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REVIEW

Lurasidone in Schizophrenia: New Information About Dosage and Place in Therapy

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ABSTRACT

Lurasidone is a newer "atypical" or "second-generation" antipsychotic that has received regulatory approval in the US and Canada for the treatment of schizophrenia. Recent changes in lurasidone product labeling include an expansion of the recommended dose range from 40–80 mg/day to 40–160 mg/day, administered once-daily with food. The recommended starting dose is 40 mg/day. Initial dose titration is not required. Efficacy for the treatment of acute episodes of schizophrenia was established in five, 6-week, fixed-dose, randomized, placebo-controlled trials. Additional short-term studies in patients with schizophrenia include a 3-week, randomized, double-blind trial comparing lurasidone with ziprasidone on safety and tolerability outcomes, and a 6-week, randomized, open-label switch study. Available long-term data includes a 12-month, double-blind safety and tolerability study comparing lurasidone with risperidone; a 6-month, open-label extension study for one of the short-term registration studies where patients were initially randomized to receive lurasidone, olanzapine, or placebo; and a 12-month, double-blind extension study comparing lurasidone with quetiapine extended-release after having received lurasidone, quetiapine extended-release, or placebo for 6 weeks. The totality of the evidence supports the overall tolerability of lurasidone, with minimal weight gain and no clinically-meaningful alterations in glucose, lipids, or the electrocardiogram corrected QT (ECG QTc) interval. The most commonly encountered adverse events that can be observed with lurasidone are somnolence, akathisia, nausea, and parkinsonism. Additional clinical trials are underway for the use of lurasidone in patients with bipolar disorder, including major depressive episodes in patients with bipolar I disorder, and in bipolar and schizophrenia

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maintenance. Principal advantages over some other second-generation antipsychotics are lurasidone's highly favorable metabolic profile and once-daily dosing regimen. Additional studies are desirable to directly compare and contrast lurasidone's efficacy with other antipsychotic agents.

Keywords: Dosing; Efficacy; Lurasidone; Psychiatry; Safety; Schizophrenia; Tolerability

INTRODUCTION

Lurasidone is a second-generation antipsychotic medication that received regulatory approval in the US on October 28, 2010 [1] and in Canada on June 15, 2012 [2]. Lurasidone is currently approved for the treatment of adults with schizophrenia based on an extensive clinical trial program that established efficacy within a dose range of 40–160 mg/day administered once-daily with food [3, 4]. Dosage strengths include 20, 40, 80, and 120-mg tablets [3]. Despite the availability of many different antipsychotic medications, schizophrenia is complex and remains a significant clinical challenge to treat. There is substantial heterogeneity in an individual patient's response to medication in terms of efficacy and tolerability and each antipsychotic option has its own profile of most commonly encountered adverse events (AEs) [5]. In order to ensure adequate adherence to therapy, patient preference also needs to be considered in terms of prioritization of symptoms to be treated and AEs to be avoided. Thus, new treatments with different profiles are welcomed. This review will include a discussion of lurasidone's clinical utility in treating schizophrenia based on short- and long-term randomized controlled trial data, and new guidance offered in revised product labeling [3]. Prior reviews can be consulted for additional details [6–9].

METHODS

This narrative review builds upon the author's prior systematic review [6] by the inclusion of new study reports as identified by an online PubMed query on June 20, 2012 and September 5, 2012 using the search term "lurasidone," and as reported in posters presented at scientific meetings held in 2011 and 2012, and by inspection of the newly revised product labeling for lurasidone.

PHARMACODYNAMICS AND PHARMACOKINETICS

Similar to most other second-generation antipsychotics, lurasidone is a full antagonist at dopamine D2 and serotonin 5HT2A receptors [3]. However, lurasidone also has high affinity for serotonin 5HT7 receptors (comparable to dopamine D2 and 5HT2A receptors) and is a partial agonist at 5HT1A receptors. Lurasidone has moderate affinity for alpha 2C noradrenergic receptors. Differences among antipsychotics in these and other binding characteristics may offer an explanation for the heterogeneity of effects observed between drugs and among different patients.

