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Zuranolone

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Zuranolone is an oral neuroactive steroid under development by Sage Therapeutics and Biogen (SAGE-217/BIIB125). It is currently being evaluated as a treatment option for postpartum depression (PPD) and major depressive disorder (MDD) [1].

MDD is one of the most frequent mental disorders; for example, in the United States, it affects more than 8 % of adults every year. On the other hand, PPD is one of the most common medical complications during and after pregnancy and is estimated to affect approximately one in eight women who have given birth. Although clinical presentation of MDD and PPD varies, patients frequently experience feelings of hopelessness, anxiety or sadness which, consequently, affect their quality of life, in terms of ability to work, maintenance of relationships and school attendance. In severe cases, risk of suicide can be substantial. As for the treatment of these disorders, current guidelines include a multitude of approved antidepressants which can help alleviate symptoms for most patients. However, these medications in general require four to six weeks to work. In translation that means patients must endure their symptoms for a month or more after starting a treatment to see if it helps.

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The GABA system is the major inhibitory signalling pathway of the brain and central nervous system. It is important in regulation of brain function, while altered GABA neurotransmission has been implicated in the pathogenesis of depression. Zuranolone is thought to work via positive allosteric modulation of GABA - A receptors and the drug targets brain networks that are responsible for functions such as mood, arousal, behaviour, and cognition [2].

Zuranolone could help in reduction of depressive psychopathology more quickly than standard medications. This investigational drug is being evaluated as a rapid-acting, once-daily, 14 - day oral short course therapy for adult patients with MDD and PPD. The new drug Application submission for zuranolone consists of data from the NEST and LANDSCAPE clinical development programs. The NEST program includes 2 studies (ROBIN and SKYLARK) of zuranolone in adult women with PPD. The LANDSCAPE program includes 5 studies (MDD -201B, MOUNTAIN, SHORELINE, WATERFALL, and CORAL) of zuranolone, which were conducted in adult patients with MDD. In the Phase 3 CORAL study on MDD, the primary endpoint was a reduction in depressive symptoms at day 3 over a 14 - day treatment period. The results were statistically significant on day 3. In Phase 3 WATERFALL study, MDD patients taking zuranolone had a statistically significant improvement in depressive symptoms over placebo at day 15. The ongoing SHORELINE

study in patients with MDD found the median time to the first repeat treatment course for patients who responded to the initial 14 - day treatment course was 135 days for the completed 30 mg cohort and 249 days for the ongoing 50 mg cohort. Studies indicate that zuranolone has shown prompt and continuous improvement of depressive symptoms and has been found to have a consistent safety profile and to be generally well-tolerated [3,4].

Zuranolone was granted fast track designation by the United States Food & Drug Administration in 2017 and Breakthrough Therapy Designation for MDD in 2018. The Food & Drug Administration also granted Fast Track Designation for PPD in 2022. As of December 2022, zuranolone is in preregistration for MDD and PPD [5].

All in all, even though numerous antidepressants are already available and readily utilized in treatment of depression, this disorder is still a foremost contributor of disability worldwide. In the area of unmet needs, zuranolone could diversify the treatment landscape for depression since, in clinical development projects, it has demonstrated significant, consistent, rapid and permanent reduction in depressive symptoms (including anxiety), as well as good tolerability and safety.

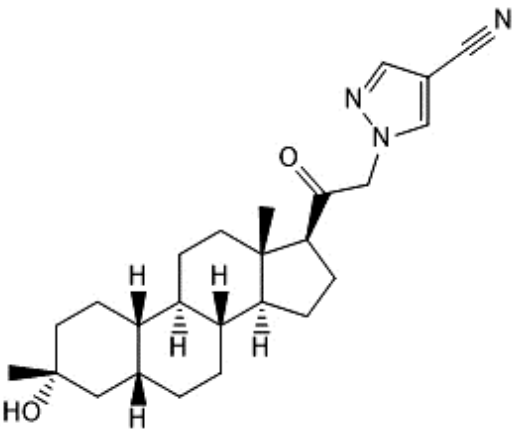

Figure 1. The chemical structure of zuranolone

References

1. Drugs.com. Zuranolone FDA approval status [Internet]. Dallas (US): Drugs.com; 2023 [updated 2022; cited 2023 Jan 20]. Available from: https://www.drugs.com/history/zuranolone.html
2. Gunduz-Bruce H. Zuranolone - An investigational oral neuroactive steroid and positive allosteric modulator of GABA type A receptors for postpartum depression and major depressive disorder [Internet]. New York (US): touchNeurology; 2023 [updated 2023; cited 2023 Jan 20]. Available from:https://touchneurology.com/psychiatric-disorders/journal-articles/zuranolone-an-investigational-oral-neuroactive-steroid-and-positive-allosteric-modulator-of-gaba-type-a-receptors-for-postpartum-depression-and-major-depressive-disorder/
3. BioSpace. Sage therapeutics and biogen announce the phase 3 CORAL study met its primary and key secondary endpoints [Internet]. Des Moines (US): Biospace; 2023 [updated 2022; cited 2023 Jan 20]. Available from: https://www.biospace.com/article/sage-therapeutics-and-biogen-announce-the-phase-3-coral-study-met-its-primary-and-key-secondary-endpoints/
4. Businesswire. Sage therapeutics and biogen present new analyses at psych congress further evaluating the efficacy and safety of zuranolone [Internet]. San Francisko (US): Businesswire; 2023 [updated 2022; cited 2023 Jan 20]. Available from:https://www.businesswire.com/news/home/20220918005062/en/Sage-Therapeutics-and-Biogen-Present-New-Analyses-at-Psych-Congress-Further-Evaluating-the-Efficacy-and-Safety-of-Zuranolone
5. Biogen. Biogen and sage therapeutics complete rolling submission of new drug application for zuranolone in the treatment of major depressive disorder and postpartum depression [Internet]. Cambridge (US): Biogen; 2023 [updated 2022; cited 2023 Jan 20]. Available from:https://investors.biogen.com/news-releases/news-release-details/biogen-and-sage-therapeutics-complete-rolling-submission-new