



FDA approves its first cannabis based medicine

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The US Food and Drug Administration has approved the first prescription drug derived from marijuana for treating two rare and severe forms of epilepsy.

Epidiolex has been approved for treating seizures associated with Lennox-Gastaut syndrome or Dravet syndrome in patients aged 2 years or older.¹ These forms of epilepsy are frequently resistant to currently available treatments.

The oral solution, developed by the UK based company GW Pharmaceuticals, contains purified cannabidiol (CBD), a chemical component of the *Cannabis sativa* plant. However, CBD does not cause the intoxication or euphoria that comes from tetrahydrocannabinol (THC). Before the drug can be marketed the Drug Enforcement Administration must reclassify cannabidiol: it is currently considered a schedule drug, meaning that it has no medical value and a high risk of misuse. It is expected to be reclassified in the next 90 days.

The European Medicines Agency is also reviewing Epidiolex for treating seizures associated with these two forms of epilepsy, and a decision is expected in the first quarter of 2019.

The FDA's approval follows three randomised, double blind, placebo controlled trials reported in the *New England Journal of Medicine* and the *Lancet*, involving a total of 516 patients. Cannabidiol, added to a regimen of conventional antiepileptic treatment, considerably reduced the frequency of drop seizures in patients with Lennox-Gastaut syndrome or Dravet syndrome.²⁻⁴

Ley Sander, medical director of the UK Epilepsy Society and professor of neurology at University College London's Institute of Neurology, commented, "The approval of any new epilepsy drug which has gone through rigorous regulatory trials has to be welcomed. This cannabidiol based drug shows promise for children with Dravet and Lennox-Gastaut syndromes, particularly for drop attacks.

"As with the complete armamentarium of epilepsy drugs, however, cannabidiol seems to work for some but not for others. It is not a magic bullet. Response is very individual, underlining the need to identify individual biomarkers of response so that we can predict for each individual which drug will work best from the point of diagnosis."

He added, "If the drug is approved in the UK then NICE [the National Institute for Health and Care Excellence] will need to assess it for effectiveness before it becomes available on the NHS. The issue then will be how the drug will be commissioned.

"It is likely that it will be centrally commissioned for children but it may be that, for adults, local commissioners will have to introduce it into their formularies."

Epidiolex is essentially a pharmaceutical grade version of CBD oil that some parents already use to treat children with epilepsy.

A recent media storm surrounded 12 year old Billy Caldwell, who had his imported cannabis oil confiscated.⁵ His mother said that it had kept Billy seizure-free for 250 days, but after the oil was confiscated his seizures started again, and he was admitted to hospital in London. After sustained media and political pressure Sajid Javid, home secretary, granted a temporary licence for cannabis oil to treat Billy's epilepsy.

The UK has seen increasing calls for more research into the medical uses of cannabis and for doctors to be able to prescribe it legally. Twenty prominent clinicians and academics wrote a letter to the *Times* on 20 June urging the government to reclassify cannabis from schedule 1 to schedule 2 under the UK's Misuse of Drugs Regulations 2001.⁶ Javid has now said that a panel will be set up to review the evidence for medical cannabis that could see the drug reclassified.

GW Pharmaceuticals has not yet announced a price for Epidiolex, but Wall Street analysts have predicted that it could cost \$25 000 (£19 000; €21 500) a year. Sativex, an oromucosal spray containing both THC and CBD made by the same company, has been licensed as a treatment in the UK for patients with multiple sclerosis. However, NICE found it not to be cost effective, and it is not available to NHS patients.

1 Food and Drug Administration. FDA approves first drug comprised of an active ingredient derived from marijuana to treat rare, severe forms of epilepsy. 25 June 2018. <https://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm611046.htm>.

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3 Devinsky O, Cross JH, Laux L, et al. Cannabidiol in Dravet Syndrome Study Group. Trial of cannabidiol for drug-resistant seizures in the Dravet syndrome. *N Engl J Med* 2017;376:2011-20. 10.1056/NEJMoa1611618 28538134

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5 Hurley R. Cannabis, cannabis everywhere: UK to review medical cannabis policy as Canada plans imminent legalisation for all uses. *BMJ* 2018;361:k2695. 10.1136/bmj.k2695 29921612

6 Hurley R. "Illogical" cannabis regulation blocks research into therapeutic uses, say doctors. *BMJ* 2018;361:k2780. 10.1136/bmj.k2780 29941429

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