Psychedelic Therapies in End-of-Life Care
By Claudia Moretti*[1]

"In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering."

Declaration of Helsinki on Biomedicine

In recent years, several countries, including Australia, Israel, Canada, and the United States, have authorized the therapeutic and compassionate use of psychedelic-assisted psychotherapy, allowing a limited, cautious, and rigorous application of compounds and substances that, outside medical-scientific contexts, would otherwise be prohibited. These therapeutic innovations or updates involve the engagement of ethics committees and physicians who adhere to strict and prudent procedures, ensuring full compliance with international obligations arising from the three United Nations Conventions on psychotropic and narcotic substances[2].

These exceptions to the general rule reflect a shift in priority from public order and health protection to the prevailing interest in safeguarding the health of terminally ill individuals. The ultimate goal is to alleviate suffering while respecting the so-called "right to science," which mandates that states ensure the right to "enjoy the benefits of scientific progress and its applications," regardless of where such advancements occur[3].

Is it possible to implement a similar approach in Italy within the current legal framework? And is it feasible without legislative amendments?

There is a longstanding societal awareness, including in Italy, that seeks to uphold end-of-life rights, complementing active treatments and survival therapies with an ethical approach to accompanying the dying. The process of dying has become a time when, thanks to technological and scientific progress, individuals can make varied and even opposing choices. It is no longer solely a phase where one passively undergoes end-of-life circumstances and decisions made by others.

End-of-life therapeutic strategies vary and are often in opposition to one another. On the one hand, there exists a strategy of denial and control, aimed at shielding the dying individual from awareness of their impending death, distancing family members and healthcare personnel from

---

[1] The drafting of this document involved Federico Di Vita and Marco Perduca.

[2] Regarding the general legality of using narcotic substances for medical purposes, see the **Single Convention on Narcotic Drugs of 1961**, as amended by the **Protocol of 25 March 1972**: Preamble: The Parties, concerned with the physical and moral health of humanity, recognizing that the medical use of narcotic drugs remains indispensable for pain relief and that appropriate measures must be taken to ensure their availability for this purpose...

[3] See **Article 15 of the International Covenant on Economic, Social, and Cultural Rights**: https://unic.un.org/aroundworld/unics/common/documents/publications/intlconvenantshumanrights/brussels_intlconvenantshumanrights_italian.pdf.

death itself, and directing every therapeutic effort against it, even at the risk of hastening the process.

On the other hand, there is the more recent strategy of accompaniment, wherein the therapeutic objective shifts from curing (when no longer possible) to caring for the individual, providing emotional support in the process of dying, and resisting the temptation to hasten the course of events.

Summary of Clinical Studies

Challenging the stigma that has surrounded the international socio-cultural debate on psychedelic compounds for over 50 years, the scientific community has recently resumed research and clinical trials with renewed vigor and promising results regarding their actual and effective therapeutic applications. Such research and trials originally began in earlier times (from the 1920s to the late 1960s) but were suspended due to international scheduling[4].

At present, only **ketamine** and its derivative, **esketamine**, are officially recognized as pharmaceuticals at the international level and could therefore be included in palliative treatments already available, even on an off-label basis, as is already the case in psychiatric clinical practice.

Regarding other compounds, particularly **psilocybin** (which holds the greatest promise for end-of-life care[5] and the accompaniment of dying individuals), advanced studies exist, including **Phase 2 trials**, which render it potentially usable for compassionate purposes under existing regulations that already permit the administration of experimental medicines for this purpose.

Another experimental research area concerns **post-traumatic stress disorder (PTSD)** studies, particularly in the United States and more recently in Ukraine, focusing on military veterans[6]. Trials have been conducted with various substances, including ketamine and MDMA, with the latter appearing to be the most effective. The primary study on MDMA and veterans is the **Phase 2 trial conducted in the U.S. by the non-profit organization MAPS** (Multidisciplinary Association for Psychedelic Studies). **Phase 3 studies are currently underway, with publications expected soon, and the FDA is anticipated to approve MDMA by August 2024.**

End-of-Life Care, Pain Therapy, and Compassionate Use

With Law No. 219/2017 (on Advance Healthcare Directives), the right to receive end-of-life care with minimal suffering has been established as an "essential level of care," meaning it is a guaranteed and free right throughout the national territory. Currently, alongside the right to refuse treatment, the right to avoid unreasonable therapeutic obstinacy, the right to access medically assisted death (subject to the four conditions set forth in the Constitutional Court ruling No. 242/2019, "Cappato-Antoniani"), the right to draft a living will, and the right to participate in shared decision-making regarding one's treatment; the legal framework also recognizes the right to receive pain therapy (previously introduced for therapeutic opioids and extended to cannabis in 2019) and the right to palliative sedation.

