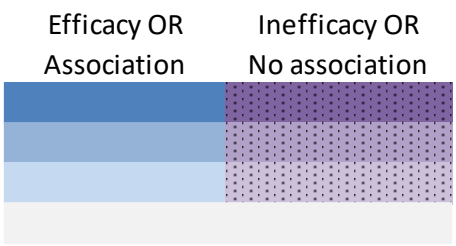
Health effects	Level of evidence of the effect
Positifs	
1) To treat the symptoms of a disease	
*** biological symptoms**	
chronic pain	cannabis
spasticity (multiple sclerosis), assessed by the patient	cannabinoids
spasticity (multiple sclerosis), assessed by the clinician	cannabinoids
spasticity (paralysis, spinal cord injury)	cannabinoids
chemotherapy-induced nausea and vomiting	cannabinoids
appetite and weight loss (HIV/AIDS)	cannabis and cannabinoids
cancers	cannabinoids
anorexia et cachexia (cancer)	cannabinoids
epilepsy	cannabinoids ¤
irritable bowel disease	cannabinoids (THC)
intraocular pressure (glaucoma)	cannabinoids
amyotrophic lateral sclerosis	cannabinoids
motor system symptoms (Parkinson's disease)	cannabinoids
dystonia (involuntary muscle contractions)	cannabinoids (THC)
*** behavioral symptoms**	
sleep disturbances (sleep apnoea, fibromyalgia, chronic pain, multiple sclerosis, etc.)	cannabinoids (THC + CBD)
anxiety	cannabinoids (CBD)
symptoms of Tourette syndrome	cannabinoids (THC)
symptoms of post-traumatic stress disorder	cannabinoids (THC)
symptoms of dementia	cannabinoids
depressive symptoms (chronic pain and dementia)	cannabinoids (THC + CBD)
behavioural symptoms (schizophrenic disorders)	cannabinoids (CBD)
behavioural symptoms (Huntington's disease)	cannabinoids
addictions	cannabinoids
2) Positive effects without a therapeutic effect being sought	
decreased risk of metabolic syndrome and diabetes	cannabis
increased pulmonary capacity	cannabis
Negative	
3) On the development of cancers	
lung cancers	cannabis
head and neck cancers	cannabis
testicular cancers (non-seminoma-type germ cell tumours)	cannabis
oesopharyngeal cancers)	cannabis
non-Hodgkin lymphoma, malignant gliomas, prostate cancer, cervical cancer, anal cancer	cannabis
leukaemias and brain cancers, in offspring	cannabis (parents)
4) On cardiometabolic and respiratory risks	
myocardial infarction (chronic use)	cannabis
myocardial infarction (occasional use)	cannabis
stroke	cannabis
risk of prediabetes	cannabis
chronic bronchitis symptoms	cannabis
improvements in respiratory symptoms	cannabis (cessation)
chronic obstructive pulmonary dis. if combined with tobacco use	cannabis
asthma	cannabis

Adapted from: The National Academies of Sciences, Engineering and Medicine. *(2017).* The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. ¤ : *Since this document was published at the start of 2017, the level of evidence may have changed for some effects. In particular, this is the case for epilepsy, with Epidyolex having been granted a European marketing authorisation for Dravet syndrome and Lennox-Gastaut syndrome.*

5) On the immune system	
decrease in inflammatory markers	cannabis
liver fibrosis (hepatitis C)	cannabis
immune status in individuals with HIV	cannabis
6) On accidents	
motor vehicle accidents	cannabis
overdoses in children	cannabis
occupational accidents	cannabis
mortality - cannabis overdose	cannabis
mortality - all causes	cannabis
7) For prenatal, perinatal and neonatal exposure	
low birth weight	cannabis
pregnancy complications	cannabis
admission of the infant to the neonatal intensive care unit	cannabis
long-term outcomes in the offspring (sudden infant death syndrome, academic achievement, cannabis use, etc.)	cannabis
8) On psychosocial risks	
cognitive impairement (memory, attention, learning)	cannabis
impaired academic achievement	cannabis
increased rates of unemployment and low income	cannabis
impaired social and relational capacities	cannabis
9) On mental health	
schizophrenia and other psychoses	cannabis
better cognitive performance (individuals with psychotic disorders using cannabis)	cannabis
worsening of negative symptoms of schizophrenia	cannabis
worsening of postive symptoms of schizophrenia	cannabis
development of depressing disorders	cannabis
improvement/worsening of depression	cannabis
suicide attempts	cannabis
development of social anxiety disorder	cannabis
development of other anxiety disorders	cannabis
development of bipolar disorders	cannabis
worsening of bipolar disorders	cannabis
development of post-traumatic stress disorder	cannabis
worsening of symptoms of post-traumatic stress disorder	cannabis



