# Lurasidone for Schizophrenia: A Brief Review of a New Second-Generation Antipsychotic

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## Abstract

Lurasidone is a second-generation antipsychotic newly approved by the U.S. Food and Drug Administration for the treatment of schizophrenia. Similar to most other second-generation antipsychotics, lurasidone is a full antagonist at dopamine D2 and serotonin 5HT2A receptors. Efficacy within the dose range of 40–120 mg/d was established in four 6-week, randomized, controlled trials. The recommended starting dose is 40 mg/d and the maximum recommended dose is 80 mg/d. Doses above 80 mg/d do not appear to confer added benefit and may be associated with a dose-related increase in certain adverse reactions such as somnolence and akathisia. Lurasidone is administered once daily with at least 350 calories of food in order to optimize bioavailability. Lurasidone is primarily metabolized in the liver through the CYP3A4 enzyme system, and coadministration with drugs that are strong inhibitors of CYP3A4 (such as ketocon-azole) or strong inducers (such as rifampin) are contraindicated. Lurasidone is associated with minimal weight gain and no clinically meaningful alterations in glucose, lipids, or the ECG QT interval.

Key Words: Lurasidone, Schizophrenia, Antipsychotic, Efficacy, Tolerability

## Introduction

Lurasidone received regulatory approval by the U.S. Food and Drug Administration (FDA) on 28 October 2010 (1, 2). It is the third new agent to be approved within the period of 2009–2010 for the treatment of schizophrenia, joining iloperidone (3) and asenapine (4) as new options that have potentially more benign metabolic adverse effect profiles than some older second-generation antipsychotic medications (5). For an extended review of lurasidone that includes additional information on all the registered clinical studies of lurasidone and a comprehensive examination of number needed to treat, number needed to harm, and likelihood to be helped or harmed, the reader is referred to (2).

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Submitted: November 10, 2010; Revised: November 24, 2010; Accepted: December 13, 2010

## **How it Works**

Lurasidone belongs to the chemical class of benzoisothiazol derivatives (6). Lurasidone is a full antagonist at dopamine D2 and serotonin 5HT2A receptors, properties shared by most second-generation antipsychotics. Lurasidone also has high affinity for serotonin 5HT7 (higher relative in vitro binding than for dopamine D2 and 5HT2A) and is a partial agonist at 5HT1A receptors; it is believed that these properties can be potentially related to effects on cognition and mood (7-9). However, specifically designed clinical trials examining cognitive and mood outcomes are necessary in order to demonstrate the utility of lurasidone on these therapeutic dimensions. Lurasidone has moderate affinity for alpha 2C noradrenergic receptors (6). Lurasidone's minimal affinity for alpha 1 noradrenergic receptors predicts a lower risk for orthostatic hypotension than compounds with higher affinity for this receptor (9). Lurasidone's minimal affinity for 5HT2C receptors and virtually no affinity for histamine H1 predicts a lower liability for weight gain as well (10). Lurasidone's lack of affinity for cholinergic M1 receptors predicts a low propensity for anticholinergic side effects (9). These pharmacodynamic effects of lurasidone were studied using cloned human receptors or membrane fractions prepared from animal tissue and, thus, may not always reflect biological activity in a patient. Predicting potential effects of a medication from specific receptor binding affinity can also be misleading. For example, although somnolence/sedation is often mediated through H1 and/or alpha 1 noradrenergic receptor activity, it can also occur via other mechanisms and has been observed with lurasidone. Some have speculated that sedation may be attributable to an as yet uncharacterized property of potent 5HT7 antagonism (11).

The blocking of 60–80% of dopamine D2 receptors may be necessary in order to achieve a therapeutic effect. This degree of receptor occupancy was observed in a study of 21 healthy male subjects using positron-emission tomography at oral doses starting at 40 mg/d (11).

## **Pharmacokinetics**

Lurasidone is rapidly absorbed, with a time to maximum concentration of 1 to 3 hours and a mean half-life of 18 hours for 40 mg (6). Lurasidone 40 mg has a mean apparent volume of distribution of 6,173 L and apparent clearance is 3,902 mL/min. Area under the curve (AUC) and maximum concentration (Cmax) increases linearly with oral dosing within the range of 20–160 mg and steady state is reached within 7 days. Lurasidone is highly protein-bound (99.8%) with affinity for albumin and  $\alpha$ -1-glycoprotein (11). Protein binding can have implications regarding drug-drug interactions, but specific information for lurasidone is limited at this time.

Lurasidone is metabolized in the liver by the CYP3A4 enzyme system (6, 11). The use of lurasidone in the presence of strong inducers and inhibitors of CYP3A4 (such as rifampin and ketoconazole, respectively) is contraindicated. Lurasidone is not a substrate of CYP1A1, CYP1A2, CYP2A6, CYP4A11, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6 or CYP2E1 enzymes (6). Of the pharmacologically active metabolites, the most plentiful is ID-14283, representing approximately 25% of the parent exposure and has a similar pharmacological profile but a shorter half-life (7.5–10 hours) compared to lurasidone itself (11, 12).

