Explanatory memorandum

Draft Government Regulation on the conditions for the prescription, supply and use of individually prepared medicinal products containing psilocybin for therapeutic use

I. General part

1. Explanation of the need for the proposed legislation and justification of its main principles

The Ministry of Health submits a draft Government Regulation laying down the conditions for the prescription, preparation, distribution, dispensing and use of individually prepared medicinal products containing psilocybin for therapeutic use (hereinafter the 'draft Government Regulation'). The aim of this draft Government Regulation is to implement the provisions contained in Act No 378/2007 on pharmaceuticals and amending certain related acts (the Pharmaceuticals Act), as amended (hereinafter the 'Pharmaceuticals Act'), and Act No 167/1998 on addictive substances and amending certain other acts, as amended (hereinafter the 'Addictive Substances Act').

Act No 270/2025 amending Act No 40/2009, the Criminal Code, as amended, Act No 141/1961, the Code of Criminal Procedure, as amended, and other related acts (hereinafter 'Act No 270/2025') amended certain health legislation, including, inter alia, the Pharmaceuticals Act and the Addictive Substances Act. Both acts now govern the possibility of prescribing, dispensing and using psilocybin for therapeutic use and individually prepared medicinal products containing this active substance.

The draft Government Regulation aims to implement the provisions of § 79a(3) of the Pharmaceuticals Act and § 33l of the Addictive Substances Act in areas where both acts foresee the issuing of a government regulation. In practice, this involves laying down the conditions for prescribing, preparing, distributing, dispensing and using individually prepared medicinal products containing psilocybin for therapeutic use. The draft Government Regulation lays down specific therapeutic indications for which individually prepared medicinal products containing psilocybin for therapeutic use may be prescribed, sets quantitative limits for the prescription and use of psilocybin for therapeutic use over a specified period for a single patient, and lays down the duration of special supervision after administration of psilocybin for therapeutic use, depending on the dose administered.

The mental health situation in the Czech Republic is extremely serious in terms of the prevalence of mental disorders and systemic challenges, and in some respects is worse than the EU average.

Statistics show that in the Czech Republic the number of patients with mental disorders had already increased by 22 % between 2010 and 2021, which is a considerably high rate of deterioration that has significantly accelerated in recent years. Almost one in three Czech adults suffers from mental disorders, and the increase in mental illness is evident across all age groups. Furthermore, per capita healthcare expenditure in the Czech Republic is still a quarter lower than the EU average, which limits the possibilities for successful reform and expansion of care. Mortality from avoidable and treatable causes in the Czech Republic is 25 % higher than the EU average, which also indicates lower efficiency of healthcare, including mental health care.

One of the approaches chosen by the Czech Republic is the introduction of innovative therapeutic procedures, which the Czech Republic is also promoting at the European level. For these reasons, the Parliament of the Czech Republic has passed Act No 270/2025. This legislative change will allow the use of therapeutic psilocybin in the treatment of certain mental disorders from 1 January 2026.

The legislative step chosen is based on significant progress in clinical research into the use of psilocybin, which has triggered a lively debate worldwide (including the EU) on the need to adapt the legislative status of psilocybin for therapeutic use in order to align it with scientific knowledge and allow its therapeutic potential to be exploited for the benefit of patients.

In this context, it should be recalled that the Czech Republic plays a significant part in research in the field of mental health and therapeutic use of psilocybin and should therefore also actively participate in translating research results into practice in this field. The change in the legislative status of psilocybin is a logical response that may not only alleviate and shorten suffering, but also bring economic benefits by reducing incapacity for work and disability.

In view of the effective date of the relevant parts of Act No 270/2025, the proposed effective date of the draft Government Regulation is also set to ……2026.

2. Assessment of the existing legal situation and justification of the need to change it

While the current legislative status of psychedelic substances (i.e. the UN Convention on Psychotropic Substances, the Addictive Substances Act, Government Regulation No 463/2013 on the schedules of addictive substances, as amended, and its amendment No 242/2018) allowed clinical research, it prevented the translation of its results into clinical practice. This has also created the need for a legislative response in other countries. An example of this shift is the position taken by the US FDA, which in October 2018 designated psilocybin for treatment-resistant depression as a breakthrough therapy in mental health care, and a year later granted this status to psilocybin treatment for depressive disorders as such.