Efficacy OR Association	Inefficacy OR No association	Level of evidence
		Substantial or conclusive evidence
		Moderate evidence
		Limited evidence
		No or insufficient evidence

cannabinoids : cannabidiol (CBD) or tetrahydrocannabinol (THC), synthesised or extracted, oral consumption

Adapted from: The National Academies of Sciences, Engineering and Medicine. *(2017).* The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research. ¤ : *Since this document was published at the start of 2017, the level of evidence may have changed for some effects. In particular, this is the case for epilepsy, with Epidyolex having been granted a European marketing authorisation for Dravet syndrome and Lennox-Gastaut syndrome.*

*Individuals consulted**

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*– Prof. **Nicolas Authier**, psychiatrist and pharmacologist, Head of the Medical Pharmacology Department and Department Head at the Centre for Pain Assessment and Treatment, Clermont-Ferrand University Hospital, Chairman of the temporary scientific committee (CST) dedicated to the implementation of the medical cannabis trial*

*– Prof. **Amine Benyamina**, psychiatrist and addiction specialist, Head of the Department of Psychiatry and Addictology at Paul Brousse Hospital, Villejuif and Chairperson of the French Addictology Federation*

*– Mr. **François Bruneaux**, Assistant to the Deputy Director, Subdirectorate of health products policy and practice and care quality at the General Directorate for Health*

*– Mr. **Yves Christol**, General Manager of InVivo Food&Tech and Ms. **Carole Hernandez-Zakine**, Director of Public Affairs for Bioline (InVivo)*

*– Mr. **Aurélien Delecroix**, Chairman of the French Hemp Union and Founding Chairman of the company Greenleaf*

*– Prof. **Marie-Odile Krebs**, psychiatrist, Department Head at Sainte-Anne Hospital, responsible for the Pathophysiology of Psychiatric Diseases team at the Paris Institute of Psychiatry and Neurosciences*

*– Ms. **Fabienne Lopez**, Chairperson of the "Principes actifs" (Active substances) Association, Messrs. **Christian D. Muller**, pharmacologist, Senior Research Officer at the CNRS, Hubert Curien Multidisciplinary Institute, and **Bertrand Rambaud**, respectively responsible for the Scientific Division and the Patient Division of the French-speaking Union for Cannabinoids in Medicine*

*– Mr. **Olivier Manzoni**, Inserm Research Director, Joint Manager of the Adolescence and Developmental Vulnerability to Neuropsychiatric Diseases team at the Mediterranean Institute of Neurobiology*

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*– Ms **Hélène Moore**, General Manager of Aurora France*

*– Mr. **Giles Moss**, General Manager Europe at GW Pharmaceuticals, Mr. **Jean-Luc Gaunel**, Manager France and Mr. **Ben Whalley,** Research Manager at GW Pharmaceuticals*

*– Ms. **Ivana Obradovic**, sociologist, Deputy Director of the French Monitoring Centre for Drugs and Drug Addiction (OFDT) and Associate Researcher at the Centre for Sociological Research in Law and Penal Institutions (CESDIP)*

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– The Department of Science and Technology and the Department of Social Affairs at the French Embassy in Germany
– The Department of Science and Technology and the Department of Social Affairs at the French Embassy in the USA
– The Department of Internal Security at the French Embassy in Canada

** NB: The individuals consulted in some cases expressed divergent opinions concerning one or more aspects of the briefing.*
Scientific coordination by Ms. Mathilde Lecompte, Scientific Advisor

References

(1) Single Convention on Narcotic Drugs of 1961, adopted by the United Nations, as modified by the 1972 Protocol amending the Single Convention on Narcotic Drugs of 1961: https://www.unodc.org/pdf/convention_1961_fr.pdf.

(2) This is the case for Germany, Australia, several states in the USA, Israel, the Netherlands, Portugal, the United Kingdom and Switzerland, etc. European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) (2018). Medical use of cannabis and cannabinoids: questions and answers for policymaking.

