BSW Sativex® spray (delta-9-tetrahydrocannabinol (THC): cannabidiol (CBD)) for treatment for symptom improvement in adult patients with moderate to severe spasticity due to multiple sclerosis (MS):
Not routinely commissioned, application via exceptional funding route only.

Policy Statement

BSW clinical advisory group have determined that after discussion with local neurology specialists, we will not commission the use of sativex for patients with moderate to severe spasticity associated with MS (see NICE NG144[1] for details).

The Quality, and Performance Assurance Committee (QPAC) were disappointed that no studies found any significant differences in health-related quality of life (HRQoL) for MS patients using Sativex spray. QPAC also had concerns as to whether this represented a good use of local resources versus the health needs and competing priorities of our population.

What does NICE say?

NICE NG144[1] guidance says that sativex is an option that could be offered AFTER the following has been tried & failed (or contra-indicated) for pts with moderate to severe spasticity (from the NICE CG186[2] clinical guideline for MS):

1.5.19 Consider baclofen or gabapentin as a first-line drug to treat spasticity in MS depending on contraindications and the person's comorbidities and preferences. If the person with MS cannot tolerate one of these drugs consider switching to the other.

1.5.20 Consider a combination of baclofen and gabapentin for people with MS if:

- *individual drugs do not provide adequate relief or*
- *side effects from individual drugs prevent the dose being increased.*

1.5.21 Consider tizanidine or dantrolene as a second-line option to treat spasticity in people with MS.

1.5.22 Consider benzodiazepines as a third-line option to treat spasticity in MS and be aware of their potential benefit in treating nocturnal spasms.

Prescribing information[3] and monitoring: (NON-formulary on BSW formulary)

Indication: 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**.**

Pharmacological action: As part of the human endocannabinoid system (ECS), cannabinoid receptors, CB_1 and CB_2 receptors are found predominantly at nerve terminals where they have a role in retrograde regulation of synaptic function. THC acts as a partial agonist at both CB_1 and CB_2 receptors, mimicking the effects of the endocannabinoids, which may modulate the effects of neurotransmitters (e.g. reduce effects of excitatory neurotransmitters such as glutamate).

In animal models of MS and spasticity CB receptor agonists have been shown to ameliorate limb stiffness and improve motor function. These effects are prevented by CB antagonists, and CB_1 knockout mice show more severe spasticity. In the CREAE (chronic relapsing experimental autoimmune encephalomyelitis) mouse model, Sativex produced a dose-related reduction in the hind limb stiffness.

Presentation: Oromucosal spray, solution. 10 mL pack size allows delivery after priming of up to 90 actuations (sprays) of 100 microlitres.

Dose: A titration period is required to reach optimal dose. The number and timing of sprays will vary between patients. Maximum of 12 sprays per day.

Cost comparison (for general comparison only – therapeutic equivalence is not implied);

Cost per patient (at recommended dose, Drug Tariff March 2021)		
Sativex	6 to 12 sprays a day	£2436 to £4872 a year (£300 for 270 dose pack)
Gabapentin	2400mg daily (800mg tab)	£298 a year
Diazepam	15mg daily	£36 a year
Dantrolene sodium	225mg daily (25mg cap)	£554 a year
Baclofen	60mg daily	£43 a year
Tizanidine	24mg daily	£497 a year if prescribed as 2mg tabs. £731 if prescribed as 4mg tabs.

Private patients

As per this policy BSW does not routinely commission Sativex. In clinically exceptional cases an Individual Funding Request (IFR) may be initiated by an appropriate secondary care specialist. Consistent with IFR policy benefit derived from treatment accessed privately cannot be considered as part of the IFR process.

Patients pursing supply, and clinicians initiating or recommending Sativex, in a private healthcare context must ensure on-going arrangements are in place for managing prescribing and follow-up on the understanding that GPs within BSW cannot prescribe Sativex. Sativex can only be initiated by a specialist due to the supply mechanism from the manufacturer.

The NHS BSW CCG definition of exceptionality can be found here: https://bswccg.nhs.uk/docs-reports/exceptional-funding-requests/1348-exceptional-funding-requests-prior-approval-criteria-based-access-policy

Relevant NHS BSW CCG Medicines Management private prescribing advice can be found here: https://bswccg.nhs.uk/docs-reports/exceptional-funding-requests/1509-private-treatments

NICE commentary on efficacy and cost-effectiveness (NG144[1]):

NICE full evidence on spasticity (p32, https://www.nice.org.uk/guidance/ng144/evidence/c-spasticity-pdf-6963831760):

The committee agreed that there were benefits for the use of THC:CBD spray for the treatment of spasticity in multiple sclerosis. The clinical evidence showed improvements in patient-reported spasticity and could not differentiate between adverse events for THC:CBD spray and placebo. Also, economic modelling showed that THC:CBD spray would offer sufficient QALY gains if reduction in spasticity led to a halving of management costs and acquisition cost of THC:CBD spray (Sativex) was also reduced (in addition to the existing pay-for-responders scheme). Therefore, the committee agreed that under these conditions Sativex could be recommended to treat moderate to severe spasticity in adults with multiple sclerosis if other pharmacological treatments had not been effective.

P33:

The committee noted that despite THC: CBD spray being found to be clinically effective at reducing spasticity, no studies found any significant differences in health-related quality of life (HRQoL) measures whether using the EQ-5D, SF-36 or VAS 0-100 instruments. Additionally, differences in point estimates between the two arms of all trials collecting HRQoL measures were very small. They considered that this might be because HRQoL measures have some level of insensitivity to changes in spasticity NRS and are therefore not capturing the benefits of the treatment appropriately. Another contributory factor could be condition severity in the population in the trials, as patients with advanced MS typically have many other important symptoms that can influence their HRQoL and reducing spasticity might not change their self-reported scores by much.

P221:

The base-case analysis showed that compared to standard of care alone, at the new list price of £300 per pack, THC: CBD spray + SoC was associated with an ICER of £19,512 per QALY gained over a 5-year time horizon.

Adverse effects[3]

The most commonly reported adverse reactions in the first four weeks of exposure were dizziness, which occurs mainly during the initial titration period, and fatigue. These reactions are usually mild to moderate and resolve within a few days even if treatment is continued. When the recommended dose titration schedule was used, the incidence of dizziness and fatigue in the first four weeks was much reduced.

References:

1.) NICE NG144 Cannabis-based medicinal products November 2019. https://www.nice.org.uk/guidance/ng144/
2.) NICE CG186 Multiple sclerosis in adults: management October 2014 (updated Nov 19). https://www.nice.org.uk/guidance/cg186
3.) Summary of Product characteristics, Sativex, Electronic Medicines Compendium. https://www.medicines.org.uk/emc/product/602