

Results. Adult studies: In short-term studies, TEM rates were comparable in patients treated with lurasidone monotherapy 20–60 mg/d (3.7%) and 80–120 mg/d (1.9%) vs. placebo (1.9%). TEM rates were also comparable in patients treated with lurasidone 20–120 mg/d (1.1%) adjunctive to Li/VPA vs. placebo + Li/VPA (1.2%). In the monotherapy study, significant reduction in YMRS score was observed at study endpoint for the 20–60 mg/d group compared to placebo (–1.9 vs. –1.3; $p < 0.05$) with similar improvement relative to placebo in the 80–120 mg/d group. Change for YMRS score was comparable for lurasidone and placebo in the adjunctive study. In long-term studies, 1.3% of adult patients treated with lurasidone monotherapy ($n = 316$) met criteria for mania, and 3.8% of patients on adjunctive lurasidone therapy ($n = 497$) met TEM criteria. Pediatric studies: TEM rates were comparable in patients treated with lurasidone vs. placebo (1.7% vs. 2.3%). LS mean reduction in symptoms of mania from baseline to week 6 was significantly greater for lurasidone vs. placebo on YMRS score (–2.0 vs. –1.1; $p < 0.05$). Pediatric long-term studies: After two years of OL treatment with lurasidone, 5.2% of patients met TEM criteria. Mean change in YMRS total score from DB baseline to Month 24 continued to improve (–2.0).

Conclusions. Short-term and long-term treatment with lurasidone demonstrated significant improvement in manic symptoms and was not associated with an increased risk of TEM in either adult or pediatric patient populations compared to rates reported in clinical populations of patients.

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Long-Term Effectiveness of Lurasidone in Pediatric Bipolar Depression: Response, Remission and Recovery

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Abstract

Background. Bipolar disorder frequently has an early onset, with an estimated 1.8% prevalence of bipolar I disorder in children and adolescents. Childhood onset of bipolar disorder is typically associated with a chronic, severe, and disabling course of illness. Relatively few prospective studies are available that evaluate the long-term efficacy of atypical antipsychotics in achieving and sustaining response or remission in pediatric patients with bipolar depression. Lurasidone has been approved by the FDA as monotherapy for bipolar depression in pediatric patients ages 10–17 years. The aim of the current post-hoc analysis was to evaluate the long-term efficacy of lurasidone in achieving

response or remission in children and adolescents with bipolar depression followed over a two-year period.

Method. Patients 10–17 years with bipolar I depression who completed a 6-week double-blind (DB) study of lurasidone vs. placebo were eligible to enroll in a two-year, open-label (OL) extension study in which patients were continued on flexibly-dosed lurasidone (20–80 mg/d) or switched from placebo to lurasidone. Efficacy measures included the Children's Depression Rating Scale, Revised (CDRS-R) and the Clinical Global Impression, Bipolar Depression Severity scale (CGI-BP-S). Functioning was evaluated utilizing the Clinician-rated Children's Global Assessment Scale (CGAS) score, with a score > 70 indicating no clinically meaningful functional impairment. Responder criteria were met if a patient achieved criteria = 50% reduction from DB baseline in the CDRS-R total score; remission criteria were met if a patient achieved a CDRS-R Total Score = 28 and a YMRS total score = 8 and CGI-BP-S depression score = 3, and a patient was considered to have met recovery criteria if they achieved remission with a CGAS score > 70 . In addition, a more stringent outcome, sustained remission, was also analyzed, which required a patient to meet remission criteria for = 24 consecutive weeks.

Results. A total of 306 patients completed the 6-week DB study and entered the extension study; 195 (63.7%) patients completed one year of treatment and 168 (54.9%) patients completed two years of treatment. Responder rates at OL baseline, one year, and two years were: 51.0%, 88.4% and 91.1%, respectively; remission rates were 24.3%, 61.3%, and 75.6%, respectively; and recovery rates were 17.7%, 53.8%, and 73.8%. On a Pearson correlation analysis, there was a strong inverse relationship ($r = -0.71$) between CDRS-R total score, and global functioning as measured by the CGAS. Sustained remission was achieved by 37.2% of patients at one year and 57% of patients after two years.

Conclusions. In children and adolescents with bipolar depression, up to 2 years of treatment with lurasidone was associated with continued improvement in depressive symptoms, resulting in progressively higher rates of response, remission, recovery, and the more rigorously calculated outcome of sustained remission.

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Safety and Effectiveness of SEP–363856 in Schizophrenia: Results of a 6-Month, Open-Label Extension Study

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