Introduction
Cannabis is a drug that comes from Indian hemp plants such as Cannabis sativa and Cannabis indica. The main active chemical in cannabis is THC (delta-9 tetrahydrocannabinol).

Cannabis is a depressant drug. Depressant drugs do not necessarily make one feel depressed. Rather, they slow down the activity of the central nervous system and the messages going between the brain and the body. When large doses of cannabis are taken it may also produce hallucinogenic effects (DrugInfo).

Cannabis is a generic term used to denote the several psychoactive preparations of the plant Cannabis sativa. The major psychoactive constituent in cannabis is delta-9 tetrahydrocannabinol (THC). Compounds which are structurally similar to THC are referred to as cannabinoids. In addition, a number of recently identified compounds that differ structurally from cannabinoids nevertheless share many of their pharmacological properties.

The Mexican term ‘marijuana’ is frequently used in referring to cannabis leaves or other crude plant material in many countries. The unpollinated female plants are called hashish. Cannabis oil (hashish oil) is a concentrate of cannabinoids obtained by solvent extraction of the crude plant material or of the resin (World Health Organization).
The chemical composition of Cannabis has been elucidated following long-lasting research efforts. Among the nearly 500 compounds belonging to a large variety of groups, cannabinoids (66 compounds) are typical to this plant. While 9-tetrahydrocannabinol is responsible for psychoactive properties of Cannabis some of the other components modulate its activity. Investigation of the chemical composition the hemp plant, Cannabis sativa L, known for millennia for its therapeutic properties and as a recreational, psychoactive drug, has been commenced in the early 1800’s; at that time, the medical use of cannabis in the western world mostly for treatment of neurological and psychiatric diseases, became quite intensive. Early efforts targeting isolation and identification of the individual components responsible for the activity of Cannabis, believed to be alkaloids, failed due to the complexity and large number of closely related compounds, their lack of stability and to the rudimentary separation and analytical techniques available (European Monitoring Centre for Drugs and Drug Addiction).

The Legal Status of Cannabis

The legal status of cannabis for personal use is one of the most controversial policy issues in the European Union. Although Cannabis is a classified narcotic drug placed under control by the United Nations and by all EU Member States, the measures adopted to control it at national level vary considerably from country to country, as shown in the table below.

The Drugs and Drug Trafficking Act, 1992 (Act No 140 of 1992) is the controlling legislation on street drugs in South Africa including Cannabis. Cultivation, possession, use, supply and dealing in Cannabis is illegal in South Africa. The aforementioned Act allows charges to be brought under three separate provisions:

- Section 3 (cultivation, manufacture and supply)
- Section 4 (use and possession)
- Section 5 (dealing)
Acute Health Effects of Cannabis Use
The acute effects of cannabis use have been recognised for many years, and recent studies have confirmed and extended earlier findings. These may be summarised as follows:

- Cannabis impairs cognitive development (capabilities of learning), including associative processes; free recall of previously learned items is often impaired when cannabis is used both during learning and recall periods;

- Cannabis impairs psychomotor performance in a wide variety of tasks, such as motor coordination, divided attention, and operative tasks of many types. Human performance on complex machinery can be impaired for as long as 24 hours after smoking as little as 20mg of THC in cannabis. There is an increased risk of motor vehicle accidents among persons who drive when intoxicated by cannabis (National Cancer Institute).

Chronic Health Effects of Cannabis Use
The chronic effects of cannabis use have also been recognised for many years, and recent studies have confirmed and extended earlier findings. These may be summarised as follows:

- Selective impairment of cognitive functioning which include the organisation and integration of complex information involving various mechanisms of attention and memory processes

- Prolonged use may lead to greater impairment, which may not recover with cessation of use, and which could affect daily life functions

- Development of a cannabis dependence syndrome characterised by a loss of control over cannabis use is likely in chronic users

- Cannabis use can exacerbate schizophrenia in affected individuals

- Epithelial injury of the trachea and major bronchi is caused by long-term cannabis smoking