In the Czech Republic, the existing legislation on addictive and psychotropic substances is enshrined in the Addictive Substances Act. Psilocybin is listed in Annex 4 to the Government Regulation implementing the aforementioned Act. This Annex contains psychotropic substances that are subject to the strictest regime, which effectively precludes their therapeutic use. This led to a contradiction between the legislative situation and scientific knowledge.

The adoption of Act No 270/2025 resolves this contradiction and increases the possibilities for a systematic and innovative solution to the current extremely serious situation in the field of mental health in the Czech Republic.

Therefore, there is currently no applicable legislation governing the conditions for the prescription, preparation, distribution, dispensing and use of individually prepared medicinal products containing psilocybin for therapeutic use. Since, following the amendment implemented by Act No 270/2025, the Pharmaceuticals Act and the Addictive Substances Act now include provisions on psilocybin for therapeutic use, it is necessary, in those areas where the issuing of a government regulation is envisaged, to lay down those provisions by means of a government regulation. If the draft Government Regulation were not adopted, the statutory authorisation would not be fulfilled and there would be no instrument laying down binding conditions for the prescription, preparation, distribution, dispensing and use of individually prepared medicinal products containing psilocybin for therapeutic use.

3. Assessment of compliance of the draft legislation with the constitutional order and other components of the legal system of the Czech Republic

The draft Government Regulation complies with the authorisation under Act No 378/2007 on pharmaceuticals and amending certain related acts (the Pharmaceuticals Act), as amended, and with the authorisation under Act No 167/1998 on addictive substances and amending certain other acts, as amended, and also complies with the constitutional order of the Czech Republic.

4. Assessment of compliance of the draft legislation with the obligations arising for the Czech Republic from its membership of the European Union

The proposed legislation is fully compatible with EU legislation, the case-law of the courts of the European Union and the general legal principles of European Union law.

5. Assessment of compliance of the proposed legislation with international treaties binding on the Czech Republic

Psilocybin is currently included in Schedule 4 of psychotropic substances, which is set out in Annex 4 to Government Regulation No 463/2013 on the schedules of addictive substances, as amended (hereinafter ‘Government Regulation No 463/2013’). Due to the extent of their misuse, or because they pose an immediate or indirect risk to health, it is necessary to ensure that substances and preparations containing these psychotropic substances are used only for limited research, scientific and very limited therapeutic purposes, as defined in the handling permit. Schedule 4 also includes psychotropic substances classified in Schedule I of the Convention on Psychotropic Substances, promulgated under No 62/1989. The Czech Republic is bound by the Convention on Psychotropic Substances.

In view of the findings from clinical practice and the facts described above, the positive effects of psilocybin for therapeutic use have been established, hence, an amendment to Government Regulation No 463/2013 has been proposed, under which psilocybin for therapeutic use would be included in the schedule of psychotropic substances in Annex 5. Reclassification into Schedule 5 of psychotropic substances in Government Regulation No 463/2013 means that it will be included in the schedule of psychotropic substances for which, due to the extent of their misuse, or because they pose an immediate or indirect risk to health, it is necessary to allow handling only on the basis of a handling permit, or, for this reason, it is necessary to ensure that medicinal products containing these psychotropic substances are dispensed in pharmacies only on the basis

of a prescription or request form marked with a blue stripe running from the lower left corner to the upper right corner. Schedule 5 also includes psychotropic substances listed in Schedule II of the Convention on Psychotropic Substances.

The amendment to Government Regulation No 463/2013 means that, to a limited extent, it will now be possible to prescribe psilocybin for therapeutic use on a blue-stripe request form, with the rules for prescribing set out in the draft Government Regulation and the related amendment to Decree No 329/2019 on the prescription of medicinal products in the provision of health services, as amended.