(3) This is the case for Uruguay, Canada and some states of the USA. See the executive summaries of the Observatoire français des drogues et toxicomanies *(French Monitoring Centre for Drugs and Drug Addiction); "*La légalisation du cannabis au Canada : genèse et enjeux de la réforme*" ("Cannabis legalisation and regulations in Canada: background and challenges") (https://www.ofdt.fr/BDD/publications/docs/eisxioya.pdf), "*La légalisation du cannabis aux États-Unis, vers une régulation du marché ?*" ("Cannabis legalisation in the USA: towards market regulation?") (https://www.ofdt.fr/BDD/publications/docs/eisxioz6.pdf) and "*Une analyse comparée des expériences de régulation du cannabis :

Colorado, État de Washington, Uruguay" *("A comparative analysis of cannabis regulation experiences: Colorado, Washington State, Uruguay" (https://www.ofdt.fr/BDD/publications/docs/CannalexRFS.pdf).*

(4) There is little correlation between legal status and use. France has the highest use prevalence in Europe in the "recent use" (< 30 days), in 15-16 year-olds" category (ESPAD 2015 – The European school survey project on alcohol and other drugs) and in the "use in the last 12 months in 15-34 year-olds" category (report on illicit drugs in France 2017 – OFDT and European monitoring centre for drugs and drug addiction) http://www.emcdda.europa.eu/system/files/publications/3074/ESPAD_report_2015.pdf and http://www.emcdda.europa.eu/system/files/publications/4523/TD0416916ENN.pdf.

(5) The European Parliament has adopted a resolution aimed at promoting research concerning the therapeutic potential of cannabis and its derivatives and their medical use where justified. European Parliament resolution of 13 February 2019 on the use of cannabis for medicinal purposes: http://www.europarl.europa.eu/doceo/document/TA-8-2019-0113_FR.html, website consulted on 4.11.19.

(6) The demand on the part of patients was reflected in the case of an individual having taken the ethics and cancer committee and the French cancer league to court for what this individual perceived as a treatment refusal. https://www.ethique-cancer.fr/files/file_fields/2018/11/26/cec-2018-avis35-cannabis-texte-final.pdf.

7 The specific temporary scientific committee began its work in September 2018 and completed it in June 2019. https://ansm.sante.fr/L-ANSM/Comites-scientifiques-specialises-temporaires/Comites-scientifiques-temporaires/Comites-scientifiques-temporaires/CSST-Evaluation-de-la-pertinence-et-de-la-faisabilite-de-la-mise-a-disposition-du-cannabis-therapeutique-en-France, website consulted on 4.11.19.

(8) THC, or Δ9-tetrahydrocannabinol, is one of the main two cannabinoids in cannabis.

(9) The industrial hemp varieties that are allowed to be grown in France are varieties listed in a variety catalogue managed by the Ministry of Agriculture; these varieties contain less than 0.2% THC. Their cultivation is highly regulated and subject to controls, to check that the THC concentration does not exceed the legal limit. The industrial use of hemp flowers is prohibited in France. https://www.drogues.gouv.fr/actualites/cannabidiol-cbd-point-legislation, consulted on 28.10.19.

Hemp varieties contain different cannabinoid concentrations depending on the species: the Cannabis indica *species contains more THC than* Cannabis sativa*. Within each species, there is a very broad variety of strains due to the plant's considerable hybridisation capacities.*

(10) France is the biggest producer of industrial hemp in Europe. Hemp can be used for numerous industrial applications: building, packaging, motor vehicle industry, pulp for paper, food (human and animal), etc. Institut technique du chanvre *(2007).* Le chanvre industriel. Guide technique. Edition Institut technique du chanvre *and Chanebeau A. (2013).* Le chanvre, du rêve aux milles utilités ! Editions Platinium.

(11) In Europe, cannabis is most widely used in the form of blocks of resin. These blocks are composed of the resin naturally present in the plant's flowers, which has a higher cannabinoid concentration than the rest of the plant.