Lurasidone is rapidly absorbed, with a time to maximum concentration of 1–3 h and a mean half-life of 18 h for 40 mg [3]. Plasma exposure, as calculated by area under the curve (AUC) and maximum concentration (C_{max}), increases in a linear fashion with oral administration within the range of 20–160 mg. Steady state is reached within 7 days. Lurasidone is 99.8% protein-bound with affinity for albumin and alpha-1-glycoprotein [9]. The principal route of metabolism for lurasidone is in the liver by the cytochrome P450 3A4 (CYP3A4) enzyme system [3]. Consequently, the use of lurasidone in the presence of strong inducers and inhibitors of CYP3A4 (such as rifampin and ketoconazole, respectively) is contraindicated [3].

Food can affect the absorption of lurasidone, similar to what is observed with ziprasidone [10], but with a lower caloric threshold (350 calories) than required with ziprasidone (500 calories). In a food-effect study, lurasidone mean C_{max} and AUC were approximately three-times and two-times higher, respectively, when administered with food compared to the levels observed under fasting conditions [3]. Lurasidone exposure was not affected as the meal size was increased from 350 to 1,000 calories and was independent of the fat content of the meal [3].

SHORT-TERM CLINICAL TRIALS

Efficacy for the dose range of 40–160 mg/day in patients with an acute exacerbation of schizophrenia was established in five 6-week, fixed-dose, randomized, placebo-controlled trials as described in product labeling [3] and summarized in Table 1 [6, 11–14]. The older, smaller, phase 2 studies used the Brief Psychiatric Rating Scale (derived from the Positive and Negative Syndrome Scale [PANSS]) as the primary outcome measure. The more recent and larger phase 3 studies used the PANSS as the primary outcome measure. In total, 1,508 patients participated in short-term, placebo-controlled schizophrenia studies with doses of 20, 40, 80, 120, or 160 mg once daily, for which data is summarized in the product label [3]. When comparing change in these rating-scale scores from baseline to endpoint, lurasidone 40 mg/day was superior to placebo in two of the three studies that tested this dose, 80 mg/day was superior to placebo in all three studies that tested this dose, 120 mg/day was superior to placebo in two of the three studies that tested this dose, and 160 mg/day was superior to placebo in the single study that included this dose. Active controls were used in two of these studies (olanzapine 15 mg/day in one, quetiapine extended-release 600 mg/day in the other), which also statistically separated from placebo on the primary efficacy measure. An additional phase 2 trial was conducted but it was considered noninformative regarding efficacy as neither the lurasidone arms (20, 40, and 80 mg/day) nor the active control (haloperidol 10 mg/day) statistically separated from placebo on the primary efficacy outcome [6]. Three of the registration studies have been published to date [11–13], and the remainder publically disclosed in poster presentations [14] and in the drug approval package available on the US Food and Drug Administration website [15].

Based on data from the short-term registration studies, lurasidone is associated with minimal weight gain and no clinically-meaningful alterations in glucose, lipids, or the electrocardiogram corrected QT (ECG QTc) interval. The proportion of patients with prolactin elevations at least five times the upper limit of normal was 2.8% for lurasidone-treated patients versus 1.0% for placebo-treated patients [3]. The metabolic profile of lurasidone appears similar to that for ziprasidone based on a 3-week study (n = 301) comparing lurasidone and ziprasidone on safety and tolerability outcomes [16]. From the short-term registration studies, the commonly observed AEs (incidence ≥5% and at least twice the rate for placebo) included somnolence (17% for lurasidone vs. 7% for placebo), akathisia (13% vs. 3%), nausea (10% vs. 5%), and parkinsonism (10% vs. 5%) [3]. A total of 9.5% of lurasidone-treated patients versus 9.3% of placebo-treated patients discontinued due to AEs; there were no AEs associated with discontinuation in subjects treated with lurasidone that were at least 2% and at least twice that for placebo [3].

In an effort to place the efficacy and tolerability profile of lurasidone in clinical perspective, study data were pooled from the six 6-week, randomized, placebo-controlled

Table 1 Summary of short- and long-term double-blind randomized trials of lurasidone for schizophrenia, as conducted by the manufacturer