Psilocybin for therapeutic use may only be prescribed and administered on the basis of a handling permit granted by the Ministry of Health. For limited therapeutic purposes, therapeutic psilocybin may be prescribed and administered in psychiatric clinics and psychiatric hospitals that fall under the direct authority of the Ministry of Health, and in outpatient, day-care or inpatient psychiatric facilities that are part of hospitals under the direct authority of the Ministry of Health, in which cases a handling permit is not required. With regard to the requirements of Article 7 of the Convention on Psychotropic Substances, the draft Government Regulation sets quantitative limits within which therapeutic psilocybin may be prescribed and administered, depending on the patient's weight and the time period. Therapeutic psilocybin thus cannot be administered more often than stipulated by the draft Government Regulation or contrary to rules related to the patient's weight. The administration of therapeutic psilocybin is justified by the need to protect public health, as it is limited to clearly defined serious cases in the indications pursuant to § 2(1) of the draft Government Regulation. These are always cases involving the patient's severe mental condition, and the condition must also be met that an existing authorised medicinal product does not satisfy the patient's needs, i.e. there is de facto no other form of therapy that would relieve the patient's suffering. The prescription and administration of psilocybin are thus strictly limited in terms of quantity, time and indications, and subject to the condition that no other available form of treatment is effective, i.e. it has been empirically demonstrated that the patient cannot obtain relief in any other way. The aim is to ensure that patients who do not respond to conventional treatment have access to therapy using therapeutic psilocybin. The draft Government Regulation further restricts the prescription and administration of therapeutic psilocybin solely to physicians with the necessary qualifications or certification in the field of psychiatry. This will ensure that therapeutic psilocybin will be prescribed and administered only by qualified persons with the appropriate education and experience, so that the objective of relieving the patient's mental distress is upheld. This is followed by the so-called special supervision, which takes place after each administration of psilocybin for therapeutic use and is carried out by the physician who administered psilocybin for therapeutic use. This ensures that the patient will receive the necessary support if required. In accordance with the requirements of the Addictive Substances Act, the administering physician keeps records of the administration of psilocybin. It is thus ensured that the prescription and administration of therapeutic psilocybin are fully documented. Individually prepared medicinal products containing psilocybin for therapeutic use may only be prescribed on a blue-stripe request form, on which information is entered in accordance with the draft Government Regulation in conjunction with the amendment to Decree No 329/2019, which was submitted to the legislative process in parallel with this draft Government Regulation. The blue-stripe request form will include, among other things, the patient's name and surname, as well as the patient's personal identification number, thus ensuring compliance with the restrictive rules under this Government Regulation for the prescription and administration of psilocybin for therapeutic use. Furthermore, the draft Government Regulation expressly provides that if three consecutive administrations of psilocybin do not lead to a demonstrable improvement in the patient's condition, further administration is contraindicated. It can therefore be concluded that therapeutic psilocybin can only be administered under clearly defined conditions, by a person

authorised for this purpose, and that the whole process is properly documented. Any violations of the rules are punishable by sanctions under the Addictive Substances Act.

6. Expected economic and financial impacts of the proposed legislation on the state budget, other public budgets and the business environment in the Czech Republic

An impact on the state or public budgets can be expected if reimbursement under the public health insurance system is introduced, including reimbursement for the prescribed supervision, psychotherapy and the individually prepared medicinal product containing psilocybin for therapeutic use.

7. Assessment of whether the draft legislation contains a provision which by its nature would constitute a technical regulation under the legislation governing technical requirements for products and information on compliance with the notification obligation under this legislation

In light of its nature, the draft legislation will be notified in accordance with Directive (EU) 2015/1535 of the European Parliament and of the Council of 9 September 2015 laying down a procedure for the provision of information in the field of technical regulations and of rules on Information Society services.

8. Expected impact of the draft legislation, in particular

8.1 Impact on the rights and obligations of natural and legal persons

No impacts in this respect are expected.

8.2 Impact on the business environment of the Czech Republic

No impacts in this respect are expected.

8.3 Assessment of whether the draft legislation constitutes State aid

The draft Government Regulation does not constitute State aid.

8.4 Social impact, including impact on specific groups of the population, in particular the socially vulnerable, persons with disabilities and national minorities

No impacts in this respect are expected. The expansion of the possibilities for therapy using psilocybin for therapeutic use can be considered a potential positive impact, which may ultimately benefit society as a whole.

8.5 Expected impact of the draft legislation on equality between men and women, if the draft legislation regulates or affects the status of natural persons

No impacts in this respect are expected.

8.6 Environmental impact

No impacts in this respect are expected.

8.7 Impact on the protection of children's rights

No impacts in this respect are expected.

8.8 Impact on national security or defence

No impacts in this respect are expected.

8.9 Impact relating to the protection of privacy and personal data

No impacts in this respect are expected.

9. Assessment of corruption risks associated with the draft legislation

The draft Government Regulation has no potential for corruption and therefore does not pose any risk in this respect.