Food can affect the absorption of lurasidone, akin to what can be seen with ziprasidone (13, 14), but possibly with a lower caloric threshold (350 calories) than necessary with ziprasidone (500 calories). The food effect was tested in a study of 26 patients with schizophrenia, schizophreniform or schizoaffective disorder receiving lurasidone 120 mg/d, where 350 calories/high fat, 500 calories/low fat, 500 calories/high fat, 800–1,000 calories/low fat, and 800– 1,000 calories/high fat meals all yielded similar lurasidone exposures (measured by AUC) that were approximately twice that for when lurasidone was taken fasting (12). Dosing of lurasidone need not be modified for elderly patients with psychosis (ages 65–85 years), as lurasidone concentrations when dosed at 20 mg/d were similar to those in young subjects (6). Similarly, dose adjustments are not required on the basis of gender or race (6). However, patients with moderate or severe renal and hepatic impairment will require a dose adjustment to no greater than 40 mg/d (6), as plasma exposure of lurasidone was demonstrably higher in patients with this degree of organ impairment compared to healthy matched controls (6). Additionally, lurasidone dose should not exceed 40 mg/d when coadministered with a moderate CYP3A4 inhibitor such as diltiazem (6).

## **Efficacy in Clinical Trials**

A total of six short-term (6-week), randomized, controlled trials were conducted comparing lurasidone with placebo, of which 5 were used in the FDA's evaluation, with 4 considered as positive demonstrating efficacy for lurasidone (see Table 1). One study was considered a "failed trial" because neither lurasidone nor haloperidol separated statistically from placebo on the major outcomes. Mean age of subjects ranged from approximately 37 to 41 years, depending on the treatment arm, with 69 to 79% being male, and 32 to 52% being White (15). Mean baseline Positive and Negative Syndrome Scale (PANSS) total scores ranged from approximately 93 to 97, depending on the treatment arm, and mean Clinical Global Impression-Severity (CGI-S) scores ranged from 4.8 to 5.0 (15). A sixth study was completed after the manufacturer submitted their New Drug Application to the FDA (16).

Efficacy outcomes were consistently in favor of lurasidone 80 mg/d versus placebo on measures of psychopathology; however, at least 2 studies also demonstrated efficacy for the doses of 40 and 120 mg/d. See Table 1 for the specific outcomes measured. A poster presented at a scientific meeting described an integrated analysis from the 4 positive studies (15). Time of onset (within 3–7 days) and trajectory of improvement was similar across the 40–120 mg/d dose range when assessing improvement on PANSS scores. CGI-S scores suggested an earlier onset of therapeutic response for the 80–120 mg/d doses. PANSS factors were also evaluated including positive, negative, disorganized thought, depression/anxiety, and hostility (17), with lurasidone showing superiority to placebo in improving all 5 PANSS factor scores with no clear dose-response relationship.

A 3-week study was also reported that compared lurasidone with ziprasidone in stable outpatients with schizophrenia (11, 18). Overall, efficacy was similar for both treatment groups at week 3.

The long-term efficacy profile of lurasidone has been assessed in both uncontrolled and controlled clinical trials, but results have not been publically disclosed to date (2).

## Table 1

1 The Five Short-Term (6-week) Lurasidone Double-Blind Randomized Trials in Patients with Acute Schizophrenia Used by the FDA for Regulatory Approval

Study (Ref #)	Phase	N Randomized	Lurasidone Dose (N*)	Active Comparator Dose (N)	N Placebo	Comments
D1050006 <sup>†</sup> (11, 15)	II	149	40 (49) and 120 mg/d (47)	None	50	Phase II. Lurasidone 40 and 120 mg/d were each sta- tistically significantly superior to placebo at endpoint in mean changes from baseline for the BPRS total, CGI-S score, CGI-I score and between lurasidone 120 mg and placebo for PANSS total score.
D1050049 (11)	II	353	20, 40, and 80 mg/d (total N=209)	Haloperidol 10 mg/d (72)	72	Phase II. Neither haloperidol 10 mg/d nor lurasidone 20, 40, or 80 mg/d separate statistically from placebo on the major outcomes (BPRS, PANSS, CGI-S) and, thus, this is a failed study.
D1050196 <sup>†</sup> (11,15,22)	II	180	80 mg/d (90)	None	90	Phase II. Published. Lurasidone 80 mg/d was statisti- cally significantly superior to placebo on the BPRS, PANSS total score, PANSS positive subscale, negative subscale, general psychopathology subscale, and CGI-S. Other evidence of superiority was noted for the PANSS cognitive component, PANSS depression, and MADRS. Effects of lurasidone versus placebo on the BPRS, PANSS total score and CGI-S were significant starting at 3 days postrandomization.
D1050229 <sup>†</sup> , "PEARL 1" (15)	Ш	496	40 (122), 80 (119), and 120 mg/d (124)	None	127	Phase III. Lurasidone 80 mg/d, but not 40 or 120 mg/d, was statistically significantly superior to placebo on the PANSS total score and CGI-S.
*D1050231 <sup>†</sup> , "PEARL 2" (15, 23)	III	473	40 (119) and 120 mg/d (118)	Olanzapine 15 mg/d (122)	114	Phase III. Lurasidone 40 and 120 mg/d were each sta- tistically significantly superior to placebo at 6 weeks on the PANSS total score, PANSS positive subscale, PANSS negative subscale, CGI-S. Olanzapine 15 mg/ day also produced significantly greater improve- ments than placebo on the PANSS total score, PANSS positive subscale, PANSS negative subscale, and CGI-S.

