NHS
North East and North Cumbria

Shared Care Protocol

Sativex (delta-9-tetrahydrocannabinol / cannabidiol) Oromucosal Spray for the treatment of spasticity in multiple sclerosis

Note: Shared care drugs are classed as AMBER on the NENC ICB Formulary – these are drugs initiated by hospital specialist, but where continuing treatment by GPs may be appropriate under a shared care arrangement.

Specialist responsibilities

- Assess the patient and provide diagnosis; ensure that this diagnosis is within scope of this shared care protocol (section 2) and communicated to primary care.
- Use a shared decision making approach; discuss the benefits and risks of the treatment with the patient and/or their carer and provide the appropriate counselling (see section 11) to enable the patient to reach an informed decision. Obtain and document patient consent. Provide an appropriate patient information leaflet.
- Assess for contraindications and cautions (see section 4) and interactions (see section 7).
- Conduct required baseline investigations and initial monitoring (see section 8).
- Initiate and optimise treatment as outlined in section 5. Prescribe the maintenance treatment for at least 4 weeks and until optimised.
- Once treatment is optimised, complete the shared care documentation and send to patient's GP practice detailing the diagnosis, current and ongoing dose, any relevant test results and when the next monitoring is required. Include contact information (section 13).
- Prescribe sufficient medication to enable transfer to primary care, including where there are unforeseen delays to transfer of care.
- Conduct the required reviews and monitoring in section 8 and communicate the results to primary care. After each review, advise primary care whether treatment should be continued, confirm the ongoing dose, and whether the ongoing monitoring outlined in section 9 remains appropriate.
- Reassume prescribing responsibilities if a patient becomes or wishes to become pregnant.
- Provide advice to primary care on the management of adverse effects if required.

Primary care responsibilities

- Respond to the request from the specialist for shared care in writing. It is asked that this be undertaken within 14 days of the request being made, where possible.
- If accepted, prescribe ongoing treatment (monthly prescriptions) as detailed in the specialists request and as per section 5, taking into any account potential drug interactions in section 7.
- Adjust the dose prescribed as advised by the specialist.
- Manage adverse effects as detailed in section 10 and discuss with specialist team when required.
- Refer the management back to the specialist if the patient becomes or plans to become pregnant.
- Stop treatment as advised by the specialist.

Patient and/or carer responsibilities

- Attend regularly for monitoring and review appointments with primary care and specialist, and keep contact details up to date with both prescribers. Be aware that medicines may be stopped if they do not attend.
- Report adverse effects to their primary care prescriber. Seek immediate medical attention if they develop any symptoms as detailed in section 11.
- Report the use of any over the counter medications to their primary care prescriber and be aware they should discuss with their pharmacist before purchasing any OTC medicines.
- Patients of childbearing potential should take a pregnancy test if they think they could be pregnant, and inform the specialist or GP immediately if they become pregnant or wish to become pregnant.

1. Background	Recommended for use (as per NICE NG220: Multiple sclerosis in adults: management) when other agents have been tried and were ineffective / not tolerated or were not considered appropriate. And as recommended as per NICE NG144: Cannabis-based medicinal products
2. Indication(s) covered by this SCP **(Please state whether licensed or unlicensed)**	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. Sativex is intended to be used in addition to the patient's current anti-spasticity medication.
3. Locally agreed off-label use	NA
4. Contraindications and cautions Please note this does not replace the Summary of Product Characteristics (SPC) and should be read in conjunction with it.	**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

<table>
<tr><td></td><td colspan="2">underlying condition.
• Who are breast feeding.

Cautions:
Sativex is not recommended for use in children or adolescents below 18 years of age due to lack of safety and efficacy data.

Sativex is not recommended in patients with serious cardiovascular disease.

Caution should be taken when treating patients with a history of epilepsy, or recurrent seizures.

This class of medicine is in the list of drugs included in regulations under 5a of the Road Traffic Act 1988. When prescribing this medicine, patients should be told:

• The medicine is likely to affect your ability to drive
• Do not drive until you know how the medicine affects you
• It is an offence to drive while under the influence of this medicine

However, you would not be committing an offence (called 'statutory defence') if:

• The medicine has been prescribed to treat a medical problem and
• You have taken it according to the instructions given by the prescriber and in the information provided with the medicine and
• It was not affecting your ability to drive safely

Please see SPC for comprehensive information.</td></tr>
<tr><td>5. Initiation and ongoing dose regime

Note -
•Transfer of monitoring and prescribing to primary care is normally after the patient’s dose has been optimised and with satisfactory investigation results for at least 4 weeks
•The duration of treatment & frequency of review will be determined by the specialist, based on clinical response and tolerability.
•All dose or formulation adjustments will be the responsibility of the initiating specialist unless directions have been discussed and agreed with the primary care clinician
•Termination of treatment will be the responsibility of the specialist.</td><td colspan="2"><u>Initial stabilisation:</u> The MS team will initiate treatment providing a four week course (3 x 10ml) using the pay-for-responders scheme.