10. Assessment of the impact on families, in particular with regard to the fulfilment of the functions of the family, the number of dependent members, the possible presence of disabled members, single-parent families, families with three or more children, and other specific life situations, as well as strengthening family integrity and stability, enhancing family harmony, achieving a better work-family balance, and strengthening intergenerational and wider family relationships

No impacts in this respect are expected.

11. Assessment of territorial impacts, including impacts on territorial self-governing units

No impacts in this respect are expected.

12. Assessment of compliance of the proposed solution with the principles of digitally-friendly legislation, including an assessment of the risk of exclusion or restriction of access to certain services for specific groups of persons as a result of the digitalisation of their provision (digital exclusion)

The draft Government Regulation does not concern this matter.

13. Justification for any proposed derogation from the procedure for discussing the draft legislation.

In view of the proposed legislation and the need for its adoption and entry into effect at the latest by ……. 2026, when Act No 270/2025 will also come into effect, the submitter requested that the deadline for the interdepartmental commenting procedure be shortened to seven working days.

This request was granted by decision of the Minister of Justice and the Chairperson of the Legislative Council of the Government under ref. No 32644-2025-UVCR.

Also, in light of the above and considering that the legislation introducing psilocybin for therapeutic use does not allow for any solution other than the adoption of the draft Government Regulation, the submitter prepared an Overview of the Impacts of the Draft Government Regulation, and by decision of the Minister of Justice and the Chairperson of the Legislative Council of the Government, the draft Government Regulation was granted an exemption from the obligation to prepare an RIA under ref. No 32799-2025-UVCR.

The submitter further notes that the draft Government Regulation is being processed in the e-Legislativa system, whose basic template for the general part of the explanatory memorandum to the draft Government Regulation does not generate its individual points in accordance with the Government's Legislative Rules. The template has therefore been adjusted so as to at least broadly meet the requirements of the Government's Legislative Rules, and an assessment relevant to the draft Government Regulation as a type of legislation has been carried out.

II. Special part

Re § 1

The provision details the legislation that the draft Government Regulation implements. Specifically, these are the areas listed in points (a) to (c). With regard to statutory authorisations, the draft Government Regulation implements the provisions of § 79a(3)(a) and (b) of the Pharmaceuticals Act and § 33l(1) and (4) of the Addictive Substances Act.

The aim of the provision is to clarify to the addressee which areas are governed directly by the draft Government Regulation, since, in view of the statutory conditions or authorisations, the draft Government Regulation is not the only implementing legislation that further elaborates on psilocybin for therapeutic use. The proposed provision thus facilitates navigation in the draft legislation.

Re § 2

§ 2 lays down rules for the prescription and administration of an individually prepared medicinal product containing psilocybin for therapeutic use. Paragraph (1) sets out the indications for which therapeutic psilocybin may be prescribed. At the same time, this paragraph stipulates the professional qualifications of physicians who are authorised to do so. Taking into account the nature of psilocybin for therapeutic use, it is stipulated that only a physician with specialised qualifications in the field of psychiatry or with specific specialist qualifications in the subspecialty of medical psychotherapy may prescribe and administer it. Therapeutic psilocybin will only be prescribed and administered to patients who meet the expected indications, and only where treatment with authorised medicinal products has been ineffective or documented intolerance to such treatment exists. At the same time, therapeutic psilocybin should be administered in accordance with the recommended clinical procedure for assisted psychotherapy using psilocybin for therapeutic use. Individually prepared medicinal products containing psilocybin for therapeutic use should thus serve as supportive treatment when treatment with other authorised products is not effective. The primary objective is thus to bring relief to patients in an adverse mental state where other treatment is not effective.

Psilocybin belongs to the group of tryptamines, which, through their action on serotonin receptors, induce specific psychological effects, known as an altered state of consciousness, characterised by induced changes in perception, thinking and emotionality. Psilocybin has also been shown to have low toxicity, minimal to no risk of dependence, and a generally favourable safety profile (Tyls et al., 2014).

