Review

Medical cannabis for chronic pain management: questions and answers between clinical and medico-legal issues

V. Schweiger[1], B. Ganz[2], A. Martini[1], P. Sarzi-Puttini[3,4], L. Bazzichi[3], E. Bonora[1], P. Vendramin[1], M. Nizzero[1], L. Zamboni[5], L. Polati[1], F. Lugoboni[5], D. Raniero[6], E. Polati[1], G. Del Balzo[6]

[1]*Department of Anaesthesia, Intensive Care and Pain Therapy, University of Verona;*
[2]*Pain Therapy Centre, Palagi Hospital, Firenze;*
[3]*Department of Rheumatology, IRCCS Galeazzi-Sant'Ambrogio Hospital, Milano;*
[4]*Department of Biomedical and Clinical Sciences, University of Milan;*
[5]*Medical Service for Addictive Disorders, University Hospital G.B. Rossi, Verona;*
[6]*Department of Diagnostics and Public Health, Section of Forensic Medicine, University of Verona, Italy.*

Vittorio Schweiger, MD, Prof
Barbara Ganz, MD
Alvise Martini, MD
Piercarlo Sarzi-Puttini, MD, Prof
Laura Bazzichi, MD
Eleonora Bonora, MD
Patrizia Vendramin, MD
Marta Nizzero, MD
Lorenzo Zamboni, MD
Luca Polati, MD
Fabio Lugoboni, MD
Dario Raniero, MD
Enrico Polati, MD, Prof
Giovanna Del Balzo, MD

Please address correspondence to:
Vittorio Schweiger
Scienze Chirurgiche Odonto-stomatologiche e Materno-Infantile, Policlinico G.B. Rossi,
P.le L.A. Scuro 10,
37134 Verona, Italy.
E-mail: vittorio.schweiger@univr.it

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ABSTRACT

Medical cannabis (MC) has gained prominence in recent years as a potential therapeutic option for various diseases, with a particular focus on chronic pain syndromes. While its efficacy remains uncertain, the global prescription rates of MC are significantly increasing. Therefore, pain therapists must be well-informed about several aspects of MC treatments, including efficacy, safety, indications, contraindications, pharmacological interactions, dosages, possible adverse events (AEs), such as the risk of addiction, and medico-legal considerations. Based on the available literature, the efficacy of MC on pain of different origins was described by the majority of authors as statistically significant compared to placebo, with a mean reduction in NRS scale (0-10) from baseline between -0.43 and -0.70. The incidence of serious AEs was rare; however, MC may significantly increase AEs such as dizziness, tiredness, drowsiness and nausea. Common AEs included dry mouth, diarrhoea, constipation and euphoria. Absolute contraindications to MC include unstable cardiovascular diseases, psychotic symptoms, bipolar disorder, both ongoing and/or planned pregnancy and breastfeeding. Regarding addiction, the risk of cannabis use disorder (CUD) according DSM-V is about 29%. From a medico-legal perspective, the Italian legislation considers the MC a symptomatic support to standard treatments and accurately regulates its prescription on part of physicians. Moreover, the pain therapist must inform the patient about the legal implications of MC on driving (in relation to disability and license eligibility), work impairment, insurances, and the possession of firearms, in order to prevent possible negative repercussions on patients, on other subjects and on the pain therapists themselves.

Introduction

The term *cannabis* refers to a genus of angiosperm plants in the Cannabaceae family. Botanically, the main plant type is the *Cannabis Sativa*, while the other varieties (*C. Indica* and *C. Ruderalis*) are considered different phenotypes of the primary species (1). Beyond its use in textile production, cannabis plays an important role in human health due to its phytocannabinoid compounds. These products, such as D-9 tetrahydrocannabinol (THC), the cannabidiol (CBD), the D-9 tetrahydrocannabivarin (THCV) and the cannabinol (CBN), are derived from mixtures of dried female inflorescences of Cannabis, commonly known as *Marijuana* or *Hashish*. The phytocannabinoid content, particularly THC (arguably the most active compound), can vary significantly among different phenotypes (2). The human use of cannabis dates back more than 5.000 years, primarily for the production of textiles. In the Far East (China, India, Nepal), cannabis was also used in ancient times during religious ceremonies to induce sensory alterations and, in the form of beverages or smoke, to alleviate pain and toothaches. Due to the repeated migrations from the Far East, cannabis arrived in the Mediterranean basin and later spread throughout Europe. The medical use of cannabis-derived products began in the United States with its introduction in the U.S. Pharmacopoeia in 1850 for the treatment of various diseases (3). However, the approval of the Marijuana Tax Act in 1937 led to cannabis being excluded form medical use in the U.S. due to its