---

[4] **1971 UN Convention on Psychotropic Substances:** https://www.unodc.org/pdf/convention_1971_en.pdf.

[5] Summary of clinical studies on psychedelic therapies in end-of-life care (Annex 1)

[6] Summary of clinical studies on PTSD in war veterans (Annex 2)

Palliative care (regulated and defined in Article 2 of **Law No. 38/2010**[7] and further detailed in Articles 23 and 31 of the Prime Ministerial Decree of January 12, 2017[8]) is defined as "*a set of therapeutic, diagnostic, and care interventions aimed at providing active and comprehensive treatment to patients whose underlying disease, characterized by an unstoppable progression and an unfavorable prognosis, no longer responds to specific treatments*."

Pain therapy, on the other hand, is defined in the same article as "*a set of diagnostic and therapeutic interventions aimed at identifying and applying appropriate pharmacological, surgical, instrumental, psychological, and rehabilitative therapies, in an integrated manner, to chronic pathological conditions to develop suitable diagnostic-therapeutic pathways for the suppression and control of pain*."

The concepts of pain suppression and control, as well as palliative care, inherently include all protocols—whether conducted in a mixed manner (psychological-psychotherapeutic therapy, spiritual and care support, with or without the use of medicinal compounds)—designed to alleviate the existential and psychological suffering of terminally ill patients. Likewise, they encompass palliative or compassionate care for individuals with chronic treatment-resistant depression, in accordance with the latest medical and scientific research and international experiences.

Use of Experimental Medicines in Our Legal System: Compassionate Care and Reimbursement

In addition to the fundamental principles mentioned above, which reflect international obligations and constitutional provisions, our legal system contains numerous detailed regulations authorizing the treatment of patients with experimental medicines not yet approved or marketed through compassionate use procedures.

So-called compassionate care (**Article 83 of EU Regulation 726/2004**[9] and the **Italian Ministry of Health Decree of September 7, 2017**[10]) allows physicians to propose experimental

---

[7] Law No. 38/2010 (Annex 3)

[8] Articles 23 and 31 of the Prime Ministerial Decree of January 12, 2017 (Annex 4)

[9] Regulation (EC) No. 726/2004 of the European Parliament and of the Council of March 31, 2004, establishing Community procedures for the authorization and supervision of medicinal products for human and veterinary use and establishing the European Medicines Agency (Text relevant to the EEA):
Article 83:
"*1. By way of derogation from Article 6 of Directive 2001/83/EC, Member States may make available, for compassionate use, a medicinal product for human use belonging to the categories referred to in Article 3, paragraphs 1 and 2 of this Regulation.*
2. For the purposes of this Article, 'compassionate use' means making a medicinal product belonging to the categories referred to in Article 3, paragraphs 1 and 2, available for humanitarian reasons to a group of patients suffering from a chronic or seriously debilitating disease, or whose disease is considered life-threatening, and who cannot be treated satisfactorily with an authorized medicinal product. The medicinal product in question must be the subject of a marketing authorization application pursuant to Article 6 of this Regulation or be undergoing clinical trials."

[10] Decree of the Ministry of Health of September 7, 2017 – Regulation on the therapeutic use of medicinal products undergoing clinical trials (Annex 5).

therapies aimed at offering terminally ill patients the so-called "*right to try,*" as per Anglo-Saxon terminology, not necessarily to cure, but at least to maintain hope.

In extreme cases, the legal system tolerates uncertainty—otherwise inadmissible—arising from the therapeutic use of drugs or substances not yet approved, with the aim of offering the "lesser evil" to the individual patient or to groups of patients with the same condition. This is permitted provided that the following conditions are met:

a) No valid therapeutic alternatives are available;

b) There is a life-threatening condition or a serious risk to health, or the disease is severe and rapidly progressing;

c) No clinical trial is underway, and thus no existing protocol is available in which to enroll the patient;

d) The Ethics Committee of the facility has issued a favorable opinion;

e) Informed consent has been obtained;

f) There is a prescription, and the medical responsibility is clearly assumed;

g) Scientific data, including publications in international medical journals, support the therapy.

