

# Cannabis in Medicine - an Option?

## **The German Model**

From Patient Initiative to Providing Dronabinol Preparations

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# Marihuana plant



# The early products

Cannabis as an established medication up to WW II



# The 20th Century at a glance

- Cannabis extracts are very commonly used, primarily for their capacity to reduce, pain, nausea and spasticity
- massive price increase of the raw material after WW I
- Introduction of more specific medications which are able to target the disease rather than the symptom alone (vaccines)
- 1930 USA: founding of the "Federal Bureau of Narcotics" and beginning stigmatisation of cannabinoids by Harry J. Anslinger
- The widespread use of drugs during the late 60´ s leads to a virtual stop of the academic research into the medical potential of psychotropic substances as a whole. Cannabis is no exception.

# Historical Background

## 4 Trends Working Against Cannabis Extracts

- **Stigmatisation of Cannabis in the US and other countries with severe legal implications after 1937**
- **Persisting problems with standardization and stabilisation**
- **A general perception that the „NEW“ man made synthetic products are superior to the „OLD“ natural products**
- **Increasing focus on Intellectual Property and Patents in the Pharmaceutical Industry**

# The Rediscovery of Cannabinoids

- **1964**

Raphael Mechoulam and colleagues succeed in isolating the principal psychoactive constituent of Cannabis (Delta -9-tetrahydrocannabinol or „Dronabinol“) at Hebrew University, Israel

- **1980**

National Cancer Institute (NCI) developed and distributed Marinol® (The natural occurring Isomer of Delta 9 THC or Dronabinol) to cancer patients in San Francisco. The patent is sold one year later to Unimed Pharmaceuticals in New Jersey

- **1985/86**

Marinol® is granted a US license for the treatment of chemotherapy-induced nausea and emesis and for AIDS wasting syndrom. Unimed partners with Roxanne Laboratories as a distributor.

# Medicinal Cannabis in Germany

## Limitations for medicinal Cannabis :

- Prescription of Marijuana or Hash for medical purposes is in principal illegal with a number of narrowly defined exceptions
- Very difficult to find a defined dosage
- Sources tend to be illegal or expensive / no reimbursement
- Smoking as a mode of application for the medical use is generally not accepted due to the associated health risks
- Contamination risk remains high (e.g.: pesticide, mold..)

# The Specific Development in Germany

- **1995**

After having suffered a spinal cord injury in a car accident, Dr. Joachim Hartinger (like many others in German rehabilitation clinics) treats the associated painful spasticity with cannabis

**1996**

THC Pharm GmbH is founded by Dr. Hartinger and three other friends in order to create safe and legal access to prescribable cannabinoids for patients

- **1997**

Applications for the production of Cannabis extracts are turned down, The authorities do not grant licenses (but search warrants)

- **1998**

For the first time in Germany, Dronabinol by THC Pharm ist made available through the Bockapotheke in Frankfurt.



# 3 Ways To Produce the Same Product

- **From Thc rich Cannabis**

Prohibited by law in Germany until 2011

- **from fibre hemp**

The process developed by Christian Steup allowed the production of Dronabinol from a self produced fibre hemp extract. Cannabidio (CBD) is extracted, purified and converted into Dronabinol. However, variations in crop and harvest can pose a problem.

- **Fully synthetic (developed on request by Swiss authorities)**

using natural (but not hemp) starter products, CBD is produced which in turn is converted into Dronabinol (up to 99 %) . This process allows for easy scale up and is not limited in the first stages by the demands of good agricultural practice and the controlled substance act.

# The new approach



Informationen unter [www.thc-pharm.de](http://www.thc-pharm.de) oder 0800 - dronabinol

## Magistral Preparation versus Finished Dosage Form

### PRO:

- Indications are not limited
- Easy to titrate
- Fast track for unmet medical need
- Forms of application can be adapted to need of individual:
- Dronabinol Oily drops from 0.2 – 5 % THC
- Dronabinol Capsules with 2,5 mg / 5 mg / or 10 mg THC
- Dronabinol drops in ethanol for inhalation with 5 % THC

### CONTRA:

- Weak IP protection
- Limited clinical data available
- Very complex Status with Insurance Companies

# Different Forms of Applications

- Oily Drops  
(Mygliol, Sesame Oil)



- Inhalation of alcoholic Drops with an  
Inhaler Device (Volcano)

- Hard capsules (softisan)



# Dronabinol

- Defined Purity and concentration
- Defined Stability of 48 months (THC Pharm)
- Easy to dose and to titrate
- Low toxicity and well tolerated (5 -10.000 patients treated so far)



# Indications I

- complementary Therapy in Palliative Care
- Appetite Stimulation in Cachexia und AIDS Wasting  
Syndrom
- Therapy –resistent Nausea and Emesis

## Indications II

- Neurologic Syndroms  
(i.e. Tourette Syndrom)
- Spasticity / Multiple Sclerosis
- Therapy-resistant pain / neuropathic pain
- Glaucoma
- COPD

# Dosage recommendations

- Appetite stimulation and cachexia  
1 – 3 x 2,5 mg – 3 x 5 mg / day
- nausea and vomiting (higher dosage post Chemotherapy)  
3 x 2,5 mg - 5 x 10mg / day
- spasticity in tetraplegic and multiple sclerosis patients  
2 x 5mg - 3 x 10mg / day
- pain in cancer patients  
3 x 2,5mg - 4 x 10mg / day



## Dosage scheme

	in 10 ml	Oily drops
1,5%	150 mg	2 drops = 1 mg
2,5%	250 mg	3 drops = 2,5 mg
5 %	500 mg	3 drops = 5 mg

# Starter set for pharmacists



# The German Market at a Glance

- approx. 8 – 12 Kg of Dronabinol consumed annually
- approx 1500 – 5000 patients receive Dronabinol in one year
- 80 % of the market is oily drops
- 18 % capsules
- 2 % inhalation
  
- approx 2 – 3000 pharmacies have experience with Dronabinol
- is restricted to a group of narrowly defined MS patients
- several dozen patients can buy medicinal cannabis flos

# Reimbursement of Cannabinoids

- Dronabinol partially reimbursed (approx. 30 – 40 % of prescriptions)
- No reimbursement for standardized cannabis extract as magistral preparation
- No reimbursement for cannabis flos
- Sativex is reimbursed (but only for MS patients with severe spasticity and when all other therapies have failed)

# Reimbursement of Dronabinol I

- Dronabinol is regularly reimbursed until 2002
- Ground breaking legislation by the German Federal Constitutional Court eases prescription in 2005
- Federal social security Court tightens the rules for reimbursement again in 2007
- After 2007, Health Insurers increasingly refuse to pay for Dronabinol as an analgesic with the exception of the use in palliative care

# Reimbursement of Dronabinol II

- First Parliamentary Debate, initiated by THC Pharm on the Medicinal Use of Cannabinoids and the Reimbursement of Dronabinol in October 2008
- Individual negotiations of THC Pharm with one of the biggest German Health Insurers to resolve the issue break down in 2009
- New Initiatives to achieve a more reliable reimbursement for specialized palliative care patients and paediatric patients are started in 2011 / 2012
- During the second parliamentary debate in 2012 all medical professions confirm the medical benefit of cannabinoids and oppose the idea of uncontrolled growing by patients.

Thank you very much for your attention

**THC Pharm GmbH**