Hertfordshire and West Essex Integrated Care System

NHS Hertfordshire and West Essex Integrated Care Board

SATIVEX® & OTHER LICENSED CANNABIS-BASED MEDICINAL PRODUCTS

RED – NOT RECOMMENDED FOR USE IN PRIMARY CARE. PRESCRIBING RESPONSIBILITY TO BE RETAINED IN SECONDARY CARE

NAME: GENERIC (TRADE)	WHAT IT IS	LICENSED INDICATIONS	DATE DECISION LAST REVISED	DECISION STATUS	NICE GUIDANCE
Delta-9-tetrahydrocannabinol [THC] and cannabidiol [CBD] spray (Sativex®)	Cannabis extract	Spasticity in multiple sclerosis (MS)	July 2020	Final	NICE NG144 – Recommended
Nabilone	Cannabinoid	Intractable chemotherapy induced nausea and vomiting			
Cannabidiol (Epidyolex®)	Antiepileptic	Adjunctive treatment with clobazam for treating seizures associated with Dravet syndrome and Lennox-Gastaut syndrome (LGS)	February 2020	Final	NICE TA 614 & TA615 - Recommended

Recommendation:

RED STATUS - NOT RECOMMENDED FOR USE IN PRIMARY CARE.
RECOMMENDED FOR RESTRICTED USE IN SECONDARY CARE IN LINE WITH NICE NG144 & NICE TA614 & TA615.

1. Sativex® (THC:CBD spray) for moderate to severe spasticity in adults with multiple sclerosis (MS) – **hospital only prescribing (red status)** with criteria for use in accordance with NICE Guideline 144
2. Nabilone for the treatment of intractable chemotherapy induced nausea and vomiting (NICE Guideline 144) – **hospital only prescribing (red status)** as this would be prescribed short term by specialists as part of chemotherapy support.
3. Cannabidiol (Epidyolex®) with clobazam as an option for treating seizures associated with Dravet syndrome (NICE TA 614) and Lennox-Gastaut syndrome (LGS) (NICE TA 615) in people aged 2 years and older – **hospital only prescribing (red status)** as these technologies are commissioned by NHS England (NHSE) and providers are NHS hospitals.

Sativex® and nabilone for the above approved indications are the commissioning responsibility of CCGs.
Epidyolex® for seizures in Dravet syndrome & LGS is the commissioning responsibility of NHS England.

Background information

In November 2019, NICE issued a new guideline (NG144) entitled 'Cannabis-based medicinal products'. Within this guidance NICE recommend a trial of THC:CBD spray (Sativex®) to treat moderate to severe spasticity in adults with multiple sclerosis (MS) if other pharmacological treatments are not effective and the company provides THC:CBD spray according to its pay-for-responders scheme. After this trial, the THC:CBD spray should be continued if the patient has had at least a 20% reduction in spasticity related symptoms. Treatment should be initiated and supervised by a physician with specialist expertise in treating spasticity due to MS.

HMMC have previously reviewed the evidence for Sativex® for spasticity and neuropathic pain in MS and the recommendation from April 2015 stated that Sativex® is NOT recommended for prescribing in primary, secondary or tertiary care. At that time, the committee agreed to adopt the East of England Priorities Advisory Committee (EoEPAC) 'NOT SUPPORTED' recommendation (2014). Following the publication of NICE Guideline 144, EoEPAC plans to withdraw its guidance on the use of Sativex®, and a draft briefing paper has been prepared. The HMMC recommendation has therefore been reviewed and updated.

NICE has also issued guidance on nabilone for the treatment of intractable chemotherapy induced nausea and vomiting (NG 144) and cannabidiol (Epidyolex®) with clobazam as an option for treating seizures associated with Dravet syndrome and Lennox-Gastaut syndrome (LGS) (NICE TAs 614 & 615). These TAs were noted as recommended at the February 2020 HMMC meeting but highlighted as the commissioning responsibility of NHSE.