Study	Type	Duration (weeks)	Lurasidone dose (mg/day)	Comments
Ogasa et al. [13]	Phase 2 efficacy trial, fixed-dose, placebo-controlled	6	40 and 120	Lurasidone 40 and 120 mg/day were each statistically significantly superior to placebo in mean changes from baseline for the BPRSd.
Reviewed in Citrome [6]	Phase 2 efficacy trial, fixed-dose, placebo-controlled, haloperidol 10 mg/day used for assay sensitivity	6	20, 40, and 80	A failed study. Neither haloperidol 10 mg/day, nor lurasidone 20, 40, or 80 mg/day separate statistically from placebo on the BPRSd.
Nakamura et al. [11]	Phase 2 efficacy trial, placebo-controlled	6	80	Lurasidone 80 mg/day was statistically significantly superior to placebo on the BPRSd.
Reviewed in Citrome [6]	Phase 3 efficacy trial, fixed-dose, placebo-controlled	6	40, 80, and 120	Lurasidone 80 mg/day, but not 40 or 120 mg/day, was statistically significantly superior to placebo on the PANSS.
Meltzer et al. [12]	Phase 3 efficacy trial, fixed-dose, placebo-controlled, olanzapine 15 mg/day used for assay sensitivity	6	40 and 120	Lurasidone 40 and 120 mg/day, and olanzapine 15 mg/day, were each statistically significantly superior to placebo on the PANSS. The proportion of patients experiencing ≥7% weight gain was highly significantly different between groups: 5.9% for the lurasidone groups combined versus 34.4% for the olanzapine group and 7.0% for the placebo group.
Loebel et al. [14]	Phase 3 efficacy trial, fixed-dose, placebo-controlled, quetiapine XR 600 mg/day used for assay sensitivity	6	80 and 160	Lurasidone 80 and 160 mg/day, and quetiapine XR 600 mg/day, were each statistically significantly superior to placebo on the PANSS. Treatment with lurasidone 80 mg and 160 mg was associated with a mean increase in weight that was not significantly different from placebo, while the mean increase in weight was significantly higher with quetiapine XR.
Potkin et al. [16]	Phase 2 safety and tolerability trial, fixed-dose, ziprasidone 80 mg b.i.d. active comparator	3	120	Lurasidone and ziprasidone had similar effects on weight and metabolic outcomes.

Table 1 continued

Study	Type	Duration (weeks)	Lurasidone dose (mg/day)	Comments
McEvoy et al. [18]	Phase 3 safety and effectiveness switch trial, flexible-dose	6	40–120 (after 2 weeks of 40, 80, or 40 for week 1 and 80 for week 2)	Switching to lurasidone was well tolerated using a cross taper strategy regardless of initial dose used or rate of titration.
Citrome et al. [19]	Phase 3 safety and tolerability trial, flexible-dose, risperidone 2–6 mg/day active comparator	52	40–120	See text. Long-term treatment with lurasidone was generally well tolerated in this study, with minimal effects on weight and metabolic outcomes.
Loebel et al. [20]	Phase 3 extension to Loebel et al. [14], flexible-dose, quetiapine XR 200–800 mg/day active comparator	52	40–160	See text. Probability of relapse at 12 months was lower for lurasidone versus quetiapine.

b.i.d. twice daily, *BPRSd* Brief Psychiatric Rating Scale (derived from the PANSS), *PANSS* Positive and Negative Syndrome Scale, *XR* extended-release

trials mentioned above, and the data reanalyzed using the evidence-based medicine metrics of number needed to treat (NNT) and number needed to harm (NNH) [17]. Response to antipsychotics was defined by a reduction of ≥20, 30, 40, or 50% from baseline on the PANSS total score. Specific potential harms were defined as weight gain ≥7% from baseline; incidence of spontaneously reported AEs; incidence of total cholesterol ≥240 mg/dL, low-density lipoprotein cholesterol ≥160 mg/dL, fasting triglycerides ≥200 mg/dL, and glucose ≥126 mg/dL at endpoint. NNT versus placebo for PANSS reductions ≥30% were 6, 6, 7, and 4 for lurasidone doses of 40, 80, 120, and 160 mg/day, respectively, and 4 and 3 for olanzapine 15 mg/day and quetiapine extended-release 600 mg/day, respectively, with overlapping 95% confidence intervals (CIs). Table 2 lists the lurasidone responder rates versus placebo and the respective NNT for lurasidone at different response thresholds. Lurasidone was not associated with any statistically significant disadvantages over placebo for weight gain or metabolic abnormalities. NNH versus placebo for weight gain ≥7% from baseline ranged from 43–150 for lurasidone 40–160 mg/day. In contrast, NNH versus placebo for weight gain ≥7% from baseline was 4 for olanzapine and 9 for quetiapine extended-release. The five most consistently encountered AEs attributable to lurasidone were akathisia, nausea, sedation, somnolence, and parkinsonism with NNH versus placebo for lurasidone 40–120 mg/day ranging from 6 (akathisia with 120 mg/day) to 30 (parkinsonism with 80 mg/day). Of particular note, lurasidone 160 mg/day appeared better tolerated than doses of 40, 80, or 120 mg/day for akathisia, nausea, sedation, or somnolence, with no NNH values for these AEs for 160 mg/day versus placebo being statistically significant. A possible explanation for this

