs.net
Specialist or Dept sister: Liz Keenan	020 3448 3439
Specialist Pharmacist: Aoife Shields	Mobile: 07779 558994

	Email: aoifeshields@nhs.net
Further information and support: Spasticity helpline General email for referrals and queries	 020 3448 3439 uclh.referrals.admin.spasticity@nhs.net

Document control

Date	Version	Amendments
14/12/2020	V1.0	New document
22/12/2020	V1.1	Minor amends made in formatting and wording in Section 1 and contact details
10/08/2021	V1.2	Protocol wording amended to make applicable for shared care with both primary or secondary care clinicians; section 3.2 updated

Document management

Groups / Individuals who have overseen the development of this guidance:	Dr Val Stevenson – Consultant, NHNN Aoife Shields – Specialist Pharmacist, NHNN NCL CCG – Barnet JFC Support Pharmacists
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Appendix 1: xxx transfer form: from [Trust] to Primary/Secondary care organisation

Section A: to be completed by secondary care *Send to organisation*

This document is to request the shared care pathway of your patient and comprises an agreement between the primary or secondary care clinician and named consultant. The patient will continue to be seen by the named consultant as regular follow up.

Fix address label here (ensure NHS no.on)	Organisation details

Department			
Clinic phone			
Consultant		Email	
Indication for prescription			
Drug prescribed			
Date	Drug started	Current dose	
Relevant conditions			
Monitoring variations			
Date next blood test		Next disease review due in	months' time.

Section B: [Accept Shared Care] to be completed by practice *Send back **FAO referring consultant** above*

The above patient has been accepted into our monitoring service.

Practice date for next blood test		Practice stamp
Signed / Designation		
Date		

Section B: [Reject Shared Care] to be completed by practice *Send back **FAO referring consultant** above*

The above patient has not been accepted into our monitoring service.

Reason		Practice stamp
Signed / Designation		
Date		