ASSESSMENT AGAINST THE ETHICAL FRAMEWORK

Evidence of Clinical Effectiveness:

- **The full NICE evidence review for medicinal cannabis for spasticity in MS** can be accessed here: https://www.nice.org.uk/guidance/ng144/evidence/c-spasticity-pdf-6963831760

The NICE guideline committee agreed that the clinical evidence showed benefits of THC:CBD spray (Sativex®) for treating spasticity in people with multiple sclerosis. There were reductions in some measures of patient-reported spasticity and no difference in adverse events in the treatment or placebo groups, although much of the evidence was assessed as low quality. The committee agreed that the longer-term benefits of THC:CBD spray are likely to outweigh any potential harms, although it was not clear how benefits related to improvements in quality of life.

NICE recommended Sativex® for restricted use for spasticity in MS.

- **The full NICE evidence review for medicinal cannabis in chronic pain** can be accessed here: https://www.nice.org.uk/guidance/ng144/evidence/b-chronic-pain-pdf-6963831759

Of the 20 studies included, 7 looked at treatment of neuropathic pain (including multiple sclerosis, peripheral neuropathic pain and neuropathic pain characterised by allodynia). The included studies looked at the following interventions, oromucosal spray containing THC:CBD and oral delta-9-THC (dronabinol).

In general, there was limited evidence of high quality, mainly because the maintenance dose duration is relatively short in most studies. The committee agreed that a maintenance dose duration of up to 6 weeks is unrealistic for assessing chronic pain treatments. Additionally, many studies did not provide details of methods for randomisation or blinding. The majority of the RCTs are for CBD in combination with THC. The data could not differentiate THC:CBD for functional pain, change in opioid dose or quality of life. However, the committee considered these are outcomes to be less important compared with mean pain intensity which could not be differentiated between THC:CBD and placebo.

NICE do not recommend CBMPs for chronic pain.

- **The full NICE evidence review for medicinal cannabis in intractable nausea and vomiting** can be found here: https://www.nice.org.uk/guidance/ng144/evidence/a-intractable-nausea-and-vomiting-pdf-6963831758

Nabilone was effective in some outcomes when compared to placebo and prochlorperazine. Therefore, it could provide some relief to patients with persistent nausea and vomiting.

However, keeping in line with current clinical practice and the availability of new antiemetics, NICE recommended for nabilone to be considered as an add-on therapy to optimised conventional antiemetics in people in with persistent chemotherapy- induced nausea and vomiting.
Considering the adverse events and the uncertainty around dependence and development of psychological disorders, the committee noted that strong recommendations could not be made for the use of nabilone. Therefore, NICE recommend for nabilone to be considered as an adjunct treatment in adults.

- **Epidyolex with clobazam for seizures in LGS & Dravet syndrome**

NICE reviewed the evidence which is available as part of the NICE TA development process. The committee concluded that cannabidiol with clobazam reduces seizure frequency compared with usual care, but that the long-term efficacy after 3 years is uncertain.

NICE recommends cannabidiol with clobazam as an option for treating seizures associated with LGS or Dravet syndrome in people aged 2 years and older in line with TA 614 and 615 recommendations.

Cost of treatment and Cost Effectiveness:

- **Medicinal cannabis for spasticity in MS**

The NICE committee considered the evidence from 2 published economic evaluations but noted that they had contradictory conclusions about the cost effectiveness of THC:CBD spray and were subject to potentially serious limitations. So they considered results from a new economic model developed specifically for the cannabis guideline. The model included data from all relevant trials, longer-term registry data and data on adverse events.

The model predicted that the average person would receive a quality of life (QALY) gain equivalent to around 30 days perfect health with THC:CBD spray added to standard care. The acquisition costs of the treatment are offset by predicted savings in management costs. The incremental cost-effectiveness ratio (ICER) was £19,512 per QALY gained.

The model estimates that THC:CBD spray would offer sufficient QALY gains if reduction in spasticity led to a halving of management costs and the acquisition cost of THC:CBD spray was also reduced (in addition to the existing pay-for-responders scheme). The committee agreed that under these conditions THC:CBD spray could be recommended as a cost effective medicine for the treatment of spasticity in MS patients who have failed to respond to other treatments.