This can be done through a request for "nominative use" for an individual patient or through "expanded access," whereby pharmaceutical companies conducting clinical trials on their drugs offer them free of charge to groups of patients in similar conditions.

For this to occur, the following steps are required:

i) Identification of an ongoing psychedelic protocol with trial results applicable to the specific case (typically Phase 3 trials, or in specific clinical cases, even Phase 2 or Phase 1 trials); ii) Submission of an authorization request to the territorially competent Ethics Committee and communication to the Italian Medicines Agency (AIFA); iii) Identification of a drug manufactured in accordance with Good Manufacturing Practices (GMP)[11], to be provided free of charge by the manufacturer; iv) Compliance with the procedures for its importation[12].

---

[11] GMP (Good Manufacturing Practices) are international guidelines and standards issued and enforced by various international organizations and regulatory authorities in the pharmaceutical sector to ensure that drugs are manufactured safely, effectively, and with high quality. The main sources of GMP regulations include:
i) International Organizations, such as the World Health Organization (WHO), which publishes its own GMP guidelines widely recognized and used globally, and the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH), which develops internationally harmonized guidelines for the pharmaceutical industry, including GMP. ii) National Regulatory Authorities, such as the Food and Drug Administration (FDA) in the United States; the European Medicines Agency (EMA) in the European Union, which oversees manufacturing facilities for medicinal products within the EU; and the Italian Medicines Agency (AIFA) in Italy, which enforces GMP regulations applicable to drug manufacturers in Italy. iii) Industry Associations, which often publish guidelines and standards for the pharmaceutical sector, including recommendations on GMP.

[12] Excerpt from the official institutional website on drug importation procedures (Annex 6).

Two additional overlapping and complementary legal frameworks allow physicians to treat patients with experimental or off-label medicines when no therapeutic alternatives exist:

- The law on reimbursement of experimental medicines (Law No. 648/1996)[13];

---

[13] **Articles 4 and 4-bis of Law No. 648/1996**:
Article 4:
"When no valid therapeutic alternative exists, as of January 1, 1997, the National Health Service fully covers the cost of innovative medicines that are authorized for marketing in other countries but not within the national territory, medicines not yet authorized but undergoing clinical trials, and medicines used for a therapeutic indication different from the authorized one. These medicines are included in a specific list prepared and periodically updated by the Single Drug Commission, in accordance with the procedures and criteria adopted by the commission itself. The financial burden arising from this provision, quantified at 30 billion lire per year, remains covered by the National Health Service within the planned expenditure ceiling for pharmaceutical assistance."

Article 4-bis:
"Even when an authorized medicinal product offers an alternative therapeutic option, the Italian Medicines Agency (AIFA) may evaluate and include in the list referred to in Article 4 those medicines that can be used for a therapeutic indication different from the authorized one, provided that this indication is well known and aligned with research conducted within the national and international medical-scientific community, following criteria of cost-effectiveness and appropriateness. In such cases, AIFA implements appropriate monitoring tools to ensure patient safety and promptly takes the necessary measures."

- Legislative Decree No. 23/1998, converted into Law No. 94/1998[14], known as the "Di Bella Decree."

The first allows patient associations, scientific societies, local health authorities (ASL), universities, clinicians, or AIFA's Scientific and Technical Committee (CTS) to request that certain medicines be

---

[14] Law No. 94/1998, Article 3

1. Without prejudice to the provisions of paragraphs 2 and 3, when prescribing a proprietary medicinal product or any other industrially manufactured medicine, the physician must adhere to the therapeutic indications, routes, and methods of administration specified in the marketing authorization issued by the Ministry of Health.

2. In individual cases, under their direct responsibility and after informing the patient and obtaining their consent, a physician may use an industrially manufactured medicinal product for an indication, administration route, or method of use different from the authorized one, or recognized under Article 1, paragraph 4, of Decree-Law No. 536 of October 21, 1996, converted into Law No. 648 of December 23, 1996. This is allowed if the physician deems, based on documented evidence, that the patient cannot be effectively treated with medicines already approved for that therapeutic indication, administration route, or method. The off-label use must be well-known and supported by studies published in internationally recognized scientific literature.