- Airway injury, lung inflammation, and impaired pulmonary defence against infection from persistent cannabis consumption over prolonged periods

- Heavy cannabis consumption is associated with a higher prevalence of symptoms of chronic bronchitis and a higher incidence of acute bronchitis than in the non-smoking cohort

- Cannabis used during pregnancy is associated with impairment in foetal development leading to a reduction in birth weight

- Cannabis use during pregnancy may lead to postnatal risk of rare forms of cancer although more research is needed in this area

- The health consequences of cannabis use in developing countries are largely unknown because of limited and non-systematic research, but there is no reason a priori to expect that biological effects on individuals in these populations would be substantially different to what has been observed in developed countries. However,
other consequences might be different given the cultural and social differences between countries.  
(National Cancer Institute).

**Therapeutic Uses of Cannabinoids**

Several studies have demonstrated the therapeutic effects of cannabinoids for nausea and vomiting in the advanced stages of illnesses such as cancer and AIDS. Dronabinol (tetrahydrocannabinol) has been available by prescription for more than a decade in the USA. Other therapeutic uses of cannabinoids are being demonstrated by controlled studies, including treatment of asthma and glaucoma, as an antidepressant, appetite stimulant, anticonvulsant and anti-spasmodic - research in this area should continue. For example, more basic research on the central and peripheral mechanisms of the effects of cannabinoids on gastrointestinal function may improve the ability to alleviate nausea and vomiting (emesis). More research is needed on the basic neuropharmacology of THC and other cannabinoids so that better therapeutic agents can be found.

Some substances in cannabis may be helpful for treating nausea caused by chemotherapy and for treating pain that is not relieved by conventional medicines. Smoking is not a good way to take any medication because carcinogenic substances are inhaled into the lungs. More research is needed to develop other ways of administering the active ingredient of marijuana for medical use (Cancer Council New South Wales).

The National Cancer Institute, USA, refers to Cannabis as a complementary and alternative medicine (CAM). It also states that Cannabis and its components can be used as a treatment for people with cancer-related symptoms caused by the disease itself or its treatment (National Cancer Institute).

This summary of the National Cancer Institute contains the following key information:

- Cannabis has been used for medicinal purposes for thousands of years
- By federal law, the possession of Cannabis, also known as marijuana, is illegal in many of the states in the United States
- The U.S. Food and Drug Administration has not approved Cannabis as a treatment for cancer or any other medical condition
- Chemical components of Cannabis, called cannabinoids, activate specific receptors found throughout the body to produce pharmacologic effects, particularly in the central nervous system and the immune system
- Commercially available cannabinoids, such as dronabinol and nabilone, are approved for the treatment of cancer-related side effects
- Cannabinoids may have benefits in the treatment of cancer-related side effects.
The potential benefits of medicinal Cannabis for people living with cancer include antiemetic effects, appetite stimulation, pain relief, and improved sleep. Although few relevant surveys of practice patterns exist, it appears that physicians caring for cancer patients in the United States who recommend medicinal Cannabis predominantly do so for symptom management (National Cancer Institute).

Historically, the use of medical Cannabis principally was administered by smoking, but over the last 40 years there have been pharmacological advances in the way that cannabinoids are utilised for medicinal purposes (Kennen, 2008, Pertwee, 2006).

Cannabinol was the first of the plant cannabinoids to be discovered from a red oil extract of the cannabis plant at the end of the 19th Century. From this discovery, the chemical structure of the plant was revealed in the early 1930’s and from that a synthetic chemical structure was developed in the USA in the 1940’s. Cannabidiol (CBD) was isolated shortly afterwards. Following on from these discoveries, THC was first isolated from the cannabis plant in 1942 and together with CBD were synthesised in 1963 (CBD) and 1964 (THC).

While pharmacological experiments with the early cannabinoids occurred as early as the 1940’s/50’s, it was the 1960’s and 1970’s that saw testing of cannabinoids increase markedly. These experiments and trials were spurred on at the time by a virtual explosion of marijuana/cannabis use amongst young people in particular across the Western world (Pertwee, 2006).