Table 2 Responder rates and NNT versus placebo from pooled data from five short-term, randomized, placebo-controlled studies of lurasidone

Intervention	PANSS reduction ≥20%		PANSS reduction ≥30%		PANSS reduction ≥40%		PANSS reduction ≥50%	
	%	NNT (95% CI)	%	NNT (95% CI)	%	NNT (95% CI)	%	NNT (95% CI)
Placebo	45.0	N/A	31.9	N/A	23.6	N/A	15.3	N/A
Lurasidone 40 mg/day	58.3	*8 (5, 17)*	49.0	*6 (5, 10)*	37.8	*8 (5, 14)*	26.4	*10 (6, 20)*
Lurasidone 80 mg/day	64.3	*6 (4 ,8)*	48.9	*6 (5, 10)*	36.0	*9 (6, 17)*	21.6	*16 (9, 117)*
Lurasidone 120 mg/day	60.8	*7 (5, 12)*	47.6	*7 (5, 12)*	32.3	*12 (7, 47)*	20.8	19 (ns)
Lurasidone 160 mg/day	78.5	*3 (3, 4)*	62.8	*4 (3, 5)*	46.3	*5 (4, 8)*	28.9	*8 (5, 21)*

Adapted with permission from Table 2 in Citrome L. Lurasidone for the acute treatment of adults with schizophrenia: what is the number needed to treat, number needed to harm and likelihood to be helped or harmed? Clin Schizophr Relat Psychoses. 2012;6:76–85

Italicized entries represent NNT values where the 95% CI does not include infinity and, hence, is considered statistically significant

NNT number needed to treat, *ns* not significant (the 95% CI contains "infinity"), *PANSS* Positive and Negative Syndrome Scale, *XR* extended release

difference in tolerability between lurasidone 160 mg/day and doses of 40–120 mg/day is that the trial that included lurasidone 160 mg/day as a treatment arm had a different medication administration time (evening) compared to the other trials, where medication was administered in the morning.

Recently presented in poster form are the results of a 6-week switch study [18]. In this trial the safety, tolerability, and effectiveness of switching clinically stable, but symptomatic, nonacute patients with schizophrenia or schizoaffective disorder to lurasidone was assessed (n = 240). Subjects were randomized to three switch strategies involving different starting doses of lurasidone ranging from 40–80 mg/day, while the prior antipsychotic agent was tapered and discontinued over the initial 2-week study period. Switching to lurasidone was well tolerated with 81.1% of entered patients completing the 6-week study. No clinically relevant differences in efficacy or tolerability were noted when comparing the three different switch strategies. Patients switching to lurasidone demonstrated clinically relevant improvement in efficacy measures. Overall reductions in weight, lipids, and glucose were observed, and the AE profile was similar to previous lurasidone studies.

LONG-TERM CLINICAL TRIALS

Long-term data is also available and the double-blind, randomized trials are summarized in Table 1 [19, 20]. In a 12-month, double-blind safety and tolerability study, clinically-stable adult outpatients with schizophrenia (n = 629) were randomized to once-daily, flexibly-dosed lurasidone (40–120 mg) or risperidone (2–6 mg) [19]. The three most frequent AEs in the lurasidone group were nausea (16.7%), insomnia (15.8%), and sedation (14.6%); the corresponding rates of these AEs in the patients in the risperidone

group were 10.9%, 13.4%, and 13.9%, respectively. The three most frequent AEs in the risperidone group were increased weight (19.8%), somnolence (17.8%), and headache (14.9%); the corresponding rates of these AEs in the patients in the lurasidone group were 9.3%, 13.6%, and 10.0%, respectively. A greater proportion of patients receiving risperidone had a ≥7% endpoint increase in weight (14%) compared to patients receiving lurasidone (7%). The median endpoint change in prolactin was significantly higher for risperidone ($P < 0.001$). Comparable improvement in efficacy measures were observed with both agents and the rates of relapse were similar. All-cause discontinuation rates were higher for lurasidone versus risperidone. In summary, long-term treatment with lurasidone was generally well tolerated in this study, with minimal effects on weight and metabolic outcomes.