psychoactive properties and the imposition of legal penalties for possession (4). It was not until 1996 that California became the first state to allow legal access to cannabis for medicinal purposes under physician supervision, with the enactment of the Compassionate Use Act (5). In Italy, medical cannabis (MC) regulations are relatively recent, and cannabis was legalised for medical purposes only in 2018 (6). In recent years, MC has emerged as a potential pharmacological treatment for various diseases including chronic pain syndromes, particularly those of neuropathic origin (7). Additionally, MC has been considered for other types of chronic pain, including painful rheumatological diseases and fibromyalgia (8-11). Although its efficacy across different pain scenarios remains uncertain, global consumption and prescription trends of these products have increased significantly. Patterns of use and indications vary between countries (12). In Italy, the total national MC consumption increases from 58.590 grams in 2014 to 1.694.800 grams in 2024 (13). Similarly to other pain medications, such as opioids, MC prescriptions are subject to medical considerations, including indications, efficacy, contraindications and adverse events (AEs), as well as prescriptive and legislative regulations. Current observations suggest that while healthcare providers generally believe MC to be a useful therapeutic option for various pathological conditions, particularly chronic pain, many aspects regarding its efficacy, AEs and medico-legal implications require further clarification (14). To fully educate the patient and answer their concerns, MC prescribers must have an in-depth understanding of these treatments, both from a clinical and a medico-legal perspective, avoiding reliance on personal opinions. The aim of this review is to provide a practical and updated resource to highlight the scientific and medico-legal aspects of MC treatments for patients with chronic pain.

Clinical considerations

MC efficacy and safety in the setting of chronic pain treatment

With the increasing use of MC for chronic pain syndromes in recent years, numerous studies have been conducted and are now available in the literature. Since 2018, approximately 18 systematic reviews and meta-analyses have been published, evaluating the efficacy and safety of various MC products (both natural and synthetic) for different types of chronic pain. Table I summarises studies comparing MC treatments to placebo in randomised controlled trials (RCTs).

As previously mentioned, the efficacy of MC in pain management has been labelled by all authors as statistically significant when compared to placebo, but across all studies, the mean reduction in the NRS scale (0-10) from baseline ranged between -0.43 and -0.70 (15-21). This reduction, generally categorized by the same authors as very small, small, or moderate, consistently falls below the minimally important difference (MID) in pain scores required to achieve clinically significant improvement for patients (22). However, in chronic pain treatment, the MID cut-off in pain scores remains controversial and is influenced by various factors, including the specific pain conditions under which it has been evaluated (22). For these reasons, other parameters were used to evaluate improvements in quality of life (QoL) among patients undergoing MC treatment for chronic pain, such as health-related quality of life (HRQoL). Also, these outcomes demonstrated statistically significant small to moderate improvements. However, the MID in HRQoL scores required to establish a clinical relevance remains a subject of debate (23-24). Conversely, surveys conducted among patients to assess the perceived clinical significance of MC in managing chronic pain arising from various conditions revealed notable improvements in both pain levels and QoL. These findings align with and reinforce the results of previous quantitative studies carried out across multiple countries (25). Similarly, a review of 49 studies involving patients undergoing MC treatment for chronic musculoskeletal pain revealed comparable positive outcomes (26). This discrepancy between the perceived substantial improvements in pain and QoL and the limited pain reduction observed in available randomized controlled trials (RCTs) may be attributed to the pharmacological complexity of MC and its beneficial effects on anxiety, depression, and sleep disturbances (27). Moreover, the lack of standardisation in MC products, the challenges associated with conducting randomised, double-blind, placebo-controlled clinical trials, and the complex role of the placebo effect mediated by the endocannabinoid system significantly hinder the scientific evaluation of MC in humans (28). Furthermore, current evidence does not support the superiority of specific MC products or routes of administration in managing one type of pain over another (7). Similarly, the evidence for differences in the efficacy of MC in treating chronic cancer pain versus non-cancer pain remains inconsistent. Based on the available data, the EFIC Position Paper on the appropriate use of MC for chronic pain management recommends its use as an adjunctive treatment when guideline-recommended first- and second-line therapies have proven insufficient in efficacy or tolerability. It emphasises the importance of defining realistic therapeutic goals and tailoring treatments to individual patient needs (29). Finally, in 2021, the International Association for the Study of Pain (IASP) highlighted the high number needed to treat (NNT) associated with MC use in chronic non-cancer pain. Due to the lack of robust clinical evidence, the IASP has yet to endorse the widespread use of MC for pain relief in this context (30). Regarding safety, the incidence of serious AEs was rare according to all considered studies. Nevertheless, there is agreement between Authors that MC significantly increase AEs from Central Nervous System (CNS) like dizziness, tiredness, drowsiness and nausea. Other reported common AEs were dry mouth, diarrhoea, constipation and euphoria. Most of the reported AEs are similar between different types of MC and were of mild to moderate intensity and generally well tolerated. Most clinical trials did not report relevant psychoactive effects related to MC treatment (15-21).