In the mid 1980’s it was discovered that cannabinoid receptors exist within the human body and that THC was able to bind to these receptors to either act with them or block them (Pertwee, 2006 & Kennen, 2008). The two receptors are known as CB1 and CB2 receptors. CB1 receptors are located primarily in the brain and CB2 receptors are located primarily in the immune cells (Kennen, 2008). With the discovery of the cannabinoid receptors within the body, the development of synthetic cannabinoids that influence these receptors took place in the 1980’s/1990’s (Pertwee, 2006).

Cannabinoids have been used successfully since these discoveries (in those regions where cannabinoid treatment is legalised, similarly to its use in ancient times) to reduce pain and discomfort in people with debilitating diseases and conditions such as cancer (the nausea and vomiting caused by chemotherapy), multiple sclerosis (the muscle spasticity associated with it, and epilepsy) and the neuropathic pain and body wastage associated with HIV/AIDS and cancer (Seamon, et al, 2007).

Currently there are two forms of medicinal cannabinoids used in reducing pain in people living with HIV while also stimulating the appetite. These are smoked Cannabis and oral tetrahydrocannabinol (THC, dronobinol and marinol). The difference between each is significant. Oral THC is considered safe, is delivered in standardised doses but has a slow onset (peak effects in around 120 minutes). However, due to this slow onset, users find it difficult to regulate the dose to achieve the required effect. Conversely, smoked Cannabis has a relatively rapid onset and its effects can be felt almost immediately (Seamon, et al, 2007), with peak effects felt in users in around 20 minutes (Haney, et al, 2005). The cannabinoid travels from the lungs to the blood stream and to a number of the body’s organs expeditiously (Seamon, et al, 2007) and as such, users can more closely regulate the dose that is necessary to deliver the required effect (Haney, et al, 2005).

According to the AIDS Council of South Australia, cannabinoids that are currently on the market in the USA and Europe include:

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HU-211 (Dexanabinol) which is used to treat endotoxic shock, ischaemia and head trauma

Dronabinol (Marinol) is a cannabinoid prescribed as an appetite enhancer primarily for people who have HIV/AIDS, people being treated with chemotherapy and gastric bypass patients

Nabilone (Cesamet) is a synthetic copy of THC that is used to treat pain and nausea

Sativex is a nasal spray that is used to alleviate neuropathic pain and spasticity in multiple sclerosis patients

Rimonabant which is an appetite suppressant used to decrease the appetite in Cannabis smokers (Kennen, 2008).

In the United States of America patients can access medicinal Cannabis if they have been diagnosed with the following conditions/diseases:

- HIV/AIDS
- Cancer
- Multiple Sclerosis
- Spinal cord injury/disease
- Severe arthritis
- Epilepsy
- Or as part of a palliative care treatment programme

There is evidence that medicinal Cannabis/cannabinoid use aids in reducing pain and other health effects associated with illnesses and conditions such as cancer, multiple sclerosis, epilepsy, the treatment of glaucoma and secondary conditions related to HIV/AIDS (Johns, 2004). According to research, the reported benefits of Cannabis/cannabinoid use include the following:

- The control of nausea and vomiting
- The control of muscle spasticity and anti-convulsant effects
- Pain management
- Increasing appetite
- Bronchodilation (asthma treatment)

(Cannabis smokers (Kennen, 2008).)

Cannabinoids, chemical substances isolated from Cannabis, have been shown to produce pharmacologic effects, particularly in the central nervous system and the immune system. Cannabinoids may have benefits in the treatment of cancer-related side effects. However, there are no currently commercially synthetic cannabinoid-containing or THC-containing medicines available in South Africa because of the complex and strict legislation controlling Cannabis in South Africa.