(12) As a more marginal use, cannabis can be consumed in the form of an oil extract, containing cannabinoids in higher concentrations since they are lipophilic. The method of use changes the kinetics of THC and CBD distribution in the blood: smoking is the fastest route, via the air/blood interface constituted by the alveoli of the lungs, while the ingested route is the slowest, particularly if other foods are eaten at the same time (there is therefore a risk of overdose with the ingested route due to the effects that appear to be limited in the short term). Mouth sprays are relatively rapid as a result of the high number of blood vessels in the mucous membranes.

(13) Written records describing the plant and its medicinal use in India and China date back to more than a millennium BC. Mechoulam, R. (2019). Cannabinoids As Therapeutic Agents (CRC Press). ISBN: 978-0-429-53626-7.

*(14) In particular, this type of use existed in literary circles: in the 19th century, the poets Théophile Gautier and Charles Beaudelaire, for example, were members of the "*Club des Haschischins*" or "Hashish-smokers' club". This use was also popular during the hippie movement. Mechoulam, R. (2019). Cannabinoids As Therapeutic Agents (CRC Press). ISBN: 978-0-429-53626-7.*

(15) Spilka et al. (2018) Les drogues à 17 ans : analyse de l'enquête ESCAPAD 2017. Tendances. Observatoire français des drogues et toxicomanies. *https://www.ofdt.fr/BDD/publications/docs/eftxssy2.pdf.*

*(16) The average THC content of cannabis increased from 5% in 2006 to more than 10% in 2016 and 11% in 2018 for herbal cannabis and from 8% to 17% and 26.5% for resin, i.e. a trebling of the THC concentration in resin in 12 years. European monitoring centre for drugs and drug addiction. (2019). Developments in the European cannabis market. EMCDDA Papers. http://www.emcdda.europa.eu/system/files/publications/11391/TDAU19001ENN.pdf) and "*Drogues, chiffres clés*", 8th edition, OFDT, 2019 (https://www.ofdt.fr/BDD/publications/docs/DCC2019.pdf).*

'17) World Health Organisation Expert Committee on Drug Dependence. (2018). Cannabidiol, critical review report. https://www.who.int/medicines/access/controlled-substances/CannabidiolCriticalReview.pdf.

(18) Since cannabidiol is not classed as a narcotic, the sale of products containing it is possible as long as these products do not claim any therapeutic benefits – which only medicinal products may claim – if there is no reference made to cannabis and if the products contain no traces of THC. https://www.drogues.gouv.fr/actualites/cannabidiol-cbd-point-legislation, consulted on 28.10.19. However, the total absence of THC in products is limited by the fact that THC and CBD share common precursors in their biosynthesis.

It should be noted that the use of CBD in large quantities, as scheduled in the medical cannabis trial, falls within the scope of medicinal use. "Wellness" cannabis players estimate that this type of use could be characterised by a limited dose of 20 mg of CBD per day, whereas a medical effect could be achieved from doses of 60 mg/day. For example, Epidyolex® may be prescribed at doses ranging from 5 to 20 mg/kg/day, i.e., 50 to 200 mg/day for a child weighing 10 kg.

(19) Pertwee, R.G. (2006). Cannabinoid pharmacology: the first 66 years. Br J Pharmacol 147, S163–S171.

(20) The first endocannabinoids discovered were 2-arachidonylglycerol and anandamide. These are lipids, synthesised in the cell membrane. Other endocannabinoids have been discovered since, such as noladin ether, virodhamine and N-Arachidonoyl dopamine.

(21) Other receptors are also involved in the endocannabinoid system; this is the case for TRPV1. Unlike CB1 and CB2, which are "protein G-coupled" receptors, i.e., which have a relatively slow action mechanism since they are subject to a cascade of activations in the cell, the TRPV1 (transient receptor potential vanilloid 1) receptor is a channel receptor, the activation of which has an immediate effect on neuronal activity.

(22) There are no endocannabinoid reserves (lipids therefore hydrophobic) in the neurons, in contrast with hydrophilic neurotransmitters, stored in the form of vesicles. Hence, regulation of their synthesis and degradation by the enzymes performing these functions is a way of controlling their quantity and therefore their effects. These enzymes are pharmacological targets that could enable future treatments to act on the endocannabinoid system. Russo, E.B. (2016). Beyond Cannabis: Plants and the Endocannabinoid System. Trends Pharmacol. Sci. 37, 594–605 and Patel, S., Hill, M.N., Cheer, J.F.,

Wotjak, C.T., and Holmes, A. (2017). The endocannabinoid system as a target for novel anxiolytic drugs. Neuroscience & Biobehavioral Reviews 76, 56–66.