In therapeutic use, psilocybin is currently combined with structured psychotherapy, referred to as psilocybin-assisted psychotherapy (Schenberg, 2018). Both older and recently published studies demonstrate the significant effect of psilocybin, or psilocybin-assisted psychotherapy, in cases of 1) depressive disorders that do not respond to conventional treatment (pharmaco-resistant) (Carhart-Harris et al., 2016, Goodwin et al., 2022), as well as depression that does not show resistance to conventional treatment (von Rotz et al., 2023, Gukasyan et al., 2022, Carhart-Harris et al., 2021). Another important area is 2) depression in patients with cancer and/or other incurable diseases (Reiche et al., 2018, Grob et al., 2011, Ross et al., 2016, Griffiths et al., 2016). Psilocybin also shows therapeutic efficacy in other conditions, such as obsessive-compulsive disorder (Moreno et al., 2006) or alcohol and nicotine dependence (Johnson et al., 2017,

Bogenschutz et al., 2015). However, in the case of depressive disorder (including its variants accompanying oncological diseases), the findings are so convincing that they already call for a legislative response.

The main advantage of psilocybin treatment is that it speeds up the onset of an antidepressant response in depressive disorder, which is one of the most serious and common mental disorders (prevalence around 10 %, the fourth most common cause of incapacity for work overall). This type of treatment can be very helpful for patients suffering from depression, as it can substantially reduce the duration of suffering and incapacity for work.

The antidepressant potential in pharmaco-resistant depression was confirmed as early as 2017 in a study which showed that administration of psilocybin leads to an improvement in symptoms of depression after one month, with this effect lasting for at least three months in 80 % of subjects (Carhart-Harris et al., 2017). The most significant evidence was provided by an international, multicentre study involving 233 patients with pharmaco-resistant moderate (30 % of patients) and severe (68 %) depressive disorder. Czech experts also participated in this study. The study showed significant improvement for both higher doses (Goodwin et al., 2022, Goodwin et al., 2023). These results are fully consistent with a number of other studies.

In view of the change in the legislative status of psilocybin for therapeutic use, studies that compared the efficacy of psilocybin with that of standard antidepressants commonly available on the market are of great importance. These studies confirmed that psilocybin is at least as effective as standard treatment with SSRI antidepressants in patients with long-term moderate to severe depressive disorder, with the main advantage being the rapid onset of improvement in their condition (Carhart-Harris et al., 2021, Zeifman et al., 2023). Existing studies confirm a long-term antidepressant effect that persists for 3–12 weeks after psilocybin administration in patients with more severe forms of depression (Goodwin et al., 2022; Davis et al., 2021; Carhart-Harris et al., 2021). Long-term follow-up data indicate a clinical response persisting for 12 months after psilocybin administration (Gukasyan et al., 2022).

The psychological distress of patients in advanced stages of oncological diseases (or in palliative care) represents another major clinical challenge. For these patients, existing psychiatric treatment options are limited or non-existent (Ostuzzi et al., 2018). The favourable results of a series of new randomised controlled trials of psychedelic-assisted psychotherapy have brought substantial hope to these seriously ill patients. The results confirm that the antidepressant effect in these patients has a rapid onset, is long-lasting (six months after administration) and that the treatment is safe (Grob et al., 2011, Griffiths et al., 2016). Long-term improvement (6.5 months to 4.5 years) after a single dose of psilocybin is seen in 60–80 % of patients (Ross et al., 2016; Agin-Liebes et al., 2020). The robustness of these findings has also been demonstrated at the level of meta-analysis, which confirmed at least a six-month reduction in anxiety and depressive symptoms in these seriously ill patients (Goldberg et al., 2020).

Justification of indications

Currently, psilocybin is one of the most studied psychedelics, belonging to the group of so-called fast-acting antidepressants. In clinical trials, psilocybin has been shown to be relatively safe in terms of the risk of serious adverse effects (somatic risks are negligible at therapeutic doses and the risk of psychological decompensation is also minimal when major contraindications such as psychosis are excluded). At the same time, compared with other psychedelics, there is the greatest body of evidence for the efficacy of psilocybin in the treatment of neuropsychiatric

disorders, although it is important to emphasise that this evidence currently comes solely from clinical trials. More than 300 clinical trials with psilocybin are currently registered in the ClinicalTrials.gov and EudraCT clinical trial registries for a wide range of indications, primarily neuropsychiatric disorders. The most advanced (pre-authorisation phase III clinical trial) and the largest data sets currently concern clinical trials with psilocybin in the treatment of depressive disorder, including treatment-resistant depression (not only pharmaco-resistant depression). The second major indication with a high degree of evidence is the use of psilocybin-assisted therapy in the treatment of depression, existential distress and demoralisation in cancer patients and patients with incurable diseases (as part of a palliative indication). Other diagnoses for which there is increasingly robust evidence include certain anxiety disorders, such as obsessive-compulsive disorder, generalised anxiety disorder, and post-traumatic stress disorder.