CANSAs became aware that synthetic cannabinoids have become available on the streets of America as recreational drugs (see text box below). This further places pressure on any possible recognition of Cannabis or any of its cannabinoids including any of the synthetic cannabinoids.
Pharmacology of Cannabis

The active ingredients of cannabis, cannabinoids, refer to a group of related compounds that include cannabidiol and the active constituents of cannabis. These compounds activate cannabinoid receptors in the human body. Cannabinoid receptor activation by agents such as Δ(9)-tetrahydrocannabinol (THC) is known to trigger immune suppression. In a research study by Hedge, et al. (2010) it was found that administration of THC in mice leads to rapid and massive expansion of CD11b(+)Gr-1(+) myeloid-derived suppressor cells (MDSC) expressing functional arginase and exhibiting potent immunosuppressive properties both in vitro and in vivo. Their study demonstrated that cannabinoid receptor signalling may play a crucial role in immune regulation via the induction of myeloid-derived suppressor cells.

Cannabinoid receptors are activated by three major groups of ligands, endocannabinoids (produced by the mammalian body), plant cannabinoids (such as THC, produced by the cannabis plant) and synthetic cannabinoids (such as HU-210). All of the endocannabinoids and plant cannabinoids are lipophillic, i.e. fat soluble, compounds.

Recent research has shown that cannabinoids has the ability to reduce cancer cells as they have a great impact on the rebuilding of the immune system. While not every strain of cannabis has the same effect, more and more patients are experiencing success in cancer reduction in a short period of time by using cannabis. Because of the dangers associated with smoking cannabis, it is said that ingesting cannabis is the best option.

After oral administration, maximal effects occur after 1 hour or more and may last from 5 to 6 hours because of continued absorption from the gut. Some psychomotor and cognitive effects persist for much longer. Cannabinoids can also cross the placenta, enter the foetal circulation and penetrate into breast milk. It is, therefore not wise to use cannabis when pregnant of breastfeeding. Cannabis accumulates in fatty tissues from where it is released slowly back into the bloodstream. Because of this, elimination from the body is extremely slow and can take many days. With repeated dosage, cannabinoids accumulate and continue to reach the brain over a longer period (Kumar, et al, 2001).

Cannabis and the Treatment of Cancer

The Cancer Association of South Africa (CANSA) lauds Mr Oriani-Ambrosini (MP) who, last year, was diagnosed with stage four, inoperable lung cancer, for raising the issues around cannabinoids and the treatment of cancer using of cannabinoids in Parliament on 19 February 2014. This was followed by Mr Ambrosini submitting a private member’s bill to Parliament called the Medical Innovation Bill published in the Government Gazette of 18 February 2014.

The purpose of the Bill is to make provision for innovation in medical treatment and to legalise the use cannabinoids for medical purposes and beneficial commercial and industrial uses. The Bill is currently under discussion by the Ministerial Advisory Committee on Cancer.

CANSA will follow the Committee’s deliberations and will adapt its Fact Sheet
and Position Statement with regard to the use of cannabinoids in the treatment of cancer accordingly.

CANSA wishes to acknowledge the following research outcomes. This is only a short representative selection of the multitude of research publications on the use of cannabis in the treatment of various cancers:


**Gustafsson, K., Christensson, B., Sander, B. & Flygare, J.** 2006. Cannabinoid receptor-mediated apoptosis induced by r(+)-methanandamide and Win55,212-2 is associated with ceramide accumulation and p38 activation in Mantle cell lymphoma. Mol Pharmacology, 70:1612-1620. The present data suggest that targeting cannabinoid receptor-1 and cannabinoid receptor-2 may have therapeutic potential for the treatment of mantle cell lymphoma.


Ligresti, A., Moriello, A.S., Starowicz, K., Matias, I., Pisanti, S., De Petrocellis, L., Laezza, C., Portella, G., Bifulco, M. & Di Marzo, V. 2006. Anti-tumor activity of plant cannabinoids with emphasis on the effect of cannabidiol on human breast carcinoma. This study investigated the anti-tumour activities of other plant cannabinoids, i.e. cannabidiol, cannabigerol, cannabichromene, cannabidiol-acid and Δ⁸-tetrahydrocannabinol. Cannabidiol was the most potent inhibitor of cancer cell growth.