Long-term extension studies to the short-term studies have also been conducted. In the 6-month, open-label extension for the 6-week study that included olanzapine as an active control, 246 patients received flexible doses of lurasidone in the range of 40–120 mg/day [21]. Patients showed further improvement in the PANSS total score. Two AEs occurred with an incidence >10%: akathisia (13.0%) and insomnia (11.0%). Body weight remained relatively stable during the open-label extension, except for patients who had been randomized in the initial double-blind phase to olanzapine 15 mg/day where a mean reduction of –1.8 kg in weight was observed after the switch to open-label lurasidone.

A 12-month, double-blind extension to the short-term study that included quetiapine extended-release as an active control has also been presented [20]. Subjects ($n = 236$) received flexible once-daily doses of lurasidone (40–160 mg) or quetiapine extended-release (200–800 mg). Lurasidone was noninferior to quetiapine in risk for relapse over the 12-month treatment period. The risk of relapse in lurasidone-treated subjects was reduced by 27.2% (hazard ratio 0.728) compared with quetiapine and the Kaplan-Meier estimate of the probability of relapse at 12 months was lower for lurasidone versus quetiapine (0.237 vs. 0.336). Treatment with lurasidone (modal daily dose 120 mg) was associated with a significantly greater change in PANSS total scores compared with quetiapine (modal dose 600 mg). Rates of AEs ≥5% in the lurasidone group were akathisia (12.6%), headache (10.6%), insomnia (7.9%), anxiety (6.0%), parkinsonism (6.0%), and weight increase (6.0%). Weight change from acute study baseline to 12 months of treatment for observed cases was +0.7 kg with lurasidone and +1.2 kg for quetiapine.

PRODUCT LABELING REVISITED

When initially approved in the US in 2010, product labeling for lurasidone noted that efficacy within the dose range of 40–120 mg/day was established in four 6-week, randomized controlled trials and that the recommended starting dose is 40 mg/day [7]. However, at that time the maximum recommended dose in product labeling was 80 mg/day. Based on the data available then, doses above 80 mg/day did not appear to confer added benefit and the dose of 120 mg/day was associated with a dose-related increase in certain AEs, such as somnolence and akathisia. Since that time, additional data has become available, in particular the study that included lurasidone 160 mg/day [14]. Consequently, the US product label has been changed [3]. The maximum recommended dose is now 160 mg/day. Dose adjustments for special populations have also been modified. Dose adjustment is recommended in moderate and

severe renal and hepatic impairment patients with a recommended starting dose of 20 mg. The dose in moderate and severe renal impairment patients and in moderate hepatic impairment patients should not exceed 80 mg/day (prior labeling recommended a maximum of 40 mg/day). The maximum dose in severe hepatic impairment patients remains the same and should not exceed 40 mg/day. When coadministered with a moderate CYP3A4 inhibitor, such as diltiazem, the recommended starting dose of lurasidone is 20 mg/day and the maximum recommended dose is 80 mg/day (prior labeling recommended a maximum of 40 mg/day). A 120-mg tablet has been added to the label (a 20-mg tablet had been added earlier). Somnolence and akathisia are no longer listed as dose-related AEs and the akathisia data have been updated to reflect the lower incidence observed with lurasidone 160 mg/day compared with 40–120 mg/day. Although the product label does not recommend a specific time of day to administer lurasidone, tolerability appears more favorable when given in the evening, as evidenced by the study that included lurasidone 160 mg/day [14] where lurasidone was administered in the evening in contrast to earlier studies when lurasidone was administered in the morning [17] .

