Can controlled substances become the new standard-of-care for psychiatric disorders?

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Disorders such as depression and anxiety have long been treated with drugs that are associated with side effects such as blurred vision, headaches, diarrhoea, sexual dysfunction, insomnia and tremors.

First-line therapies such as Zoloft (sertraline hydrochloride) and benzodiazepines such as diazepam also come with boxed warnings due to the increased risk of suicidal tendencies. This risk is especially heightened in children, adolescents and young adults under the age of 24.

The extreme care that must be taken with prescribing these medicines, along with the fact that these drugs can take weeks to exhibit therapeutic effects, has led pharmaceutical companies to consider developing products with superior safety and efficacy profiles in comparison to treatments currently available.

Out of the 70 products in clinical development for major depressive disorder in the seven major markets (7MM: the US, France, Germany, Italy, Spain, the UK and Japan), two drug candidates, Allergan's AGN-241751 and Seelos Therapeutics' ketamine hydrochloride, were granted fast track designation by the US Food and Drug Administration (FDA). In addition, Acadia Pharmaceuticals' pimavanserin tartrate received breakthrough therapy designation from the FDA. The high level of innovation in the pipeline for psychiatric disorders can be partially explained by the urgency of treating vulnerable patients, as the prevalence of these conditions continues to increase in the 7MM.

A unique aspect of the pipeline for psychiatric disorders is the gravitation towards controlled substances such as ketamine and midomafetamine. Janssen's Spravato (esketamine) was approved for treatment-resistant depression in 2018 and midomafetamine has been granted breakthrough therapy designation for the treatment of post-traumatic stress disorder (PTSD).

Furthermore, cannabidiol, a non-psychoactive compound found in cannabis plants, is being investigated for efficacy in treating disorders such as substance addiction, anxiety and depression. In November 2019, psilocybin was granted breakthrough therapy designation by the FDA for the treatment of major depressive disorders. Psilocybin is converted into psilocin, a pharmacologically active serotonin-receptor agonist. As a Schedule 1 substance according to the Convention on Psychotropic Substances, approval to use psilocin in clinical trials has only been given to a limited number of organisations in the US, the UK and Switzerland.

Despite the potentially addictogenic properties of some controlled substances, clinical trials are demonstrating evidence that when administered in appropriate conditions, such as in combination with psychotherapy, these products can alleviate the cognitive symptoms of disorders such as PTSD.

This is considered to be one of the most important parts of recovery, as addressing cognitive disturbances will improve the quality of life of patients and reduce the frequency of intrusive thoughts. Important challenges to overcome for drug developers include restrictions on conducting research on controlled substances, gaining approval for distribution in various markets, and negotiating the pricing and reimbursement policy for products in clinical development.