Table I. Summary of the studies evaluating the randomised controlled trial (RCT) of MC treatments *vs*. placebo.

Authors (year, ref)	Patients (n)	MC Products	Pain type	Follow-up	Outcomes (pain intensity)	Effect size on pain intensity (Cohen's category)
Mücke *et al*. 2018 (15)	1750	PDC of THC/CBD Nabilone Inhaled herbal Dronabinol	Chronic neuropathic pain	2-26 weeks	NNT 50%: 20	0.2
Yanes *et al*. 2019 (16)	2248	PDC of THC/CBD Synthetic cannabinoids	Acute and chronic pain	n.a.	NRS-MD: -0.43	Between 0.5 and 0.8
Wong *et al*. 2020 (17)	3444	PDC of THC/CBD Synthetic cannabinoids	Chronic non-cancer pain	12-16 weeks	NRS-MD: -0.70	n.a.
Johal *et al*. 2020 (18)	4006	PDC of THC/CBD Inhaled herbal Synthetic cannabinoids	Chronic non-cancer pain	2 weeks	NRS-MD: -0.68	n.a.
Wang *et al*. 2021 (19)	5174	PDC of THC/CBD Synthetic cannabinoids	Chronic cancer and non-cancer pain	≥ 4 weeks	NRS-MD: -0.50	n.a.
McParland *et al*. 2022 (20)	1051	PDC of THC/CBD Synthetic cannabinoids	Chronic neuropathic pain	2-15 weeks	NRS-MD: -0.55	n.a.
Barakji *et al*. 2023 (21)	7017	PDC of THC/CBD Inhaled herbal Synthetic cannabinoids	Acute and chronic pain	1 day-14 weeks	NRS-MD: -0.43	n.a.

PDC: products derived from Cannabis; THC: tetrahydrocannabinol; CBD: cannabidiol; NNT: number needed to treat 50%; NRS: numerical rating scale; MD: mean difference; MC: medical Cannabis; n.a.: not available.
Cohen's effect size categories: 0.2: minimal clinically important improvement, 0.5: medium clinically important improvement, and 0.8: large clinically important improvement.