Massi, P., Vaccani, A., Ceruti, S., Colombo, A., Abbracchio, M.P. & Parolaro, D. 2001. Antitumor effects of cannabidiol, a non-psychoactive cannabinoid, on human glioma cell lines. http://www.ncbi.nlm.nih.gov/pubmed/14617682. This study showed that the non-psychoactive cannabidiol was able to produce significant antitumour activity in vitro and in vivo, thus suggesting a possible application of cannabidiol as an antineoplastic (inhibiting or preventing the growth and spread of tumours or malignant cells) agent.


The findings of this research support that the combined administration of TMZ and cannabinoids could be therapeutically exploited for the management of glioblastoma multiforme (most common and most aggressive malignant primary brain tumour in humans).


**CANSA’s Position**

CANSA cannot support the use of Cannabis in any form as it is still an illegal substance in South Africa. Smoking is also dangerous to health – whether one speaks of tobacco products or Cannabis. It is still not clear whether the health risks associated with the use of Cannabis outweighs the benefits thereof.

CANSA supports the World Health Organization in its guidelines for the control of cancer pain. To this end CANSA believes that there are medicines available for the control of pain. Morphine is one of the drugs of choice for the control of severe pain and is also available at a reasonable cost.

CANSA is also of the opinion that there are sufficient medicines available in South Africa for the effective treatment of nausea, vomiting and other conditions related to cancer including end-of-life care.

CANSA can further not support the use of synthetic cannabinoids and/or THC at present while these medicines are still not available in South Africa. Whenever a decision is taken to allow the legal importation and/or manufacture of medicines containing synthetic cannabinoids in South Africa, CANSA will investigate the cost effectiveness of such products and will again consider its position in this regard.

**Medical Disclaimer**

This Fact Sheet is intended to provide general information only and, as such, should not be considered as a substitute for advice, medically or otherwise, covering any specific situation. Users should seek appropriate advice before taking or refraining from taking any action in reliance on any information contained in this Fact Sheet. So far as permissible by law, the Cancer Association of South Africa (CANSA) does not accept any liability to any person (or his/her dependants/estate/heirs) relating to the use of any information contained in this Fact Sheet.
Whilst the Cancer Association of South Africa (CANSA) has taken every precaution in compiling this Fact Sheet, neither it, nor any contributor(s) to this Fact Sheet can be held responsible for any action (or the lack thereof) taken by any person or organisation wherever they shall be based, as a result, direct or otherwise, of information contained in, or accessed through, this Fact Sheet.

In 2010, in the United States of America, an estimated 11 406 emergency department (ED) visits involved a synthetic cannabinoid product, sometimes referred to as “synthetic marijuana” and commonly known by street names such as “Spice” or “K2.” Three fourths of these ED visits involved patients aged 12 to 29 (75 percent), of which 78 percent were male.
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Ambrosini
https://www.google.co.za/search?q=ambrosini+cancer&source=lnms&tbm=isch&sa=X&ei=R E4HU-__kPMr07Aa9fHQAo&ved=0CAcQ_AUoAQ&biw=1120&bih=661&dpr=0.9#facrc= &imgdii= &imgres=0XBJOs_G_JNI8LM%253A%3B90LBuEVxYt8QVM%3Bhttp%253A%252F%252Fwww.iol.co.za%252Fpolopoly_fs%252Fiol-news-pic-oriani-ambrosini-1.1649726%252Fimage%252F944389835.jpg%3Bhttp%253A%252F%252Fderivatives%252Fbox_300%252F944389835.jpg%3Bhttp%253A%252F%252Fwww.iol.co.za%252Fnews%252Fpolitics%252F Fill-mp-to-introduce-dagga-bill-1.1649727%3B300%3B225

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Cannabis and the Treatment of Cancer

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My Broadband

National Cancer Institute

No Cannabis
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Pharmaceutical Cannabinoids
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