23 The central nervous system consists of the brain and spinal cord. CB1 is present in most of the brain's structures: it is found in the cerebellum, the amygdala, the hippocampus and the prefrontal cortex, these structures being respectively associated with coordination of thoughts and actions, control of emotions, memory and higher cognitive functions (reasoning and executive functions). The CB1 receptor is almost absent from the brain stem, the structure that controls vital functions such as breathing and heart rate. The almost complete absence of cannabinoid receptors in this structure is the explanation widely given for the absence of cases of overdose due to cannabis, whereas opioid receptors, for example, are present in this part of the brain. Krebs M.O. et Jay T. (2018). Maturation cérébrale à l'adolescence et consommation de cannabis. Addictions et comorbidités psychiatriques. La revue du praticien *68, 7.*

24 The peripheral nervous system includes all the nerves that convey motor activity of the central nervous system to the muscles and sensory information from the peripheral to the central nervous system. CB1 is more expressed in the brain than in other tissues, but it is also found in the muscles, therefore also in the heart, the liver, the bowel, adipose tissue, etc. Bouquié, R., Deslandes, G., Mazaré, H., Cogné, M., Mahé, J., Grégoire, M., and Jolliet, P. (2018). Cannabis and anticancer drugs: societal usage and expected pharmacological interactions – a review. Fundamental & Clinical Pharmacology 32, 462–484.

25 Via the microglia, immune system cells in the brain, the CB2 receptor is also found in the central nervous system. The action of THC via CB2, which is anti-inflammatory, also takes place in the brain, therefore.

26 eCBs have a retrograde action, in contrast with the prevailing paradigm for neurotransmitters (carrying information from an upstream neuron to a downstream neuron): at synapse level, eCBs are synthesised by the downstream neuron and bind to the receptors of the upstream neuron, reducing the latter's activity. This method of parallel regulation (or modulation) of neuronal activity on a local level (synapse) is one of the mechanisms enabling synaptic plasticity. This phenomenon consists of mechanisms that influence the transmission of information from one neuron to another, leading to the strengthening or weakening of certain synapses. In concrete terms, these mechanisms can modulate the amount of information transmitted by the upstream neuron and the way the information is received by the downstream neuron. Synaptic plasticity and the reinforcement of certain synapses - and hence certain connections - compared to others is the basis of learning processes.

27 Roland, A.B., Ricobaraza, A., Carrel, D., Jordan, B.M., Rico, F., Simon, A., Humbert-Claude, M., Ferrier, J., McFadden, M.H., Scheuring, S., et al. (2014). Cannabinoid-induced actomyosin contractility shapes neuronal morphology and growth. Elife 3, e03159.

*28 An increase in structural connectivity (via axon bundles) and functional connectivity (the simultaneous activation of brain areas) is, along with synaptic refinement, during which some of the connections between neurons are eliminated, one of the phenomena characterising brain maturation. These phenomena are accompanied by cognitive changes. Office scientific briefing on "*Neurosciences et responsabilité de l'enfant*" ("Neurosciences and responsibility in children"), Michel Amiel, Senator, November 2019.*

29 Patel, S., Hill, M.N., Cheer, J.F., Wotjak, C.T., and Holmes, A. (2017). The endocannabinoid system as a target for novel anxiolytic drugs. Neuroscience & Biobehavioral Reviews 76, 56–66.

30 Animals used as pain models present both a higher number of central and peripheral CB1 receptors and higher eCB levels. In addition, the injection of endocannabinoids in animals has an analgesic effect. Zogopoulos, P., Vasileiou, I., Patsouris, E., and Theocharis, S.E. (2013). The role of endocannabinoids in pain modulation. Fundamental & Clinical Pharmacology 27, 64–80 and Richardson, J.D., Kilo, S., and Hargreaves, K.M. (1998). Cannabinoids reduce hyperalgesia and inflammation via interaction with peripheral CB1 receptors. Pain 75, 111–119.