<u>Maintenance dose (following initial stabilisation):</u> The initial maintenance dose must be prescribed by the initiating specialist.

<u>Conditions requiring dose adjustment:</u> The number of sprays should be increased gradually up to a maximum of 12 sprays per day (according to instructions provided in patient information leaflet), until they achieve optimum symptom relief. There should be at least a 15 minute gap between sprays.</td></tr>
<tr><td rowspan="2">6. Pharmaceutical aspects</td><td>Route of administration:</td><td>Sativex is for oromucosal use only.</td></tr>
<tr><td>Formulation:</td><td>Oromucosal spray, solution
Each single 100 microlitre spray contains:
2.7 mg delta-9-tetrahydrocannabinol (THC) and 2.5 mg cannabidiol (CBD) from Cannabis sativa L.</td></tr>
</table>

	Administration details:	The spray must be shaken before use and must be directed at different sites on the oromucosal surface, changing the application site each time the product is used. To minimise variability of bioavailability in the individual patient, administration of Sativex should be standardised as far as possible in relation to food intake. In addition, starting or stopping some concomitant medicinal products may require a new dose titration.
	Other important information:	NA

7. Significant medicine interactions
 	
For a comprehensive list consult the BNF or Summary of Product Characteristics.
SPC
	The following list is not exhaustive; please see SPC for comprehensive information and recommended management.
	
	• Sativex reversibly inhibits CYP3A4, 1A2, 2B6, 2C9 and 2C19 at high concentrations, and may inhibit CYP3A4 at clinically relevant concentrations.
	  ○ Review dosing regimen of CYP3A4 substrates if given with Sativex as the plasma concentration of concomitant drug may increase.
	• Sativex may induce CYP1A2, 2B6 and CYP3A4 and thus may reduce activity of other drugs metabolised by cytochrome P-450:
	  ○ e.g. coumarins, statins, beta-blockers and corticosteroids. Review dosing regimen of sensitive CYP substrates if co-administered with Sativex.
	• Sativex inhibits the UGT enzymes UGT1A9 and UGT2B7 at therapeutic doses.
	  ○ Caution when prescribing Sativex with drugs solely metabolised by any of these UGTs (e.g. propofol and certain antivirals).
	• Use Sativex with caution in patients with genetic glucuronidation disorders (e.g. Gilbert's disease) as they may exhibit increased serum concentrations of bilirubin.
	• Sativex is metabolised by cytochrome P-450 enzyme system.
	  ○ If concomitant treatment with CYP3A4 inhibitors (e.g. itraconazole, ritonavir, clarithromycin) is started or stopped during Sativex treatment, consider new dose titration.
	  ○ Fluconazole may inhibit metabolism of Sativex; care should be taken when co-administering Sativex with potent CYP2C9 inhibitors as may increase in exposure to THC, CBD and their metabolites.
	  ○ Avoid concomitant use of strong cytochrome P-450 enzyme inducers (e.g. rifampicin, carbamazepine, phenytoin, phenobarbital, St John's Wort) with Sativex; if use is unavoidable, careful titration is recommended, especially in two weeks following discontinuation of the inducer.
	• Concomitant use of hypnotics and drugs with sedating effects: additive effect may increase risk of falls. Sativex may interact with alcohol, affecting co-ordination, concentration and ability to respond quickly. Avoid alcohol consumption whilst taking Sativex, especially at the beginning of treatment or when changing dose; additive CNS effects may impair ability to drive or use machines and increase fall risk.
	• Sativex may reduce effectiveness of systemic hormonal contraceptives: use additional barrier methods.	

8. Baseline investigations, initial monitoring and	**Baseline investigations:** The patient will come to clinic and will be asked to complete a 0 to 10 patient-reported numeric rating scale.	

<table>
<tr><td>ongoing monitoring to be undertaken by specialist</td><td colspan="2">Initial monitoring: After the 4 week trial of Sativex the MS team will review the patient (remotely or face to face) and treatment can be continued if the person has had at least a 20% reduction in spasticity-related symptoms on a 0 to 10 patient-reported numeric rating scale. Note: For remote appointments the patient will be asked to send a picture of the 0 to 10 patient-reported numeric rating scale to the MS team. The patient will be asked to send several VAS scales so the team can get an average of how effective the Sativex is.