Mechanisms of action and comparison with standard treatment

Unlike conventional antidepressant treatment, psilocybin has a significantly different mechanism and onset of action. Primarily, its effect often begins almost immediately after exposure or after the effects of the substance have subsided. This significantly reduces the suffering of patients who, with standard treatment, often wait months for the effect (the usual time for evaluating the antidepressant effect is 6-8 weeks after setting the antidepressant dose, and not all patients respond to the first antidepressant). At the same time, if psilocybin is effective for the patient, they either do not need any antidepressants in maintenance treatment or require only lower doses of conventional medicines. This can significantly minimise the occurrence of side effects associated with conventional medicines (weight gain, sedation, sexual dysfunction, etc.). Unlike other psychotropic drugs, psilocybin has been found to have a relatively favourable safety profile in clinical trials. Its use in medical treatment is associated with a minimal incidence of serious adverse effects, which are often temporary or transient and of short duration. However, although the therapeutic potential of psilocybin is significant, there are also certain risks that need to be taken into account. Psilocybin may cause acute anxiety, panic attacks, paranoid thoughts, and dissociative or psychotic symptoms in sensitive individuals. Therefore, it is always necessary to follow the prescribed assisted-therapy procedure, i.e. to link the pharmacological effect of the substance with the structure of the psychotherapeutic process. The therapeutic framework includes three phases: preparation, the actual session under the influence of the substance, and the subsequent integration of the experience. In the preparatory phase, emphasis is placed on establishing a confidential relationship between the patient and the therapist, clarifying the objectives of the therapy and reducing the potential anxiety associated with the expectation of the experience itself. During the session, the patient is supervised by at least one, but often two, trained therapists, who do not interfere in a directive manner in the course of the experience, but create a safe and supportive framework. The patient must remain in the facility until the effects of the substance have completely subsided and their ability to function safely on their own has been restored. The subsequent integration phase is crucial for the processing of the experiences and their meaningful integration into the patient’s life. In the treatment of depression, existential distress and demoralisation in patients with cancer or incurable diseases, standard treatment with antidepressants is practically ineffective. Due to the nature of some of these diseases, there is often not even enough time to try and titrate different medications. In such cases, psilocybin may have a fundamental therapeutic effect here in the form of acceptance of a serious diagnosis and reconciliation with death or long-term disability. At the same time, however, it is necessary to emphasise that even in these indications, treatment must be conducted by an experienced and trained team.

Mechanism of the rapid antidepressant effect

There are four primary mechanisms of the rapid antidepressant effect: 1) rapid changes in receptors (e.g., downregulation of 5-HT2a receptors, which are key in mood and anxiety responses); 2) rapid change in brain function (a kind of reset of brain neural networks); 3) induction of neuroplasticity (creation of new connections between neurons and activation of new brain circuits); and 4) the psychological context (the content of the experience can provide key insights into the psychological aspects of the mental disorder and can act as an accelerator of the psychotherapeutic process).

Re § 3

§ 3 lays down the conditions for the quantitative restrictions on the administration of psilocybin for therapeutic use. The limit for the prescription, dispensing and use of an individually prepared medicinal product containing psilocybin for therapeutic use is set at a maximum total quantity of 75 mg of psilocybin for therapeutic use over a period of one calendar month. Paragraph (2) then stipulates that a single dose may not contain more than 35 mg of psilocybin for therapeutic use and that the dosage may not exceed 0.4 mg/kg of the patient's body weight. In addition, temporal restrictions on administration and conditions for contraindication are laid down. The data used for regulatory purposes are based on experience from practical use as well as on findings from clinical trials.

There are currently five clinical trials underway in the Czech Republic with psilocybin as an investigational product. These include two international and three national clinical trials, including two for patients diagnosed with pharmaco-resistant depression, two for patients diagnosed with depression associated with cancer, and one for patients diagnosed with stable ischaemic heart disease with a history of myocardial infarction at least six weeks prior to entering the clinical trial. All five studies have already commenced in the Czech Republic.