Navigating the efficacy of MC in rheumatic pain

Recent research highlights the increasing interest in MC as a therapeutic option for managing chronic pain in rheumatological disorders, a hallmark feature of conditions such as rheumatoid arthritis (RA), osteoarthritis (OA) and spondyloarthropathies. The persistent nature of chronic pain, combined with the challenges in effectively treating rheumatologic pain, has prompted this patient population to explore alternative treatments, including MC, due to the limitations of conventional therapies. The rationale for considering cannabinoids as a treatment option in rheumatology lies in their established ability to interact with the endocannabinoid system, modulating both pain and inflammation. Animal studies have demonstrated that certain cannabis compounds, including CBD, cannabigerol (CBG), and a combination of CBD and THC, can consistently reduce pro-inflammatory cytokines (31). This has been further supported by a growing body of literature, which provides initial evidence of MC's potential to alleviate pain and improve associated symptoms such as sleep disturbances and anxiety in patients with rheumatological disorders. Since the first studies on MC in rheumatologic conditions in the early 2000s (32), which focused primarily on its effects on chronic pain and inflammation, research has expanded to explore its impact on related symptoms such as sleep disturbances and anxiety. These findings suggest that MC may have dual benefits: alleviating pain and improving associated symptoms (33-36). Additionally, Rampakakis *et al*. reported that MC use among rheumatology patients in Ontario was higher compared to the general population, with pain identified as the most commonly treated symptom (37). Ouatah *et al*. echoed similar observations in a letter to the editor published the same year, noting active cannabis use for symptom management among patients with RA or spondyloarthropathies. Their findings highlighted reduced pain intensity and improved QoL following MC use (38). Nonetheless, rheumatologists researching this topic have expressed concerns regarding the lack of robust evidence, including the absence of large-scale RCTs, the need for standardisation, and gaps in knowledge about long-term effects. These limitations make it challenging to interpret and reliably endorse the purported benefits of MC in the rheumatologic setting.

Contraindications to MC: a therapeutic solution with limited restrictions

According to the recent literature, absolute contraindications to MC include unstable cardiovascular conditions (*e.g*. acute congestive heart failure, critical aortic stenosis, poorly controlled atrial fibrillation and coronary artery disease and others), due to THC's potential to cause acute cardiovascular effects such as tachycardia and postural hypotension (39). Smoked MC preparations should also be avoided in patients with acute or chronic respiratory diseases as they may worsen respiratory symptoms. Conversely, oral forms of MC are considered safe for these patients. MC is contraindicated in individuals with psychosis or bipolar disorder, as it may exacerbate symptoms or trigger psychotic

episodes in susceptible patients, particularly those with genetic predisposition or a history of early life stressors, but also consequently to an early age of initiation and regular cannabis use, the use of high THC-containing products, and a personal or family history of these conditions. Additionally, the use of MC is contraindicated during pregnancy or while planning a pregnancy, as it poses potential risks to foetal development and neonatal morbidity, which are particularly pronounced in the first trimester. MC use must be avoided during breastfeeding for transplacental diffusion (40). In patients under 25 years, exposure to high doses of THC and regular use has been associated with risks such as persistent cognitive impairment, social dysfunction, anxiety, depression, and cannabis dependence. Consequently, MC products, particularly those containing THC, are relatively contraindicated in patients with an active or prior history of cannabis use disorder (CUD) or other substance abuse (40). In individuals with severe liver or renal dysfunction, as well as those with chronic hepatitis type C, MC treatment requires careful evaluation due to the increased risk of developing or exacerbating hepatic steatosis. Due to physiological changes associated with aging, such as reduced fat-free body mass, impaired cognitive function, decreased metabolic capacity, and varying degrees of organ dysfunction, initiating treatment with MC in elderly patients must be approached with caution. AEs may be more frequent and pronounced, and the risk of drug interactions is higher. Therefore, in this specific population, low-dose regimens and slow titration strategies are recommended. Another group of patients in whom MC treatment should be approached with caution is immunocompromised individuals. Cannabis products from regulated sources are preferable due to cannabis inherent risk of contamination. Furthermore, cannabinoids have been shown to exhibit anti-inflammatory and immunomodulatory effects at both molecular (cytokines) and cellular (primarily lymphocytes) levels. Therefore, in cases of immune dysregulation, MC treatment should be initiated with full awareness of the specific risks by both the patient and prescriber and maintained under stricter follow-up schedules. Absolute and relative contraindications, along with precautions for MC treatment are summarised in Table II.

Table II. Absolute/relative contraindications and precautions of MC treatment. Specific precautions and considerations should be considered before initiating treatment with MC for the listed conditions.