Advise patient that it might take up to 2 weeks to find the optimal dose and that undesirable effects can occur during this time, most commonly dizziness. These undesirable effects are usually mild and resolve in a few days. Specialist should consider maintaining the current dose, reducing the dose or interrupting, at least temporarily, the treatment depending on seriousness and intensity.

If the patient responded to treatment the patient will be provided with a further month of treatment from the Trust whilst prescribing is transferred to the patient's GP.

Ongoing monitoring: an annual review will performed by the MS team to confirm that the patient is continuing to respond to treatment. The MS team will inform the GP if the Sativex is to be continued or not.</td></tr>
<tr><td rowspan="2">9. Ongoing monitoring requirements to be undertaken by primary care

See section 10 for further guidance on management of adverse effects/ responding to monitoring results.</td><td>Monitoring</td><td>Frequency</td></tr>
<tr><td>None required</td><td>NA</td></tr>
<tr><td rowspan="3">10. Adverse effects and management

Any serious adverse reactions should be reported to the MHRA via the Yellow Card scheme www.mhra.gov.uk/yellowcard</td><td>Result</td><td>Action for primary care</td></tr>
<tr><td>Significant psychiatric side effects (e.g. psychosis, suicidal thoughts).</td><td>To stop medication and contact MS team immediately, as well as psychiatry, if required.</td></tr>
<tr><td>Significant side effects or concerns about efficacy.</td><td>Refer back to specialist team.</td></tr>
<tr><td>11. Advice to patients and carers
The specialist will counsel the patient with regard to the benefits and risks of treatment and will provide the patient with any relevant information and advice, including patient information leaflets on individual medicines.</td><td colspan="2">The patient should be advised to report any of the following signs or symptoms to their primary care prescriber without delay:
• Psychosis, suicidal thoughts

Patient information on this medicine can be found at the following links:
Sativex Oromucosal Spray - Patient Information Leaflet (PIL) - (emc) (medicines.org.uk)</td></tr>
<tr><td>12. Pregnancy, paternal exposure and breast feeding
It is the responsibility of the specialist to provide advice on the need for contraception to male and female patients on initiation and at each review but the ongoing responsibility for providing this advice rests with both the primary care prescriber and the specialist.</td><td colspan="2"><u>Pregnancy</u>:
Women of childbearing potential must use highly effective contraception whilst taking Sativex. The effects on hormonal contraception are unknown, therefore women should use an additional method of contraception both during and for 3 months after discontinuation.

<u>Breastfeeding</u>:
Sativex is contraindicated during breast-feeding</td></tr>
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13. Specialist contact information	**Newcastle Upon Tyne Hospitals NHS FT** Name: MS specialist nurses Daytime telephone number: 0191 2825403 Out of hours contact details: Neurology on-call Dr via switch board 0191 23361661 **South Tyneside & Sunderland FT** Victoria Jones – MS co-ordinator: 0191 5656256 Ext 5656256 MS Specialist Nurse – Carmel Wilkinson: Working hours: Monday to Thursday 08.30-5pm Contact details Bleep : 52076 Secretary :Victoria Jones Telephone :0191 5656256 Ext:: 47152 Consultant Kate Petheram: Working hours Monday to Wednesday. Secretary Sue Berry 0191 5656256 Ext: 42778 Consultant Gemma Maxwell: Working hours Monday to Thursday. Secretary Cindy Morrow 0191 5656256 Ext: 42552 **CNTW** Consultant Elizabeth Davis: Working hours Monday to Friday. Secretary Deborah Turnbull 0191 2875121 Consultant Alison Burbidge: Working hours Mon, Weds, Thurs, Friday. Secretary Carol Kelly 0191 2875116 Consultant Duncan Mitchell. Secretary Carol Kelly 0191 2875116. Advanced Physiotherapy Practitioner / Non medical prescriber Dave Purdy: Working hours Monday to Friday. Secretary 0191 2875080 Rehabilitation Nurse Lucy Gibbison: Working hours Monday to Thursday. Secretary 0191 2875080 **South Tees Hosptials NHS FT** Samantha Hewson – MS Coordinator working hours Tuesday to Friday 01642 282761 Consultant – James Chapman working hours Mon, Tues, Thurs, Friday james.chapman1@nhs.net
14. Additional information	Where patient care is transferred from one specialist service or GP practice to another, a new shared care agreement must be completed.
15. References	• Overview | Multiple sclerosis in adults: management | Guidance | NICE • Overview | Cannabis-based medicinal products | Guidance | NICE
16. To be read in conjunction with the following documents	• RMOC Shared Care Guidance • NHSE/NHSCC guidance – items which should not be routinely prescribed in primary care: guidance for CCGs • NHSE policy- Responsibility for prescribing between Primary & Secondary/Tertiary Care
17. Local arrangements for seeking specialist advice	**The following circumstances/ changes in the patient's condition require discussion with the specialist team:** • If pregnancy occurs or if the patient is planning to become pregnant or breastfeed. • If non-compliance is suspected or the patient fails to attend monitoring appointments and the primary care prescriber considers it no longer safe to continue prescribing. (All appropriate steps must first be taken by primary care to reinforce the importance of attendance to the patient)

