Association of British Neurologists

ABN interim guidelines December 2018

Use of cannabis-based products in neurology

Background
The government has recently announced plans to reschedule cannabis-based products for medicinal use. Moving cannabis-based products from Schedule 1 to Schedule 2 will allow these products to be prescribed where there is an unmet clinical need, is supported by clear clinical evidence or published guidelines and where alternative treatments have been unsuccessful. However, a more detailed policy on how it will be provided to patients has not yet been published. Plans are in place for a formal NICE review and a guideline scoping document for this review has now been published. The ABN welcomes the commitment to develop formal guidelines through this process and has registered as a stakeholder to help with this. We also welcome opportunities for further research in this area. In the interim the ABN has provided the following clinical guidelines:

What this means for neurologists:
These products are only likely to be prescribed for the following neurological disorders:

1. People with very rare severe forms of epilepsy
2. Adults with spasticity caused by multiple sclerosis

Other potential indications currently include chronic pain and intractable chemotherapy induced nausea and vomiting, although it is expected that prescriptions for these indications would only be provided in non-neurological specialist clinics (see RCP recommendations). Cannabis based products for spasticity driven by non-MS conditions are currently not indicated although the ABN will be asking for this to be considered within the NICE review.

1. EPILEPSY
Published evidence for efficacy is currently only in Dravet Syndrome and Lennox-Gastaut Syndromes. Cases need to be carefully diagnosed.

Dravet syndrome; defined as age of onset of seizures <15m, prolonged (>15 mins) unilateral or bilateral motor seizures in first year often triggered by fever, emergence of other seizure types between 1 and 5 years including focal onset seizures, atypical absence, myoclonic jerks, unprovoked generalised tonic-clonic seizures (that may continue to be prolonged). Neurodevelopment normal in first year; slowing and plateau from second year.

Lennox Gastaut syndrome: Onset from 2 years of age (may evolve from spasms in first year). Multiple seizure types including tonic seizures (especially from sleep), atypical absence and atonic drop seizures. Neurodevelopmental slowing, with likely later severe intellectual disability and behaviour disorder. EEG demonstrates slow spike and wave (<2.5/s) with paroxysmal fast activity seen in sleep.

For these conditions prescriptions should only be for cannabidiol. Use in these syndromes is subject to several requirements, as helpfully summarised in the BPNA interim guidance which we would strongly advise consulting.

Epilepsy additional notes
The 'Lennox-Gastaut' label is often broadly applied to severe epilepsies with compatible seizure types and intellectual disability, but in this context syndromic diagnosis should be rigorous.
Liver function tests need to be monitored regularly, especially if used in conjunction with valproate and/or clobazam, and if LFTs are abnormal before initiation of treatment.

There is currently little available information on teratogenic and neurodevelopmental effects for cannabidiol. In addition concerns remain for the effect of some cannabis-derived products on post-natal neurodevelopment.

We recognise that there is likely to be pressure for prescription of cannabis-based products for other severe epilepsies. However, at present there is either no or very little evidence for benefit in other forms of epilepsies. Until there is more evidence and the anticipated NICE guidelines published, we would advise extreme caution if these products are being considered for any other form of epilepsy.

Epilepsy specific prescribing notes
Dosing data for cannabidiol in adults is very limited, although more information from GW Pharma will hopefully be available shortly. The regime used for children is as follows: dosing starts at 2mg/kg/day and is increased weekly by 2mg/kg/day until seizures are reduced or the patient experiences adverse effects that lead to discontinuation. The maximal recommended dose is 20mg/kg/day. Liver function tests should be taken at baseline, 2-weeks post the initiation of therapy and 2-weeks after each increment in dose. They should then be performed 3 monthly or on the occurrence of a clinically relevant event. Cannabidiol may need to introduce more slowly in patients on valproate because of concern about transaminitis.

2.MULTIPLE SCLEROSIS
Results from clinical trials of cannabinoids on spasticity in MS have been inconsistent: A large study of oral cannabis extract (the "CAMS" study) showed no effect on spasticity due to multiple sclerosis when assessed by the Ashworth scale although mobility and patient-reported measures improved (albeit with a degree of unblinding). A later study (the "MUSEC" trial) showed a positive effect of oral cannabis extract on muscle stiffness in MS, measured by a novel category scale.

Sativex® (delta-9-tetrahydrocannabinol/cannabidiol) spray is already licensed as an add-on treatment, for symptom improvement in patients with moderate to severe spasticity due to 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. It is initially prescribed for a 4 week trial period and stopped if ineffective (response is defined as a ≥20% reduction vs baseline which can be objective or patient reported). Approximately 50% of patients respond to treatment.

Though effective, current NICE guidance 2014 is not to offer Sativex as it is not deemed to be a cost effective treatment, although it is provided in some specialist settings or via private prescription. The Scottish Medicines consortium in 2011 could not recommend its use as they had not received relevant submissions. In 2014 the All Wales Medicines Strategy Group recommended Sativex for use in moderate-severe MS spasticity and it is currently being prescribed in Wales by MS specialists.

Cannabinoids do not affect multiple sclerosis disease activity or disability accumulation.

Multiple sclerosis additional notes

There is considerable patient demand for cannabinoids, because it is perceived as a natural and side-effect free way of treating troublesome multiple symptoms, such as pain and spasticity, and many patients will already have experience of non-prescription cannabis. Nonetheless, we advise that cannabis based products are used only in people who have had an unsatisfactory response to conventional spasticity drugs, as per the Sativex indication.
We note that spasms associated with spasticity respond to Sativex. However, while spasticity is measurable in clinic objectively, spasms may be infrequent and may not be easy to measure. In particular, spasms in the absence of spasticity will be reliant entirely

on patient history. In addition, stopping treatment pose challenges and clear criteria have yet to be agreed.

Multiple sclerosis specific prescribing notes

There is very limited information on dosing of cannabinoids outside of Sativex. Patients should be evaluated after 4 weeks trial period for evidence of clinical response sufficient to justify ongoing prescription, similar to the licensed titration of Sativex.

There are likely to be large numbers of MS patients who may potentially benefit from these drugs and all patients will need to be assessed within specialist clinics and subsequently reassessed for benefit as well as continuing benefit. Ongoing prescriptions are time consuming and need GP involvement. Dispensing is currently done only through hospital pharmacies, but may need to be provided through community pharmacies.

Important general points for clinicians considering the prescription of cannabis-based products:

1. The guidelines only relate to medicinal grade cannabis-based products where the content of cannabinoid constituents (i.e. THC/CBD, as appropriate) in the product is known and declared on the product label (not being dronabinol or its stereoisomers).
2. All cannabis-based products are considered unlicensed medications apart from Sativex®, (which has a market authorisation) and would be prescribed on a named-patient basis only.
3. Cannabis-based products should only be available from clinicians on the specialist register and within their age-appropriate area of expertise
4. Any decision to prescribe should be documented and supported by a multidisciplinary team.
5. No additional funding has been made available for these products and decisions on funding are currently up to individual hospital trusts.
6. Patients taking cannabis-based products should be aware that it may affect their ability to drive.
7. Clinicians prescribing these products should be aware of important drug interactions.
8. Rigorous and auditable safeguards around prescribing of an unlicensed product will need to be followed, alongside existing protocols on controlled drugs.
9. Treating clinicians will be expected to maintain a detailed assessment of clinical and patient outcome measures.
10. If travelling patients need to be aware that cannabis-based products remain illegal in some parts of the world.