Contraindications and precautions of MC treatment
Absolute contraindications
Unstable cardiovascular diseases
Acute or chronic respiratory diseases (only for smoke preparations)
Personal or strong family history of psychosis or bipolar disorders
Pregnancy, planning a pregnancy and breastfeeding
Relative contraindications
Past or current CUD
Past or current substance use disorder
Patients <25 Years of age
Precaution and special considerations
Severe liver and/or renal dysfunction/disease
Medications associated with sedation or cognitive impairment
Medications metabolised by cytochromes P450 (particularly CYP3A4)
Strong inducers/inhibitors of cytochromes P450
Elderly patients
Immunocompromised patients

MC: medical Cannabis; CUD: Cannabis use disorder .

Pharmacological interactions of MC: main considerations

From a pharmacokinetic perspective, MC is metabolised through isoenzymes of the cytochrome P450 system. Drugs that interfere with these enzymes can either enhance the effects of MC and its associated AEs or diminish its efficacy through metabolic induction. For instance, the concurrent use of certain antibiotics (*e.g.* rifampicin, clarithromycin, erythromycin), antifungals (*e.g.* itraconazole, fluconazole, ketoconazole, miconazole), and HIV protease inhibitors (*e.g.* ritonavir) can increase the bioavailability of MC. Conversely, other drugs, such as carbamazepine, phenobarbital, phenytoin, primidone, rifabutin, troglitazone, and Hypericum perforatum (St. John's wort), tend to accelerate MC metabolism, thereby reducing its pharmacological efficacy. Additionally, the inhibitory action of THC and CBD on specific cytochrome P450 isoenzymes may amplify the pharmacological effects of drugs such as amitriptyline, phenacetin, granisetron, dacarbazine, and flutamide. Notably, CBD is a potent inhibitor of CYP3A4, necessitating dose adjustments for therapies involving CYP3A4 substrates, particularly medications with a narrow therapeutic index (*e.g.*, tacrolimus). From a pharmacodynamic perspective, the concurrent use of central nervous system (CNS) depressants may result in additive effects of MC, such as sedation or cognitive impairment, which are critical concerns for prescribers. MC can potentiate the sedative effects of psychotropic substances, including alcohol, benzodiazepines, antidepressants (*e.g.* fluoxetine, fluvoxamine, nefazodone), antiepileptics, barbiturates, and opioids (40). Given the extent and complexity of potential drug interactions, clinicians should carefully screen for any potentially interacting medications, including over-the-counter regimens, before initiating MC treatment (40).

MC and cannabis use disorder

The cannabis use disorder (CUD) is defined as the inability to stop consuming cannabis even when it is causing physical or psychological harm (41-42). Until recently, data on CUD primarily originated from studies on recreational cannabis use, with estimated prevalence rates ranging between 8.9% and 22% (43-44). The risk of developing CUD was found to increase four to seven times among individuals who began using cannabis before the age of 18. Moreover, regular use of THC

at higher concentrations (>12.5%) has been linked to an elevated risk of CUD, whereas CBD appears to exhibit protective anti-CUD properties (44). Recent research has also addressed the risk of CUD in patients undergoing MC treatment. In a prospective observational cohort study involving 167 adults treated with MC for pain, insomnia, anxiety, and depression, 11.7% of all participants and 17.1% of those using MC daily or nearly daily developed CUD after 12 months (45). Among 125 patients admitted to an inpatient addiction medicine service (AMS) in southwestern Ontario, Canada, 42% reported exclusive MC use, while 58% reported both MC and recreational cannabis use (dual motives). For CUD, 28% of medical-oly users and 51% of dual-use users met the diagnostic criteria (p=0.016). High psychiatric comorbidities such as anxiety, depression, and PTSD were prevalent among these patients (46). A systematic review of 14 studies involving 3681 participants using MC within the past 6-12 months reported a CUD prevalence of 29% (95% CI: 21–38%) according to DSM-5 criteria. Mental health disorders were strongly associated with an increased risk of CUD (47). Based on this evidence, it is critical to inform MC users for chronic pain about the potential risk of developing CUD. Comprehensive patient evaluations, including assessments of substance use history, screening questionnaires, and regular monitoring, are essential to mitigate the risk of CUD when considering MC treatments (48). Additionally, the latest guidelines recommend avoiding the prescription of MC products with high THC concentrations (>12.5%) (49).

MC discontinuation and cannabis withdrawal syndrome

Numerous studies have investigated AEs leading to the discontinuation of MC. Regarding the cannabis withdrawal syndrome (CWS), data from the recreational use assessed the likelihood of CWS as extremely low and characterised predominantly by craving, anxiety, restlessness, irritability, anorexia, disturbed sleep, vivid dreams, gastrointestinal tract symptoms, night sweats and tremor (50-54). Notably, the majority of CWS were reported in studies with longer follow-up periods. Nevertheless, a recent systematic review and meta-analysis reported the prevalence of CWS among regular or dependent Cannabinoid users of 47%, while the quality of the literature was rated as being low for the majority of the analysed studies (55). However, the risk of CWS in MC user it has not yet been clarified in the literature. For this reason, long-term monitoring of patients undergoing MC therapy remains essential to identify and manage any potential cases of CWS (54). Further research is warranted to reinforce this safety aspect.

MC use and opioid consumption in chronic pain patients

The opioid epidemic in the USA has underscored the need for pharmacological therapies that can reduce or replace opioids in the management of chronic pain. In this context, MC treatment has been considered a potential alternative. A cohort study reported an association between MC treatment and opioid reduction, along with improved QoL (56). However, these findings were not consistently supported by earlier studies (57). More recent evidence suggests that MC may play a significant role in reducing opioid use, although further research is required to substantiate this conclusion (58-59).

MC treatment titration in patients with chronic pain

MC treatment should ideally start with a low dose of non-inhaled CBD products (5 mg once daily), with up-titration by 5–10 mg every 2–3 days, up to a maximum of 40 mg/day, administered twice daily if necessary. If this approach proves ineffective, the addition of 1 mg of THC may be considered, with weekly titration by 1 mg up to a maximum of 40 mg/day, while maintaining the same CBD dose. If the patient does not respond to a 40 mg dose of THC, further dose escalation is not recommended, and a gradual discontinuation should be considered (30). While the differences in treatment effects among various MC formulations, as well as the optimal doses, formulations, and methods of administration for chronic pain remain topics of debate, there is consensus that the daily THC dose should not exceed 40 mg (60). This limit is presently based on expert opinions, due to the lack of confirmatory studies in the literature. If the clinician and patient are considering exceeding the 40 mg daily limit, expert consultation is recommended (61). Furthermore, as previously noted, inhaled forms of cannabis are not advised due to pulmonary risks associated with particulate matter and toxins (60).

Medico-legal considerations in MC prescription and use

MC regulations in Europe

European legislation establishes precise requirements and marketing procedures for MC products across all EU member states (62). However, there is no unified regulatory framework for magistral and officinal preparations containing cannabinoids, as these are exempt from marketing authorisation. Consequently, the regulation of MC products is determined by individual member states and often varies significantly due to cultural and historical considerations (63). Currently, eight European countries (21%) oppose MC, nine (23%) have adopted a pharmaceuticalisation approach (allowing cannabinoid-based pharmaceuticals, but not herbal cannabis), and 22 (56%) embrace medicalisation (using herbal cannabis as magistral preparations from raw sources or under government agency licensure for cultivation or distribution) as their clinical policy (64). Germany has the highest number of MC prescriptions in Europe, which increased substantially following regulatory changes in 2017. By 2018, approximately 80,000 patients in Germany had received MC prescriptions (65). Health insurers in Germany are obligated to reimburse treatment costs for patients who demonstrate refractoriness to other therapies, though no standardized protocols currently define universal reimbursement criteria (66). In the Netherlands, cannabis flowers with distinct cannabinoid profiles may be prescribed by any physician for conditions such as multiple sclerosis-related spasticity, spinal cord injury, chronic pain, palliative care, cancer complica-

tions, HIV, and hepatitis C (67). However, it is estimated that around half a million individuals in the Netherlands use cannabis for medical purposes, with the majority doing so without a prescription or medical supervision (68).