	• The patient's clinical condition deteriorates such that the primary care prescriber feels a dose change is required/ the patient no longer appears to be benefiting from therapy
18. Version Control	Version: 1 Date of Issue / Review: 20/06/2023 Date for next Review: 20/06/2025 Approved by: NENC Medicines Subcommittee

Appendix 1: Shared Care Request letter (Specialist to Primary Care Prescriber)

Dear *[insert Primary Care Prescriber's name]*

Patient name: *[insert patient's name]*
Date of birth: *[insert date of birth]*
NHS Number*: [insert NHS Number]*
Diagnosis: *[insert diagnosis]*

As per the agreed *[insert APC name]*shared care protocol for *[insert medicine name]* for the treatment of *[insert indication],* this patient is now suitable for prescribing to move to primary care.

The patient fulfils criteria for shared care and I am therefore requesting your agreement to participate in shared care. Where baseline investigations are set out in the shared care protocol, I have carried these out.

I can confirm that the following has happened regarding this treatment:

	Specialist to complete
The patient has been initiated on this therapy and has been on an optimised dose for the following period of time:	
Baseline investigation and monitoring as set out in the shared care documents have been completed and were satisfactory	Yes / No
The condition being treated has a predictable course of progression and the patient can be suitably maintained by primary care	Yes / No
The risks and benefits of treatment have been explained to the patient	Yes / No
The roles of the specialist/specialist team/ Primary Care Prescriber / Patient and pharmacist have been explained and agreed	Yes / No
The patient has agreed to this shared care arrangement, understands the need for ongoing monitoring, and has agreed to attend all necessary appointments	Yes / No
I have enclosed a copy of the shared care protocol which covers this treatment/the SCP can be found here (insert electronic/ web link)	Yes / No
I have included with the letter copies of the information the patient has received	Yes / No
I have provided the patient with sufficient medication to last until	
I have arranged a follow up with this patient in the following timescale	

Treatment was started on *[insert date started]* and the current dose is *[insert dose and frequency]*.

If you are in agreement, please undertake monitoring and treatment from *[insert date]* NB: date must be at least 1 month from initiation of treatment.

The next blood monitoring is due on *[insert date]* and should be continued in line with the shared care guideline.

Please could you reply to this request for shared care and initiation of the suggested medication to either accept or decline within 14 days.

Name: *[insert name]*
Role and specialty: *[insert role and specialty]*
Daytime telephone number: *[insert daytime telephone number]*
Email address: *[insert email address]*
Alternative contact: *[insert contact information, e.g. for clinic or specialist nurse]*
Out of hours contact details: *[insert contact information, e.g. for duty doctor]*

Appendix 2: Shared Care Agreement Letter (Primary Care Prescriber to Specialist)

Primary Care Prescriber Response

Dear *[insert Doctor's name]*

Patient *[insert Patient's name]*

NHS Number *[insert NHS Number]*

Identifier *[insert patient's date of birth and/oraddress]*

Thank you for your request for me to accept prescribing responsibility for this patient under a shared care agreement and to provide the following treatment

Medicine	Route	Dose & frequency

I can confirm that

☐ I am willing to take on this responsibility from *[insert date]* and will complete the monitoring as set out in the shared care protocol for this medicine/condition.

☐ I am NOT willing to take on this responsibility due to the following reason/s (please specify):

……
……
……
……
……

I would be willing to consider prescribing for this patient once the above criteria have been met for this treatment. If these/this is met by you please resubmit your request to share care.

Primary Care Prescriber signature: _____ Date: _____

Primary Care Prescriber address/practice stamp: