

## **POSITION STATEMENT Medical Use of Cannabis (Marijuana)**



### **KEY MESSAGES**

- Cancer Council NSW acknowledges that cannabis may be of medical benefit to cancer patients where conventional treatments are unsuccessful, in the following circumstances:
  - in relieving nausea and vomiting in patients undergoing chemotherapy;
  - as an adjunctive analgesic in patients with moderate to severe pain; and/or
  - as an appetite stimulant for cancer patients experiencing weight loss and muscle wasting.
- Smoking is a particularly harmful route of cannabis (marijuana) administration, largely because carcinogenic substances are inhaled into the lungs.
- Synthetic cannabis products, particularly Nabiximols delivered via an oral spray, offer advantages in providing symptom relief without unwanted psychological or tetrahydrocannabinol (THC) related effects, as well as being a preferable route of administration for anti-emetic therapy.
- Natural and synthetic forms of cannabis are currently illegal in Australia.
- Cancer Council NSW supports limited exemptions from criminal prosecution, such as those provided by the Cannabis Cautioning Scheme, for cancer patients who have been certified by an approved medical practitioner as having particular conditions, and who have been counselled by such a practitioner about the risks of smoking cannabis.
- Cancer Council NSW supports the current clinical trial of the synthetic cannabis product Nabiximols via oral spray for relieving uncontrolled persistent pain in patients with advanced cancer, part of which is being conducted in Australia.

### **BACKGROUND**

#### **Cannabis use in Australia (NSW)**

Cannabis is the most commonly used illicit drug in Australia. In 2010, around 1.9 million Australians aged 14 years or older reported using cannabis in the previous 12 months, including 9.1% of the NSW adult population.<sup>1</sup> Rates of cannabis use are higher in males and among young adults. The highest proportion of males who had used cannabis in the last 12 months were those aged 20-29 years (25%), and for females, those aged 18-19 years (19.3%). Most cannabis use is occasional, with the largest proportion (34.6%) of recent users reporting cannabis use once or twice in the past 12 months.<sup>1</sup>

## **Cannabis**

### *Natural cannabis*

Cannabis, also known as grass, pot, hash, and marijuana, is made from the dried flowers and leaves of a plant called *Cannabis sativa*. The *Cannabis sativa* plant contains cannabinoids, which are chemicals that act upon cannabinoid receptors in the body (CB<sub>1</sub> and CB<sub>2</sub>). The most well known and researched cannabinoids are tetrahydrocannabinol (THC) and cannabidiol (CBD). THC is the primary psychoactive component of cannabis and is the most effective cannabinoid for alleviating nausea and vomiting and stimulating appetite.<sup>2,3</sup>

### *Synthetic cannabis*

Cannabinoids also refer to synthetic drugs developed in pharmaceutical laboratories. These act in the same way in the body as the natural plant product. Currently the three main synthetic cannabinoids are:

- Dronabinol, a synthetic form of THC;
- Nabilone, a synthetic form of THC; and
- Nabiximols, a chemically pure 50:50 mixture of THC and CBD.<sup>3,4</sup>

### *Therapeutic benefits of cannabis use*

A working party on the use of cannabis for medical purposes established by the NSW Government concluded in its final report (August 2000)<sup>3</sup> that medical conditions for which cannabis may be of medical benefit include:

- As an appetite stimulant for cancer and HIV related wasting;
- Pain unrelieved by conventional treatments;
- Neurological disorders, such as multiple sclerosis; and
- Nausea and vomiting in cancer patients undergoing chemotherapy which do not respond to conventional treatment.

These conclusions were consistent with a report prepared in 1998 by the Drug and Alcohol Services Council of South Australia for the Ministerial Council on Drug Strategy.<sup>5</sup>

The Australian Medical Association also considers cannabis may be of medical benefit as an appetite stimulant and as an anti-emetic, but believes that more research is needed to determine the benefits for neurological disorders and pain relief, as well as the safe and effective routes of administration.<sup>6</sup>

In 2004, researchers at the National Drug and Alcohol Research Centre of the University of New South Wales recruited Australian adults who had used cannabis for medical purposes.

One hundred and twenty-eight respondents completed questionnaires anonymously, and the majority (58%) were NSW residents. Participants reported the use of cannabis to relieve a number of medical conditions. Cannabis use was perceived to provide substantial relief from symptoms such as pain and nausea.<sup>7</sup>

In North America and some European countries, Dronabinol, Nabilone and Nabiximols are used to treat nausea and vomiting caused by chemotherapy in people who do not respond to conventional treatment. Dronabinol and Nabiximols are also used to treat loss of appetite and weight loss in cancer patients.<sup>8-10</sup> Additionally, Nabiximols are used as an adjunctive analgesic treatment in adult patients with advanced cancer who experience moderate to severe pain.<sup>11</sup>

#### *Adverse effects of cannabis use*

The short term effects of plant-based (natural) cannabis include loss of inhibition, anxiety or paranoia, difficulty concentrating, faster heart rate, dry mouth and throat, vomiting, and hallucinations. Additionally, adverse health effects are associated with chronic cannabis use, including increased risk of bronchitis, lung cancer and other diseases of the respiratory system, cannabis dependence (addiction), depression and decreased concentration, memory and ability to learn new things.<sup>12</sup> Most of what is known about the adverse effects of smoked cannabis comes from studies of long-term recreational users rather than medical users. People who smoke cannabis for medicinal purposes usually use smaller quantities over shorter time periods compared to recreational users. There is potential for follow up studies of patients in countries such as Canada and the Netherlands, where medical programs involving smoked cannabis currently exist, to investigate the risk of these adverse events in this population.<sup>13</sup>

A systematic review of the adverse effects associated with the use of synthetic cannabis products found that there was no increased risk of serious adverse events, such as vomiting and urinary tract infections. Non-serious adverse events such as dizziness, dry mouth, confusion, anxiety and nausea have, however, been associated with use of synthetic cannabis products.<sup>4,8,9,14</sup>

#### *Routes of administration*

Cannabis is usually smoked in hand-rolled cigarettes (joints), with many users mixing it with tobacco before smoking it, or water pipes (bongs). Sometimes it is mixed with foods (cakes or cookies) and eaten or brewed as tea.<sup>12</sup>

Dronabinol and Nabilone are taken orally in capsule form.<sup>8,9</sup> Nabiximols is administered as an oral spray which is absorbed in the patient's mouth.<sup>15</sup>

There is considerable debate as to the optimal route of administration of cannabinoids in treating cancer and other illnesses. The smoking of cannabis is not recommended by health authorities, as the smoked form contains at least 50 of the same carcinogens as tobacco,<sup>3,16</sup> and is unlikely to be prescribed in Australia because smoked plant products will not satisfy requirements to be classed as a therapeutic good.<sup>3</sup> Dronabinol and Nabilone are not popular or widely used by eligible patients in the United Kingdom (UK) and United States (US) as the drugs need to be taken orally and the beneficial components are not well absorbed into the body.<sup>3</sup>

The effects and benefits of Nabiximols oral spray are currently being investigated in a number of locations including, the US, UK, Mexico, Germany and the Czech Republic.<sup>17</sup> It is expected that the oral spray form of Nabiximols will be the preferred option for synthetic cannabinoid, because the spray delivery system prevents THC from entering the blood too quickly, and the formulation enhances the therapeutic benefits, while minimising unwanted psychological and other THC-related effects.<sup>15</sup>

### **Australian and NSW law**

Australia is a signatory to two international agreements relating to the use of cannabis for medical purposes. The United Nations' *Single Convention on Narcotic Drugs (1961)* aims to combat drug abuse by coordinated international action, by limiting the possession, use, trade in, distribution, import, export, manufacture and production of drugs exclusively to medical and scientific purposes and to deter and discourage drug traffickers.<sup>18</sup> The United Nations' *Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances (1988)* extended the provisions of the Single Convention to a range of behaviour- and mood-altering drugs, but distinguished between those which are totally prohibited and those, such as cannabis, which may be of benefit for restricted medical purposes.<sup>3</sup>

Cannabis is listed as an illicit drug under Australian federal law, specifically the *Crimes (Traffic in Narcotic Drugs and Psychotropic Substances) Act 1990* and the *Customs Act 1901*. It is encompassed by law under the *Narcotics Drugs Act 1967* and the *Therapeutic Goods Act 1989*. The existing legal framework in Australia prohibits the cultivation of plants containing narcotic or psychotropic substances, including cannabis.<sup>2,3</sup> Neither cannabis nor its synthetic forms are currently approved by the Therapeutic Goods Administration (TGA) for therapeutic use in Australia.

Under NSW law, cannabis is a prohibited substance. Under the *Drugs Misuse and Trafficking Act 1985*, it is an offence to cultivate, supply or possess the drug. The NSW Working Party on the Use of Cannabis for Medical Purposes recommended in August 2000 that, pending the development and availability of safer and more efficient methods to deliver cannabinoids, NSW introduce a compassionate regime to assist those suffering from the range of illnesses identified in their report to gain the benefits associated with the use of cannabis without the risk of criminal sanctions.<sup>3</sup>

The Cannabis Cautioning Scheme was instituted in April 2000, after a recommendation from the 1999 NSW Drug Summit. Administered by the NSW Police Force, it aims to educate minor cannabis offenders about the legal and health implications of cannabis use. The scheme gives police discretion to issue a caution to adults who commit minor cannabis offences. Along with the caution, offenders are provided information regarding support services and treatment.<sup>19</sup>

In the 2010 National Drug Strategy Household Survey conducted by the Australian Institute of Health and Welfare, 69% of participants supported legislative change that permitted medical use of cannabis; and 74% supported clinical trials investigating the benefits of cannabis use for the treatment of medical conditions.<sup>1</sup>

### **Medical cannabis in the international context**

The World Health Organization (WHO) acknowledges the therapeutic benefits of cannabinoids for nausea and vomiting in advanced stage cancer patients. WHO also notes that further research is needed on the central and peripheral mechanisms of the effects of cannabinoids in reducing nausea; along with investigation of the mechanisms by which THC and cannabinoids affect cellular function in the nervous system, so that better therapeutic agents can be developed.<sup>20</sup>

#### *United States*

The US Institutes of Medicine conducted an extensive investigation of the medical use of cannabis in 1999. The Institutes of Medicine report<sup>21</sup> made a number of key recommendations which included:

- Research should continue into the physiological effects of synthetic and plant-derived cannabinoids and the natural function of cannabinoids found in the body; and
- Clinical trials of cannabinoid drugs for symptom management should be conducted with the goal of developing rapid onset, reliable, and safe delivery systems.

Plant-based medical cannabis programs exist in 16 jurisdictions in the US, including Alaska, California, Hawaii, Maine, Nevada, Oregon, and Washington. These plant-based medical cannabis programs vary in format across the different states. One example is the Oregon Medical Marijuana Program. This program allows registered patients to use cannabis for medical conditions outlined in the Oregon Medical Marijuana Act. Along with an application, patients must send identification, an annual registration fee and submit a statement of support from an attending physician, stating that the patient has a qualifying condition for which cannabis may help. Patients can opt to grow their own medicine, have someone grow it for them or designate a caregiver to manage their supply. The Oregon Medical Marijuana Program does not provide information on where to source cannabis.<sup>22</sup>

Synthetic cannabis products are available for cancer patients in the US. Dronabinol and Nabilone have been approved by the US Food and Drug Administration (FDA) to relieve nausea and vomiting and increase appetite in cancer patients since 1985. Nabiximols, however are still being tested in the US for effectiveness in relieving cancer pain.<sup>17,23</sup>

#### *United Kingdom*

In the UK, the Select Committee on Science and Technology of the House of Lords in 1998 recommended that there was an urgent need for clinical trials of natural cannabis for the treatment of multiple sclerosis and chronic pain. The Select Committee recommended research be undertaken into alternative routes of administration that would retain the benefit of the quick absorption offered by smoking without the adverse effects.<sup>24</sup> The report acknowledged that synthetic cannabis products were available in the UK, and that research comparing the effectiveness of natural and synthetic cannabis would be welcomed.<sup>24</sup> Nabiximols is currently being tested in the UK for its effectiveness in relieving cancer pain.<sup>17</sup>

#### *Canada*

In 2001, Health Canada implemented the *Marihuana Medical Access Regulations* which defined the conditions in which access to cannabis for medical purposes would be permitted. The regulations allow people who experience severe pain, cachexia, anorexia, weight loss, and/or severe nausea from cancer, with a declaration from a medical practitioner, to apply to possess cannabis for medical purposes. People order and pay for cannabis seeds and/or dried cannabis through Health Canada. Health Canada's cannabis is supplied by a company that specialises in growing, harvesting and processing plants for pharmaceuticals and research and produces a standardised, safe, homogenous supply of cannabis.<sup>25</sup>

In 2007 Health Canada approved Nabiximols, with conditions, under the Notice of Compliance with Conditions policy, for adult patients with advanced cancer who experience moderate or severe pain unrelieved by conventional treatment.<sup>26</sup>

### *The Netherlands*

Medical cannabis was permitted in the Netherlands from 2003 and involves the use of plant based substances. The Office of Medicinal Cannabis in the Ministry of Health, Welfare and Sport licences companies to grow cannabis which is supplied to pharmacies in the form of dried cannabis.<sup>27</sup> For cancer patients, a doctor can prescribe medicinal cannabis to help relieve nausea, reduced appetite and weight loss, and nausea and vomiting caused by chemotherapy and radiotherapy. Patients are advised to dilute the cannabis into tea or inhale using a vaporiser.<sup>28</sup>

### *Australia*

Following recommendations in the report of the working party on the use of cannabis for medical purposes, the 2003 NSW Government proposed a four year clinical trial of medical cannabis. This trial did not commence under the Carr Government, nor has it progressed under subsequent NSW premiers.<sup>27,29</sup> John Kaye, Greens NSW Member for Parliament, tabled a motion in the Upper House in late 2011 calling on the Minister for Health to establish a one year trial of medically prescribed cannabis and circulated a discussion paper. The paper is currently open for discussion, with the intention to move a motion in spring 2012 to call on the NSW Government to begin the process of establishing a trial.<sup>29</sup> As the paper is currently at the discussion stage there is no clear outline of the research design of a proposed trial of medical cannabis. Cancer Council NSW will be interested in the development of this proposal and the nature of the trial that is proposed. Given the health and legal implications involved with a natural medical cannabis program, Cancer Council NSW supports development of a trial using synthetic cannabis products. In particular, Nabiximols via oral spray offer advantages in treating the symptoms without the associated 'high', and is a more acceptable method of administration of anti-emetic therapy for patients that have difficulty swallowing or digesting tablets.<sup>30</sup>

### **Current Clinical Trials**

In December 2010, GW Pharmaceuticals commenced a Phase III trial (NCT01262651) to use Sativex (oral spray of Nabiximols) for relieving persistent pain in patients with advanced.<sup>31,32</sup> This followed after Phase IIa and IIb trials demonstrated the effectiveness of Nabiximols for pain relief in patients with advanced cancer pain, that was not fully relieved by

strong opioids.<sup>33</sup> The study is being conducted in Europe, North America, Latin America, and Asia, and is anticipated to be completed by August 2014.<sup>17</sup>

GW Pharmaceutical is also currently running an international synthetic cannabis clinical trial (NCT01424566). This trial includes 11 Australian research sites, three of which are currently recruiting. The trial aims to determine the efficacy of Sativex (oral spray form of Nabiximols), compared with placebo, as an adjunctive medication in relieving persistent chronic pain in advanced cancer patients. The trial began in January 2012 with an estimated study completion date of December 2015.<sup>34</sup>

### **Conclusion**

Synthetic cannabis products have the potential to offer cancer patients relief from symptoms such as nausea and vomiting while undergoing chemotherapy, pain unrelieved by conventional treatments, and as an appetite stimulant for cancer related weight loss and muscle wasting. In particular when administered in a spray form, these products are able to address symptoms without the patient experiencing the unwanted psychological or THC-related effects, exposing themselves to the carcinogens associated with smoking cannabis, and administered in a form suitable as anti-emetic therapy. Successive NSW Governments have discussed the potential benefits and harms of medical cannabis use for more than a decade, but have nevertheless demonstrated limited political will to change the status quo. Cancer Council NSW understands that a range of health and regulatory issues surround a medical cannabis program, but recommends that the NSW Government reconsider their position, particularly in light of the new GW Pharmaceuticals clinical trial of Nabiximols that includes Australian sites.



## References

1. Australian Institute of Health and Welfare. *2010 National Drug Strategy Household Survey Report*. Drug Statistics series no. 25. Cat. no. PHE 145 Canberra: AIHW; 2011.
2. Griffith G and Swain M. *The medical use of cannabis: recent developments*. NSW Parliamentary Library Research Services, Briefing Paper No 11/99 ; 1999.
3. Working Party on the Use of Cannabis for Medical Purposes. *Report of the Working Party on the use of cannabis for medical purposes*. Sydney: NSW Parliament; 2000. Vol 2.
4. Portenoy R, Ganae-Motan E, Allende S, Yanagiharra R, Shaiova L, Weinstein S, et al. Nabiximols for opioid-treated cancer patients with poorly-controlled chronic pain: a randomized, placebo-controlled, graded-dose trial. *Journal of Pain*. 2012;13(5).
5. Gowing L, Ali R, Christie Pand White J. (1996); Therapeutic uses of cannabis. DASSA Monograph No 1. Adelaide: Drug & Alcohol Services South Australia.
6. *Cannabis 2006*. Australian Medical Association.; 2006 [cited 2012 Jul 26]. Available from: <http://ama.com.au/node/2556>
7. Swift W, Gates P, Dillon P. Survey of Australians using cannabis for medical purposes. *Harm Reduction Journal*. 2005;2(18).
8. *Dronabinol*. Medline Plus.; 2012 [cited 2012 May 10]. Available from: <http://www.nlm.nih.gov/medlineplus/druginfo/meds/a607054.html>
9. *Nabilone*. Medline Plus.; 2012 [cited 2012 May 10]. Available from: <http://www.nlm.nih.gov/medlineplus/druginfo/meds/a607048.html>
10. *Sativex therapeutic uses, other*. GW Pharmaceuticals.; 2012 [cited 2012 May 10]. Available from: <http://www.gwpharm.com/other-targets.aspx>
11. *Sativex therapeutic uses, cancer pain*. GW Pharmaceuticals.; 2012 [cited 2012 May 10]. Available from: <http://www.gwpharm.com/cancer-pain.aspx>
12. *Cannabis factsheet*. NSW Government Health.; 2011 [cited 2012 May 11]. Available from: <http://www.health.nsw.gov.au/factsheets/drugandalcohol/marijuana.html>
13. Degenhardt L, Hall W. The adverse effects of cannabinoids: implications for use of medical marijuana. *CMAJ*. 2008;178(13):1685-6.
14. Wang T, Collet J, Shapiro S, Ware M. Adverse effects of medical cannabinoids: a systematic review. *CMAJ*. 2008;178(13):1669-78.
15. *What is Sativex?* GW Pharmaceuticals.; 2012 [cited 2012 May 10]. Available from: <http://www.gwpharm.com/sativex-faqs.aspx>
16. *Does smoking cannabis cause cancer?* Cancer Research UK.; 2010 [cited 2012 May 11]. Available from: <http://cancerhelp.cancerresearchuk.org/about-cancer/cancer-questions/does-smoking-cannabis-cause-cancer>
17. *Sativex for relieving persistent pain in patients with advanced cancer (SPRAY III)*. Clinical Trials, NIH.; 2012 [cited 2012 May 15]. Available from: [http://clinicaltrials.gov/ct2/show/study/NCT01361607?show\\_locs=Y#locn](http://clinicaltrials.gov/ct2/show/study/NCT01361607?show_locs=Y#locn)

18. *Single Convention on Narcotic Drugs, 1961*. United Nations Office on Drugs and Crime.; 2012 [cited 2012 May 14]. Available from:  
<http://www.unodc.org/unodc/en/treaties/single-convention.html>
19. *Cannabis Cautioning Scheme*. NSW Government NSW Police Force.; 2012 [cited 2012 May 14]. Available from:  
[http://www.police.nsw.gov.au/community\\_issues/drugs/cannabis\\_cautioning\\_scheme](http://www.police.nsw.gov.au/community_issues/drugs/cannabis_cautioning_scheme)
20. *Cannabis*. World Health Organization.; 2012 [cited 2012 May 15]. Available from:  
[http://www.who.int/substance\\_abuse/facts/cannabis/en/](http://www.who.int/substance_abuse/facts/cannabis/en/)
21. Mack A and Joy J. *Marijuana as medicine?: the science beyond the controversy*. Washington, DC: National Academy Press; 2001.
22. *Oregon Medical Marijuana Program*. Oregon Health Authority.; 2012 [cited 2012 Jul 6]. Available from:  
<http://public.health.oregon.gov/DiseasesConditions/ChronicDisease/medicalmarijuanaprogram/Pages/index.aspx>
23. *Marijuana*. American Cancer Society.; 2012 [cited 2012 May 10]. Available from:  
<http://www.cancer.org/Treatment/TreatmentsandSideEffects/ComplementaryandAlternativeMedicine/HerbsVitaminsandMinerals/marijuana>
24. Select Committee on Science and Technology. *Cannabis: the scientific and medical evidence*. HL paper 151 1997-1998 ; 1998. 9th.
25. *Medical use of marihuana*. Health Canada.; 2011 [cited 2012 May 15]. Available from:  
<http://www.hc-sc.gc.ca/dhp-mps/marihuana/index-eng.php>
26. *Factsheet - Sativex*. Health Canada.; 2007 [cited 2012 May 10]. Available from:  
[http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/conditions/sativex\\_fs\\_fd\\_109461-eng.php](http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/conditions/sativex_fs_fd_109461-eng.php)
27. Topp L. (2006); *Medical cannabis: lost in politics*. *Of Substance*. 4.
28. *Medical cannabis*. Office of Medical Cannabis, Ministry of Health, Welfare and Sport.; 2012 [cited 2012 May 15]. Available from:  
<http://www.cannabisbureau.nl/en/MedicinalCannabis/>
29. John Kaye. *Medical cannabis: time to trial* John Kaye, Greens NSW Member of Parliament.; 2012 [cited 2012 May 28]. Available from: <http://johnkaye.org.au/medicinal-cannabis-time-to-trial/?searchterm=cannabis>
30. *Oral spray delivery of ondansetron bioequivalent to tablets*. Cancer Network.; 2006 [cited 2012 Jul 27]. Available from:  
<http://www.cancernetwork.com/news/display/article/10165/108458>
31. *Sativex enters phase III clinical programme in cancer pain*. GW Pharmaceuticals.; 2012 [cited 2012 May 17]. Available from:  
<http://www.gwpharm.com/Sativex%20Enters%20Phase%20III%20Clinical%20Programme%20In%20Cancer%20Pain.aspx>
32. US National Institutes of Health. *A study of Sativex (R) for relieving persistent pain in patients with advanced cancer* National Institutes of Health.; 2012 [cited 2012 Nov 9]. Available from:  
[http://www.clinicaltrials.gov/ct2/show/study/NCT01262651?term=sativex&rank=32&show\\_locs=Y#locn](http://www.clinicaltrials.gov/ct2/show/study/NCT01262651?term=sativex&rank=32&show_locs=Y#locn)

33. Johnson J, Burnell-Nugent M, Lossignol D, Ganae-Motan E, Potts R, Fallon M. Multicenter, double-blind, randomized, placebo-controlled, parallel-group study of the efficacy, safety, and tolerability of THC:CBD extract in patients with intractable cancer-related pain. *Journal of Pain and Symptom Management*. 2010;39(2).
34. National Institutes of Health. *A two-part study of Sativex (R) oromucosal spray for relieving uncontrolled persistent pain in patients with advanced cancer* National Institutes of Health.; 12 A.D. [cited 2012 Nov 9]. Available from: [http://clinicaltrials.gov/ct2/show/study/NCT01424566?term=NCT01424566&rank=1&show\\_locs=Y#locn](http://clinicaltrials.gov/ct2/show/study/NCT01424566?term=NCT01424566&rank=1&show_locs=Y#locn)

#### **VALIDATION**

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#### **FURTHER INFORMATION**

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