The international clinical trial, sponsored by Compass Pathfinder Limited (UK), is focused on identifying an appropriate dose of the medicinal product. The planned 568 participants diagnosed with pharmaco-resistant depression from nine EU Member States are to be assigned in a ratio of 2:1:1 to one of three treatment groups. All participants will receive a single dose of COMP360, which is synthetic psilocybin, in doses of 25 mg, 10 mg or 1 mg. The clinical trial has been approved and commenced.

The second academic clinical trial, sponsored by the University Medical Centre Groningen (NL), includes patients with depression related to cancer. The clinical trial will include 100 patients from four Member States, all of whom will be given psilocybin in two doses (15 mg and 25 mg vs. 1 mg and 1 mg). The clinical trial has been approved and commenced.

The other three clinical trials are national and have a planned enrolment of 60 patients each. For two of them, the sponsor is the National Institute of Mental Health (Národní ústav duševního zdraví, NÚDZ) in Klecánky. The first is for patients diagnosed with pharmaco-resistant depression and the second is for patients diagnosed with depression associated with cancer. Both clinical trials are designed as comparative clinical trials. Patients are divided into three treatment groups of 20, with the first group receiving psilocybin, the second ketamine and the third midazolam (as a 'placebo'). The clinical trials are ongoing and the results are not yet available.

The last clinical trial is sponsored by Psyon s.r.o., which is also associated with physicians from NÚDZ, and includes patients diagnosed with stable ischaemic heart disease with a history of

myocardial infarction. Patients will be divided in a 1:1 ratio into a 20 mg psilocybin treatment group or a 5 mg midazolam treatment group. The product will be administered as a single dose. The clinical trial has commenced, but results are not yet available.

The European Clinical Trials Register now lists 19 approved and ongoing clinical trials with psilocybin, including the five mentioned above. One additional study has been completed, but the results are not yet available.

Justification of dosing schemes and doses

In treatment using psilocybin-assisted therapy, several basic treatment regimens are used, based on historical evidence and experience from current clinical trials. From a temporal perspective, treatment can be divided into an induction phase followed by a maintenance phase.

During the induction phase, it is essential to consider whether the patient is coming into contact with this type of treatment for the first time, or whether it is being used, for example, to treat another episode of the same illness (typically a relapse of a depressive episode). In the case of first administration, in particular in patients with no previous experience of psychedelic drugs, it is crucial to place maximum emphasis on educating the patient about the somatic and psychological effects of the substance and on how treatment is conducted during preparatory sessions (managing any physical and psychological discomfort, working with music, working with the body during the session, etc.). In the case of patients who have already had one or more such experiences, it is possible to focus more on the psychotherapy itself, in other words, on exploring questions and relating to their specific difficulties. In both cases, it is essential to establish a safe framework for the administration of the substance. Most studies today work in the context of psychedelic therapy with full psychedelic doses, which are typically between 20-35 mg per adult. Usually, a fixed dose is used; nevertheless, some protocols also use a conversion to kilograms of body weight, typically from 0.2 to 0.4 mg/kg. Doses exceeding 35 mg per individual are not currently used in therapeutic indications, but have been used in clinical studies focusing on safety and pharmacokinetics in healthy volunteers.

Single versus repeated administration

In studies, we encounter both single-dose administration followed by observation of how long the effect persists, and a two-dose model, often in a dose-escalation regimen (gradually increasing doses) with subsequent open-label extensions. The indication for another dose is often determined by the patient’s clinical condition, i.e. if the therapeutic effect wears off, another session with another dose is indicated as soon as possible. These schemes apply not only to psilocybin, but also, for example, to the related substance 5-MeO-DMT (5-methoxy-N,N-dimethyltryptamine) or DMT (N,N-dimethyltryptamine). At the same time, the degree and duration of an antidepressant or other therapeutic response has been shown to be directly related to the intensity of the effect and to the psychedelic or mythical experience. Furthermore, experience with off-label treatment of depression and other disorders using the dissociative anaesthetic ketamine in sub-anaesthetic doses (which then has certain psychotomimetic effects similar to serotonergic psychedelics) also shows that regimens involving repeated, serial administration of ketamine are more effective than a single-dose administration. These schemes also achieve a longer duration of antidepressant response, which after a single intervention typically lasts several days, at most a few weeks. On the basis of extrapolation from these data and from studies in which multiple doses of psilocybin were used, it can therefore be clinically

extrapolated and assumed that, in the case of psilocybin, too, administration in a series of several consecutive doses (two to three) will produce a greater and longer-lasting therapeutic effect.

