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Evaluating the Efficacy of Gepirone in Major Depressive Disorder: A Systematic Review

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ADMINISTRATIVE INFORMATION

Support - N/A.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 03 February 2024 and was last updated on 03 February 2024.

INTRODUCTION

Review question / Objective This systematic review aims to examine randomized controlled trials to determine the efficacy of gepirone as a treatment for MDD in patients aged 17-years and older, as well as the adverse effects experienced by patients taking gepirone in this patient population.

Rationale Bristol-Myers Squibb initially created Gepirone in the 1980s before being licensed to Fabre-Kramer Pharmaceuticals (Fabre-Kramer) for development and marketing. Since its inception, gepirone was denied approval for the treatment of MDD by the U.S. Food and Drug Administration (FDA) in 2002, 2004, and 2007 for its inability to produce sufficient positive studies to mitigate opposing studies with negative results.14 Although no additional clinical trials were performed since the early 2000s, Fabre-Kramer resubmitted another appeal, leading to the approval to market Exxua (gepirone) as a treatment option for MDD, highly distinguished from SSRIs for its improvement of sexual dysfunction and neutral effect on weight.

Condition being studied Major depressive disorder.

METHODS

Search strategy The Boolean/Phrase search feature was used with the terms in EBSCOhost: (gepirone or Exxua or N06AX19) AND (depression OR depressive disorder OR depressive symptoms OR major depressive disorder OR MDD). The Boolean/Phrase search feature was used with the terms in PubMed: (gepirone OR Exxua OR N06AX19) AND (depression OR depressive

disorder OR depressive symptoms OR major depressive disorder OR MDD).

Participant or population Participants aged 17 and older diagnosed with Major depressive disorder.

Intervention Gepirone.

Comparator Placebo.

Study designs to be included Randomized-Controlled Trials.

Eligibility criteria Inclusion criteria consisted of randomized controlled trials, English language, human studies, and patients at least 17-years-old, without a restriction on publication dates. Studies involving the use of gepirone for indications other than major depressive disorder, concomitant drug use for treatment of major depressive disorder, and patients younger than 17-years-old were excluded.

Information sources EBSCOhost was utilized to simultaneously search Academic Search Primer, APA PsycArticles, APA PsycInfo, CINAHL Ultimate, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and MEDLINE. An additional search was conducted using PubMed.

Main outcome(s) The main outcome was impact on the Hamilton Depression Rating Scale.

Data management Authors used covidence.org to facilitate independent data screening.

Quality assessment / Risk of bias analysis Risk of bias was assessed for all included studies using RoB2, a revised Cochrane risk-of-bias assessment tool used for randomized trials. It uses 5 domains to assess bias from randomization process, deviations from intended interventions due to missing outcome data, measurement of outcome, and in selection of the reported result. It concludes risk of bias as “low risk of bias”, “some concerns” and “high risk of bias” to assess the study’s quality.

Strategy of data synthesis Authors employed a qualitative data synthesis strategy. Clinical significance is recognized as a ≥ 50% symptom reduction. To analyze the clinical significance, the percent change of the HAM-D17 score is calculated using the mean difference in HAM-D17 score from baseline to endpoint.

Subgroup analysis All data were categorized into “early” and “late” response. “Early response” represents data points reported within 5 weeks or less of drug administration, while “late response” is 6 weeks or more. This timeline represents data closest to the 4 and 8 week benchmarks in clinical practice, which are generally used to determine a patient’s response to antidepressants.

Sensitivity analysis N/A.

Language restriction English.

Country(ies) involved United States.

Keywords Gepirone; Major Depressive Disorder; Hamilton Rating Scale for Depression; Systematic Review.

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