The committee agreed that the evidence for the effectiveness and safety of other cannabis-based medicinal products was much more limited. There is also currently no evidence on the cost effectiveness of products other than THC:CBD spray.

Potential local implications for Sativex® in MS
The NICE resource impact template predicts the following:

	ENHCCG	HVCCG
Predicted number of patients already receiving treatment	8	8
Predicted number of patients at the end of year 3 after gradual uptake	33	34
Predicted cost impact from year 4 onwards	£77,953	£79,828

- The figures for the end of year 3 are based on 90% uptake within the eligible population.
- It is assumed that everyone would have their first 3 vials for free (1 pack), so 8 packs have been assumed in the first year cost and 9 for subsequent years.

- It is assumed that the eligible population will remain the same, due to increases in the prevalent population matching the number discontinuing treatment, each year.

Each 10ml Spray contains approximately 90 sprays. If the average number of sprays per day in the clinical trials was 8 and the cost per 270 sprays is £300, then the annual cost per patient will be £3,200. Sativex® for spasticity in MS is a RED drug so is for hospital only prescribing. It is included in the national tariff so funding would come from the hospital trusts.

Current primary and secondary care prescribing of Sativex® is minimal

- **Medicinal cannabis in chronic pain**

For all treatment and condition specific subgroups the economic model used in the guidance produced ICERs far in excess of the usually accepted £20,000-£30,000/QALY range. This was principally due to the modest treatment effects and the high and ongoing cost of treatment with CBMPs. The model had a number of limitations including the lack of long term data on almost all parameters but no plausible variations in any of the model's input parameters produced ICERs close to £20,000-£30,000/QALY.

Using the economic model developed for the guideline, THC:CBD spray, which is the cheapest CBMP with a publicly available price, an incremental cost-effectiveness ratio (ICER) of over £150,000/QALY gained over the standard of care, a value far higher than the commonly accepted decision threshold of £20,000-£30,000/QAL gained was produced.

The committee indicated that this finding was not surprising as CBMPs are not expected to extend life or be fundamentally disease modifying, treatment effects relating to symptom alleviation are modest (about a 0.4 improvement in pain on a 0 to 10 scale on average) and the cost of the treatments is high.

The committee concluded that, at current prices, these CBMPs do not represent an effective use of resources in the management of chronic pain. NICE are not recommending use in chronic pain indications, including neuropathic pain associated with MS. Neuropathic pain in people with MS should be treated according to the NICE guideline on neuropathic pain in adults with referral to pain services if appropriate.

- **Medicinal cannabis in intractable nausea and vomiting**

No published economic evidence was identified. The cost of nabilone was estimated to be £20-59 per day of treatment. The committee considered that any resource impact would be unlikely to be significant as nabilone would typically not be offered continuously. Given that persistent chemotherapy-induced nausea and vomiting could lead to additional health care resources, such as a hospital stay and patients would be unlikely to continue treatment for long if it was not providing benefit, the committee concluded that nabilone could be a cost-effective add-on treatment option.

- **Epidyolex with clobazam for seizures in LGS & Dravet syndrome**

Costs, cost-effectiveness and cost impact available as part of NICE TA and associated costing documents.
This combination is commissioned by NHS England and providers are NHS hospitals. NHSE Specialised commissioning has confirmed that the care of patients with Dravet syndrome and LGS who are on this combination will stay with NHSE on reaching adulthood, assuming the treatment doesn't change).
Although shared care is technically possible for these indications, the Patient Access Scheme (PAS) price is not available in primary care and this is a highly specialised area of therapeutics.

The needs of the population

Alternative treatment options are available for all indications and therefore these treatments are additive to the current treatment pathways. There may be patients where current treatment is ineffective or not tolerated.

The needs of the community

Only a very small group of patients may benefit from these treatments. However, treatment costs are high so there may be a cost pressure to the local health economy. Sativex® is included in the National Tariff which would mean that funding of treatment would be the responsibility of provider Trusts. It is suggested that successful treatment may lead to a reduction in other care costs which may offset the increase to some degree.