31 The action mechanism(s) of CBD is/are not fully understood; the biological targets of CBD are very varied. In vitro, CBD has an antagonistic effect on the CB1 receptor (it reduces the likelihood of THC activating the receptor), but at very high concentrations, not realistic with respect to recreational or medicinal use (McPartland et al*, 2015). A recent study suggests that this antagonistic effect may occur at lower concentrations, but it needs to be repeated by other research teams to be confirmed (Tham* et al*, 2019). The effects of CBD, and in particular the anti-epileptic effects, probably come from other targets; the interactions between CBD and receptors such as TRPV1 or serotonin receptors are being studied.*

McPartland, J.M., Duncan, M., Marzo, V.D., and Pertwee, R.G. (2015). Are cannabidiol and Δ9-tetrahydrocannabivarin negative modulators of the endocannabinoid system? A systematic review. British Journal of Pharmacology 172, 737–753.
Tham, M., Yilmaz, O., Alaverdashvili, M., Kelly, M.E.M., Denovan-Wright, E.M., and Laprairie, R.B. (2019). Allosteric and orthosteric pharmacology of cannabidiol and cannabidiol-dimethylheptyl at the type 1 and type 2 cannabinoid receptors. British Journal of Pharmacology 176, 1455–1469.

32 eCBs work on a time scale in the range of a second, since they are quickly degraded, whereas phytocannabinoids persist in the brain for up to several hours. In addition, the prolonged activation of CB1 by phytocannabinoids results in cascades of cell events, which are the source of the durability of the effects of cannabis use – lasting from one hour to around ten hours.

33 The multiple different ways of using cannabis (smoked, with or without tobacco, by spraying, by ingestion, etc.) and the difficulty of knowing the patient's exact consumption history (cannabis, tobacco, alcohol, etc.) are additional complications when it comes to collating studies and reaching conclusions. The National Academies of Sciences, Engineering and Medicine. (2017) The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research.

34 The National Academies of Sciences, Engineering and Medicine. (2017) The Health Effects of Cannabis and Cannabinoids: The Current State of Evidence and Recommendations for Research.

35 Mücke, M., Phillips, T., Radbruch, L., Petzke, F., and Häuser, W. (2018). Cannabis-based medicines for chronic neuropathic pain in adults. Cochrane Database of Systematic Reviews.

36 Smith, L.A., Azariah, F., Lavender, V.T., Stoner, N.S., and Bettiol, S. (2015). Cannabinoids for nausea and vomiting in adults with cancer receiving chemotherapy. Cochrane Database of Systematic Reviews.

37 These are painful, uncontrolled muscle contractions, causing pain and spasms.

38 However, conclusions vary greatly depending on the studies. A recent meta-analysis pointed to the lack of high-quality studies, particularly in this field, and concluded that there was insufficient evidence to support the use of cannabinoids in the treatment of psychiatric disorders. Black, N., Stockings, E., Campbell, G., Tran, L.T., Zagic, D., Hall, W.D., Farrell, M., and Degenhardt, L. (2019). Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis. The Lancet Psychiatry In Press.

39 Decree No. 2013-473 of 5 June 2013 lifted the ban on using cannabis derivatives in the case of medicinal products (article R. 5132-86 of the French Public Health Code).

40 However Sativex® is still not available in France, due to the absence of an agreement concerning the price of the medicine. In 2014, the Haute Autorité de Santé *(French National Authority for Health) awarded Sativex® a low actual clinical benefit and no clinical added value compared to existing medicinal products. Sativex® contains THC and CBD in a ratio of 1: 1.*

41 Epidyolex® had been available in France since 2018 thanks to a "Temporary Authorisation for Use" (ATU) early access programme. It was granted a European MA in 2019. Epidyolex® contains only CBD. Another medicine containing cannabinoids, Marinol®, is available on an ATU early access programme basis. The active substance – dronabinol – of this product is synthetic THC, not THC extracted from the plant, as is the case in Sativex®. Marinol® is indicated for cases of central and peripheral neuropathic pain following the failure of currently available treatments.

42 France's Assemblée nationale *(National Assembly) adopted an amendment made by the general rapporteur for the draft social security funding law (PLFSS) for 2020, Olivier Véran, upon the first reading of this PLFSS (amendment No. AS721), which notably schedules that the conditions for implementation of the trial will be set using a regulatory process. The PLFSS 2020 will be examined in the Senate in early November, then submitted to a joint committee. Text of the adopted amendment:*

"I. – On an experimental basis, for a period of two years, the State may authorise the medical use of cannabis in the form of products meeting pharmaceutical standards, in certain indications or clinical situations refractory to accessible indicated treatments.