Maintenance treatment and dosage

There is not much information available about maintenance treatment in recent research, but current clinical trials are focusing on how long the effect of treatment lasts after a single dose and how it can subsequently be enhanced or prolonged on the basis of the patient's clinical condition. Most studies therefore offer an open-label extension. In addition, in some countries, an extended access programme has been approved for certain diagnoses, i.e. patients who responded to treatment in a study may have access to continued treatment with an unauthorised medicinal product. Based on existing data from controlled trials and case studies, there is relatively robust evidence that the effects of psilocybin can last from several days to several months, and sometimes even up to one year.

The doses used in clinical studies can be divided into low (5-15 mg or equivalents in mg/kg), medium (15-25 mg or equivalents in mg/kg), and higher doses (25-35 mg or equivalents in mg/kg). High doses (35-50 mg) have not yet been used in therapeutic indications. By combining the dose and treatment scheme, it is possible to estimate a maximum safe monthly dose, taking into account the clinical condition and response, as well as any individual sensitivity to the effects. If we take into account that up to three doses can be used in the induction phase in a dose-escalation regimen, then, for example, doses of 15-25 and 30 mg can be used with a minimum interval of one week, or three doses of 25 mg. It should be noted that an interval between two doses shorter than one week is not justified, since administration leads to practically immediate internalisation and thus downregulation of 5-HT2A receptors, which are primarily responsible for the acute effect of psilocybin, and this downregulation persists at least one week after exposure to psilocybin. As a result, there is virtually no rationale for administering further doses at shorter intervals. Summarising these facts, we arrive at a maximum dose of 70-75 mg per month.

Re § 4

This provision implements the authorisation set out in the Addictive Substances Act and specifies the duration of special supervision depending on the dose of psilocybin for therapeutic use that is administered.

Paragraph (1) lays down the limits for the administration of an individually prepared medicinal product and the corresponding period of special supervision. Where the dose does not exceed 14.99 mg of psilocybin for therapeutic use, the period of special supervision is set at 4 hours. A dose exceeding this value, i.e. from 15 mg of psilocybin for therapeutic use, requires special supervision for 6 hours. What is important for the conduct of special supervision is the fact that the periods laid down are only minimum durations. Therefore, there is no option to shorten the period of special supervision depending on the dose administered.

Paragraph (2) then follows on from paragraph (1), stipulating that special supervision may only be terminated after the effects of the individually prepared medicinal product containing psilocybin for therapeutic use have completely subsided, as determined by the physician who administered it. Thus, if the effects of the administration persist after the period of special supervision provided for in paragraph (1) has passed, special supervision must continue until it is established that the effects of the product have ceased. This may be determined only by the physician who administered the individually prepared medicinal product containing psilocybin for therapeutic use. Only that physician has a complete overview and information on the dose

administered and on how the administration proceeded. The condition that the effects must have ceased was laid down with a view to protecting the patient's life and health and in accordance with the principle of prevention – a patient who has been administered an individually prepared medicinal product containing psilocybin for therapeutic use will remain under the supervision of a physician so that any required medical care or support can be provided if necessary.

Re § 5

In light of the nature of the proposed Government Regulation, the draft legislation will be notified in accordance with Directive (EU) 2015/1535 of the European Parliament and of the Council of 9 September 2015 laying down a procedure for the provision of information in the field of technical regulations and of rules on Information Society services.

Re § 6

The effective date of the draft Government Regulation is set in accordance with the requirements of Act No 222/2016 on the Collection of Laws and International Treaties and on the creation of legislation promulgated in the Collection of Laws and International Treaties (the Act on the Collection of Laws and International Treaties), as amended, i.e. as of ..... 2026. At the same time, the amendments to the Pharmaceuticals Act and the Addictive Substances Act implemented by Act No 270/2025 will come into effect on …… 2026. In view of the fact that it is an implementing Government Regulation which implements certain provisions of the Pharmaceuticals Act and the Addictive Substances Act, it is desirable that the effective date of this Government Regulation be set to coincide with the effective date of the amendments to the Pharmaceuticals Act and the Addictive Substances Act.