MC regulations in Italy

Italy ranks second only to Germany in the number of MC prescriptions within the European Union (68). The Italian legislation does not consider MC a targeted therapy, but rather a symptomatic support for standard treatments when these fail to produce the desired effects, because of intolerable AEs, or require dose increases that could lead to AEs. Consequently, in Italy MC is always prescribed as "off-label use," potentially for any disease (69). However, full reimbursement is only available for specific clinical conditions. For pain management, MC can be prescribed with reimbursement for patients experiencing painful spasticity due to multiple sclerosis or spinal cord injuries resistant to conventional therapies, as well as in cases of chronic pain (particularly neurogenic in origin) where treatments with non-steroidal anti-inflammatory drugs (NSAIDs), steroids, or opioids have proven ineffective (70). Reimbursement policies may vary across different Italian regions (70-71). Some regions require a specific therapeutic plan and only provide reimbursement for selected painful conditions, while others restrict reimbursement to certain MC products. Moreover, some Italian regions have yet to entirely implement the MC prescription process.

The prescribing physician in Italy

MC can be prescribed in Italy by any medical doctors registered with the National Medical Registry, through a non-repeatable prescription, with the total cost borne by the patient (69). For full reimbursement by the Italian Health System, the prescribing physician, employed by or affiliated with the Health System, must draw up a specific therapeutic plan after obtaining the patient's informed consent. Certain pain centres are specifically authorised to prescribe MC. For instance, in the Tuscany Region, within public health or affiliated hospitals, MC prescriptions with reimbursement can be issued only by oncologists, neurologists, palliative care physicians, and pain specialists (70). In the Veneto Region, rheumatologists can also prescribe MC for pain treatment (71). To date, the drafting of a therapeutic plan in some Italian regions has been conducted and updated through a centralised digital platform.

Medico-legal implications of MC use in Italy

The medico-legal implications of MC prescriptions in Italy encompass several key aspects. As far as driving is concerned, the issue or renewal of a driving license for patients with prescription of MC containing THC requires evaluation by a local Medical Commission. This commission assesses the risk-benefit ratio of driving under the influence of MC and may issue a license with limited validity and periodic renewal (72). Neuropsychological assessments, including reaction tests, simulator evaluations, or on-road driving tests, may also be conducted. Additionally, specific restrictions, such as driving only during daylight hours, limiting journey distances, prohibiting passengers, setting speed limits, or disallowing trailers and highway usage, may be imposed. The consumption of alcohol and other substances while driving is strictly forbidden (73). The prescribing physician is obligated to inform the patient that, under Article 187 of the updated Italian New Traffic Law, driving after consuming narcotic or psychotropic substances, including MC products containing THC, is punishable. Furthermore, THC and its metabolites can persist in biological fluids for several days following MC consumption (74). Therefore, MC prescriptions must always be accompanied by a comprehensive patient information sheet detailing potential adverse effects (AEs) and interactions with other substances, particularly sedatives, muscle relaxants, antidepressants or alcohol. An informed consent form, signed by both the patient and the physician, is also mandatory at the start, renewal or modification of the prescription (75). Concerning work ability, the occupational physician must assess a patient's suitability for employment upon disclosure of MC treatment. Workers may also be subjected to unannounced toxicological tests mandated by law to confirm abstinence from MC (76). From an insurance perspective, the detection of THC in blood samples may nullify coverage, exclude compensation, or even prompt legal action against drivers or workers. Finally, firearms licenses are not issued to individuals undergoing MC treatment, and existing licenses may be suspended as a result (77).

Conclusion

MC treatments for chronic pain are becoming increasingly widespread. It is anticipated that, over the next few years, further studies will provide greater clarity regarding their efficacy in these patients. However, due to the numerous clinical and medico-legal considerations associated with cannabis-derived products, pain therapists must be thoroughly informed about their indications, contraindications, precautions, pharmacological interactions, dosages, and potential adverse events (AEs), including the risk of dependence in specific patient populations. Furthermore, prescribers must possess a comprehensive understanding of the medico-legal implications within their country to effectively mitigate potential risks for patients, others, and themselves.

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