Equity & Equality

A positive impact is anticipated for some patients with a disability as these treatments have not been recommended previously.
There is no differential impact expected on one or more equality groups differently to others Age; Gender reassignment; Marriage & Civil Partnership; Pregnancy & Maternity; Race; Religion & Belief; Sex; Sexual orientation.

Policy Drivers

- **National guidelines** - NICE NG 144, CG 173 & 186, NICE TAs 614 & 615
- **Bedfordshire and Luton Joint Prescribing Committee (BLJPC) position statement**
  BLJPC has adopted the criteria proposed in this paper.
- **Milton Keynes Prescribing Advisory Group (MKPAG) decision.**
  MKPAG has approved the use of Sativex® (Cannabis extract) for hospital prescribing only, subject to a 6 month audit of patients.
- **North Central London Joint Formulary Committee (NCLJFC) position statement**
  3 products approved for specialist/hospital use:
  - Cannabidiol oral solution (Epidyolex®): with clobazam is approved for patients ≥ 2years with a form of rare epilepsy (either Dravet syndrome or Lennox-Gastaut syndrome) within the recommended criteria in the NICE TAs (614 & 615) and is commissioned by NHS England.
  - Cannabidiol and delta-9-tetrahydrocannabinol oromucosal spray (Sativex®): on formulary for the treatment of severe spasticity in multiple sclerosis restricted to a specialist spasticity clinic at University College London Hospitals. A four-week trial of Sativex® is offered initially and only continued if the patient has had at least a 20% reduction in spasticity-related symptoms on a 0 to 10 patient-reported numeric rating scale.
  - Nabilone capsules: on formulary for the treatment of chemotherapy induced nausea and vomiting which persists with optimised conventional antiemetics at University College London Hospitals, Royal Free London, North Middlesex University Hospital and Whittington Hospital.

  No cannabis-based medicinal products are on formulary in NCL for use in chronic pain.
  Applications to use cannabis-based medicinal products for indications that are not currently on the Joint Formulary (including dronabinol and those other available products used in an off-label indication) will be considered through the usual process. The only exemption to this position statement is where the cannabis-based medicinal product is an investigational medicinal product within clinical trial regulations.
- **Cambridge & Peterborough JPG - CUHFT only:** The prescribing of THC:CBD spray (Sativex®) is supported for adults with multiple sclerosis (MS) with severe spasticity, whose only remaining option for the management of spasticity is intrathecal baclofen.
  Nabilone approved as hospital only.

Implementability:
No issues identified as the specified medications are only approved for specialist prescribing in secondary care.

References

1. NICE guideline (NG144) - Cannabis-based medicinal products, November 2019 https://www.nice.org.uk/guidance/ng144
2. NICE TA 614 - Cannabidiol with clobazam for treating seizures associated with Dravet syndrome, Dec 2019 https://www.nice.org.uk/guidance/ta614
3. NICE TA 615 - Cannabidiol with clobazam for treating seizures associated with Lennox–Gastaut syndrome, Dec 2019 https://www.nice.org.uk/guidance/ta615
4. NICE Clinical Guideline (CG 173) - Neuropathic pain in adults: pharmacological management in adults in non-specialist settings, November 2013. http://www.nice.org.uk/guidance/CG173
5. NICE Clinical Guideline (NG 220) - Multiple sclerosis in adults: Management, June 2022. http://www.nice.org.uk/guidance/ng220
6. NCL JFC Cannabis-based medicinal Products Position Statement. 21/02/2020 https://nclhealthandcare.org.uk/wp-content/uploads/2023/09/4_Cannabis_position_statement.pdf

Version	2.0 Harmonisation of Hertfordshire Medicines Management Committee (HMMC) guidance and West Essex Medicines Optimisation Programme Board (WEMOPB) guidance updates include: • Rebadging with HWE ICB and removal of ENHCCG and HVCCG headers • Review date removed and replaced with standard statement.
Developed by	Pharmacy and Medicines Optimisation Team
Approved by	HMMC
Date approved/updated	July 2020 December 2024
Review date:	The recommendation is based upon the evidence available at the time of publication. This recommendation will be reviewed upon request in the light of new evidence becoming available.
Superseded version	Original v1.0