3. Until the conclusion of the clinical trials referred to in Article 1, physicians who, exclusively in the field of oncology, have used or are using octreotide- or somatostatin-based medicines will not be held liable, provided that the patient has given written consent acknowledging that the medicines in use are still under clinical investigation.

3-bis. In the cases regulated by paragraphs 2 and 3, the physician must record a numerical or alphanumeric reference in the prescription, without disclosing the patient's personal details. This reference should allow, if requested by health authorities, the identification of the treated patient from archived records held by the prescribing physician.

4. Under no circumstances can the physician's use of the provisions in paragraphs 2 and 3 be considered as granting the patient the right to obtain the medicines at the expense of the National Health Service, except in cases regulated by Article 1, paragraph 4, of Decree-Law No. 536 of October 21, 1996, converted into Law No. 648 of December 23, 1996.

5. Any violation of the provisions of this article by a physician is subject to disciplinary proceedings under Legislative Decree No. 233 of September 13, 1946.

- According to Article 1, paragraph 796, of Law No. 296 of December 27, 2006, these provisions do not apply when the systematic and widespread use of pharmacological therapies within hospitals or other healthcare settings constitutes an alternative therapeutic option outside the authorized marketing conditions, targeting patients with conditions for which approved treatments already exist. Additionally, Article 2, paragraph 348, of Law No. 244 of December 24, 2007, prohibits physicians from prescribing an industrially manufactured medicine for an off-label therapeutic indication unless at least phase II clinical

included in a list of drugs reimbursable by the state when no valid therapeutic alternative exists, including:

- Innovative medicines marketed in other countries but not yet approved in Italy;
- Medicines still undergoing clinical trials;
- Off-label medicines.

Article 14 authorizes the physician, under their sole responsibility in individual cases, to use off-label medicines at no cost to the State, provided that phase II clinical trial results already exist for the intended use.

Psychedelic Therapies and Drug Regulation

The "right to health" takes precedence over other protected interests (public order and public health, precautionary principle) under drug legislation (Presidential Decree 309/1990).

Within the normative framework outlined above, embedded in the constitutional and international context recognizing the right to health and freedom of therapeutic choice—almost fully recognized even in end-of-life situations—the promising outcomes of applied research on psychedelic-assisted therapies, some of which are in advanced stages, can only legitimize their exceptional, palliative, and compassionate (psycho)therapeutic use in Italy, where evidence has already justified their use elsewhere.

Such legitimacy is not precluded by their generic inclusion in Table 1 of Presidential Decree 309/90 or by the criminal provisions therein, which do not inherently prevent the application of the aforementioned end-of-life regulations.

Law 94/1998, Article 3

1. Without prejudice to the provisions of paragraphs 2 and 3, when prescribing a medicinal product, the physician adheres to the therapeutic indications, routes, and methods of administration specified in the marketing authorization granted by the Ministry of Health.
2. In individual cases, the physician may, under their direct responsibility, after informing the patient and obtaining their consent, employ an industrially manufactured medicinal product for an indication, route of administration, or method of use different from those authorized, provided that the physician deems, based on documentable data, that the patient cannot be effectively treated with medicines already approved for that indication or route of administration. The off-label use must be known and consistent with studies published in internationally accredited scientific journals.
3. Until the end of the trial mentioned in Article 1, the actions of an oncologist using octreotide or somatostatin remain valid, provided that the patient gives written consent acknowledging that the medicines are under clinical trial.
4. The unauthorized use of medicinal products under paragraphs 2 and 3 does not entitle patients to reimbursement by the National Health Service, except as provided in Article 1, paragraph 4, of Decree-Law No. 536 of October 21, 1996.
5. Physicians violating this article are subject to disciplinary proceedings under Decree-Law No. 233 of September 13, 1946.

The Constitutional Court, in its ruling No. 185 of May 26, 1998, declared the unconstitutionality of this provision insofar as it did not provide for the reimbursement of experimental cancer drugs for economically disadvantaged patients.

Legal Framework for Psychedelic Therapies

Firstly, the entire Presidential Decree 309/90 operates on a separate, parallel track, preserving medical/therapeutic use by prescribing professionals while regulating the non-personal use of scheduled plants and molecules, including specific sanctions[15].