OVERALL PLACE OF LURASIDONE IN THERAPY

Lurasidone joins a crowded marketplace where there are several newly-commercialized second-generation antipsychotics competing for attention [22]. Cost is similar to that for other branded oral second-generation antipsychotics. Similar to ziprasidone, aripiprazole, asenapine, and iloperidone, lurasidone is metabolically "friendly" compared to agents such as olanzapine. However, there are also differences in

Table 3 Highlights of differences and similarities among lurasidone, ziprasidone, aripiprazole, iloperidone and asenapine regarding their adverse event profiles in acute schizophrenia in adults as reported in product labeling

	Lurasidone	**Ziprasidone**	**Aripiprazole**	**Iloperidone**	**Asenapine**
Spontaneous AE with incidence ≥5% and twice placebo	Somnolence, akathisia, nausea, and parkinsonism	Somnolence, respiratory tract infection	Akathisia	Dizziness, dry mouth, fatigue, nasal congestion, orthostatic hypotension, somnolence, tachycardia, and weight increase	Akathisia, oral hypoesthesia, and somnolence
NNH AE somnolence	10	15	20	16	17
NNH AE akathisia	10	100	25	Rate lower than placebo	33
NNH weight gain ≥7%	67	17	20	12	35
Prolactin warning?	Yes	Yes	No	Yes	Yes
QT warning?	No	Yes	No	Yes	Yes

Data from Citrome & Nasrallah [23] and the most recent product label for lurasidone [3]
AE adverse event, *NNH* number needed to harm

terms of commonly encountered AEs (Table 3). When examining effects on short-term weight gain, lurasidone has the smallest difference from placebo on the categorical outcome of weight gain of at least 7% from baseline [23]. In contrast to many of the alternatives, lurasidone is dosed once daily and does not require initial dose titration. Although it is recommended to be administered with food, the caloric threshold currently suggested (350 calories) is modest. Extrapyramidal side effects and akathisia may occur; akathisia appeared to be dose-related in earlier studies; however, this was not observed in the study where 160 mg/day was administered in the evening. At present, available data are limited to trials with constrained inclusion/exclusion criteria that can limit their generalizability.

Logical candidates for lurasidone treatment would be adults with schizophrenia for whom metabolic or cardiovascular risk is a concern, and for whom weight gain is to be minimized or avoided. Dosing is relatively simple, enabling adherence. Patients who are sensitive to somnolence, akathisia, nausea, and parkinsonism will need to be monitored these AEs.

POTENTIAL FUTURE USES

Preliminary findings are available from two 6-week, placebo-controlled trials in major depressive episodes in patients with bipolar I disorder (with or without rapid cycling and without psychotic features): a monotherapy study [24], and an adjunctive therapy trial [25]. In the monotherapy trial [24], lurasidone was flexibly dosed at 20–60 mg/day or 80–120 mg/day. Lurasidone treatment resulted in significantly greater Montgomery Asberg Depression Rating Scale (MADRS) score reduction at the week 6 endpoint for both dose groups compared with placebo. In the adjunctive therapy trial [25], flexibly-dosed lurasidone (20–120 mg/day) adjunctive to ongoing treatment with either lithium or valproate was associated with a significantly greater MADRS score reduction compared with placebo. The tolerability and safety outcomes were consistent with that observed in the trials in patients with schizophrenia.

Descriptions of studies at www.clinicaltrials.gov can be found for protocols examining lurasidone for bipolar maintenance, in subjects with major depressive disorder with mixed features, schizophrenia maintenance, high dose strategies (240 mg/day) for treatment resistant schizophrenia, and clinical and biomarker assessment of efficacy of cognitive remediation in patients with schizophrenia or schizoaffective disorder stabilized on lurasidone.

CONCLUSION

Lurasidone is a new second-generation antipsychotic and has received regulatory approval in the US and Canada. Based on short- and long-term studies in adults with schizophrenia, lurasidone in the range of 40–160 mg/day dosed once daily with food is efficacious and reasonably well tolerated. The recommended starting dose is 40 mg/day and no initial titration is necessary. Lurasidone does not appear to be associated with medically-relevant effects on weight, lipids, and glucose. The most commonly encountered AEs that can be observed with lurasidone are somnolence, akathisia, nausea, and parkinsonism. Tolerability outcomes from the long-term studies have been consistent with the short-term studies. Additional clinical trials are underway for the use of lurasidone in patients with bipolar disorder; two positive trials in bipolar depression have been reported. Principal advantages over some other second-generation antipsychotics are lurasidone's highly favorable metabolic profile and once-daily

dosing regimen. Additional studies are desirable to directly compare and contrast lurasidone's efficacy with other antipsychotic agents.

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