II. – The conditions for implementation of the trial are defined by the regulations. In particular, these specify the treatment conditions, the number of patients concerned, arrangements for importing, production, procurement, prescribing and dispensing by hospital and community pharmacies, along with conditions for patient information and follow-up and health professional training.

III. – Within a period of six months following the end of the trial, the Government shall submit to Parliament a report concerning, in particular, the medical use of cannabis for patients, their follow-up, organisation of prescribing and dispensing channels, as well as the associated spending. This report shall specifically examine the relevance of extending the recourse to medical use of cannabis at the end of the trial and, if applicable, the conditions for its funding by the national health insurance system."

43 These concern Lennox-Gastaut syndrome and Dravet syndrome.

44 Estimates made by players in the field suggest that these indications could concern 300,000 to 600,000 people in France. An extension of the indications could increase the number of potential users to 1 to 2 million.

45 Cannabis extracts will probably be proposed in the form of oil, capsules or a mouth spray. Several types of cannabis will be available, with THC: CBD ratios capable of covering the spectrum of conditions to be alleviated. The THC: CBD ratios (expressing active substance concentration ratios) of 1: 1 and 5: 20 could be intended for neuropathic pain, including spasticity in multiple sclerosis, the high THC ratio (20: 1) for palliative care and the high CBD ratios (1: 20 and 1: 50) for rare epilepsy cases.

46 Pain management centres, specialised multiple sclerosis centres, etc.

47 A general practitioner, who has also taken the training, will then be able to take over management of the treatment. It is scheduled that training of doctors and the registry that will be used for patient follow-up and analysis of trial efficacy will be funded by the national health insurance system, while the products distributed to patients will be supplied free of charge by foreign companies who already have expertise in medical cannabis, the list of which has not been unveiled (however, it may be assumed that these could be Aurora, Canopy Growth, Bedrocan, etc.). The products will be dispensed by hospital and community pharmacies and pharmacists will have received specific training for this purpose.

48 A proper assessment of patient needs, as well as their rigorous follow-up, appear to be important in view of the fact that a third of patients having used medical cannabis in Germany stopped it following the development of adverse reactions and/or due to a lack of treatment efficacy (non-exhaustive preliminary data supplied by the scientific department of the French Embassy in Germany). This high level of adverse reactions is consistent with what is observed in clinical studies testing cannabis or cannabinoids in the treatment of diseases. The adverse reactions observed include dizziness, dry mouth, disorientation, nausea, euphoria, confusion or drowsiness. Hallucinations, paranoia and psychotic disorders can also occur.

49 Évaluation des médicaments en vue de leur remboursement – Haute Autorité de santé *(Assessment of medicinal products with a view to their reimbursement – Haute Autorité de santé). https://webzine.has-sante.fr/upload/docs/application/pdf/2017-03/dir4/v13ok-circuit_medicament_ct_ceesp-160317.pdf.*

50 In particular, the potential of CBD as a treatment for alcohol addiction is being explored. De Ternay, J., Naassila, M., Nourredine, M., Louvet, A., Bailly, F., Sescousse, G., Maurage, P., Cottencin, O., Carrieri, P.M., and Rolland, B. (2019). Therapeutic Prospects of Cannabidiol for Alcohol Use Disorder and Alcohol-Related Damages on the Liver and the Brain. Front Pharmacol 10, 627.

51 Research work is currently under way to study the potential therapeutic virtues of cannabis, particularly in the treatment of cancer. Relatively positive results have been obtained in vitro on pancreatic tumour cell cultures, but these cannot justify use in humans for curative purposes at present. Moreau, M., Ibeh, U., Decosmo, K., Bih, N., Yasmin-Karim, S., Toyang, N., Lowe, H., and Ngwa, W. (2019). Flavonoid Derivative of Cannabis Demonstrates Therapeutic Potential in Preclinical Models of Metastatic Pancreatic Cancer. Front. Oncol. 9.

52 This wealth of compounds - some of which are psychoactive and others simply aromatic - explains the large number of uses of cannabis, in contrast with other drugs. Russo, E.B. (2011). Taming THC: potential cannabis synergy and phytocannabinoid-terpenoid entourage effects. British Journal of Pharmacology 163, 1344–1364.

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