There is, therefore, no conflict between the general prohibitions and requirements of the law and the possible, legitimate adoption of psychedelic (psycho)therapies, whether as palliative care, pain management, or compassionate treatment. The periodic update of the drug schedules in Article 13 of Presidential Decree 309/90, under the Ministry of Health's authority, allows for the exceptional medical use of these therapies.

Balancing the apparent conflict between different legal values (simplified as: individual health/life/therapeutic freedom vs. public order, public health, and precaution), the legislator has already chosen, through rigorous legal protocols, to prioritize alleviating human suffering in a manner deemed appropriate and sufficiently safe by the international scientific community.

Encouraging studies, research, and initial applications suggest that psychedelic-assisted psychotherapies effectively relieve end-of-life pain in its various physical, psychological, and existential forms. If this is the case, a solid legal framework for their use already exists in Italy.

Policy Proposals for Psychedelic Medicines in Pain Therapy

Given these premises, we urge the Ministry of Health, through the incumbent Minister, to:

i) Engage with medical professionals and researchers in a clinical and scientific debate;

ii) Include validated psychedelic medicinal compounds in the existing schedules for pain therapy drugs, facilitating access to these therapies already in use abroad. This follows the precedent of listing opioid, coca leaf derivatives, and amphetamine-based medicines for therapeutic use;

iii) Clarify that this inclusion does not disrupt or innovate the legal framework but merely enforces the constitutional principle (affirmed in Constitutional Court ruling No. 282/2002) that medicine is not a governmental prerogative. Governments do not select specific therapeutic practices; rather, they must heed the scientific community, which dictates its own standards and precautions. Compliance with international legal obligations, including those under the International Covenant on Economic, Social, and Cultural Rights, is essential.

Residents of Italy have the same right to benefit from scientific progress and its applications as those in other jurisdictions where these end-of-life treatments have been validated. If the results prove convincing, promising, and relatively safe (within the tolerable uncertainty for other end-of-

---

[15] **Article 72 of Presidential Decree No. 309/1990**
"... The therapeutic use of medicinal preparations containing narcotic or psychotropic substances is permitted, provided they are duly prescribed according to the treatment needs related to the patient's specific pathological conditions." The **Criminal Court of Cassation, Section VI, ruling of March 13, 2013, No. 16581**, with a well-established interpretation, clarifies that:
"The administration of medicinal preparations containing narcotic substances is permitted under Article 72, paragraph 2, of Presidential Decree No. 309 of 1990, only if the physician genuinely acts for therapeutic purposes, administering a duly prescribed treatment in accordance with Article 43 of the Unified Text and in line, based on current scientific knowledge, with the clinical objectives pursued."

life treatments), they should be addressed institutionally as matters of legality rather than mere personal freedoms.

Immediate Actions

While awaiting institutional debate informed by global scientific evidence and subsequent legislative adjustments from the Ministry of Health, the following actions should be pursued:

1. Legally, scientifically, and administratively support physicians and patients seeking compassionate use of psychedelic-assisted therapies within existing legal frameworks.
2. Assist companies seeking expanded access for experimental drugs to patients who, though ineligible for trials, are in similar clinical conditions.
3. Maintain dialogue with European institutions and regulatory agencies overseeing clinical trials and pharmacovigilance.
4. Foster collaboration among medical and scientific experts to ensure rapid and coordinated therapeutic responses.

* Claudia Moretti is a lawyer at the Florence Bar and a civil rights activist. She primarily practices law in the healthcare and social welfare sectors. Within her professional expertise, she is actively involved in organizing training events for her professional order, both independently and through **COGISS** (Italian Jurists' Coordination for Social and Health Law), of which she is a founding member. Through COGISS, she promotes education and awareness on health law-related issues in the legal field.
She is actively engaged in end-of-life campaigns led by the **Luca Coscioni Association** and has worked on civil rights and bioethics issues since the early years of her career. For over thirty years, she has collaborated with **Aduc** (www.aduc.it – Association for Users' and Consumers' Rights), managing the **Legal Observatory** and writing legal information articles to enhance public awareness of their rights. She also represents the association in legal disputes on various matters, including freedom of expression, the right to report, and other consumer law issues.