\* Where possible, Ns in this column represent the number of patients available for efficacy analyses and obtained from (ref #15). <sup>†</sup>These were the 4 clinical trials that established efficacy (ref #6). There is another phase III clinical trial completed after the manufacturer submitted their New Drug Application to the FDA–see http://clinicaltrials.gov/ct2/show/NCT00790192 (ref #16).

BPRS=Brief Psychiatric Rating Scale; CGI-I=Clinical Global Impression-Improvement; CGI-S=Clinical Global Impression-Severity; MADRS=Montgomery-Asberg Depression Rating Scale; PANSS=Positive and Negative Syndrome Scale

## **Safety and Tolerability in Clinical Trials**

Class level warnings and precautions are listed in the product label (6), including the boxed warning for increased mortality in elderly patients with dementia-related psychosis. The most commonly observed spontaneously reported adverse events (as defined by incidence  $\geq$ 5% and at least twice the rate of placebo) in patients treated with lurasidone in short-term trials were somnolence, akathisia, nausea, parkinsonism and agitation (6).

Somnolence (broadly defined to include hypersomnia, hypersomnolence, sedation, and somnolence) during the short-term trials was observed in 22.3% of patients receiving lurasidone versus 9.9% receiving placebo (6). Another way of expressing this risk is by calculating number needed to harm (NNH), which is an effect size that indicates how many patients would need to be treated with one agent instead of the comparator in order to encounter one additional adverse outcome of interest (20). The higher the numerical value for NNH, the less frequently the adverse outcome is encountered. Single digits usually mean one would encounter the event frequently enough to make a difference in medication selection and when advising patients what effects would be most commonly experienced. For somnolence at all doses of lurasidone versus placebo, the NNH is 9, meaning that 9 patients would need to be treated with lurasidone at any dose instead of placebo before expecting to encounter one additional patient with somnolence. Somnolence is dose related, with somnolence reported in 26.5% for patients receiving lurasidone 120 mg/d (NNH versus placebo 6), compared with 23% (NNH 8) for 80 mg/d and 19% (NNH 11) for 40 mg/d.

Akathisia was reported in 15% of patients receiving lurasidone at any dose, compared with 3% for placebo, yielding a NNH of 9 (2, 6). Akathisia is dose related, with a rate of 22% for 120 mg/d (NNH 6), 15% for 80 mg/d (NNH 9) and 11% for 40 mg/d (NNH 13). The incidence of reported extrapyramidal symptom-related events, excluding akathisia and restlessness, was 14.7% for lurasidone versus 5.1% for placebo (NNH 11). Parkinsonism occurred in 11% of patients receiving lurasidone compared to 5% for placebo (NNH 17). Dystonia occurred in 4.7% of lurasidone patients, compared with 0.7% for placebo (NNH 25). The greatest frequency of parkinsonism and dystonia occurred with 120 mg/d. The proportion of patients who shifted from normal to abnormal on the Barnes Akathisia Scale was 16% for lurasidone compared to 7.6% for placebo (NNH 12). The proportion of patients who shifted from normal to abnormal on the Simpson Angus Scale for extrapyramidal symptoms was 5.3% for lurasidone compared to 2.5% for placebo (NNH 36).

Nausea and agitation are less commonly encountered than somnolence or akathisia and, as per product labeling (6), rates for these two adverse events in the short-term trials were 12 and 6% for lurasidone, compared with 6 and 3% for placebo, yielding NNHs of 17 and 34, respectively.

Among the patients receiving lurasidone in the shortterm trials, 9.4% discontinued treatment because of an adverse reaction(s), compared with 5.9% of those receiving placebo, yielding a NNH of 30 (2, 6). There were no adverse reactions associated with discontinuation in subjects treated with lurasidone that were at least 2% and at least twice the placebo rate (6).

Lurasidone appears to have a benign weight and metabolic profile (2, 6). Mean weight changes from baseline in short-term trials were +0.67, +1.14, and +0.68 kg for lurasidone 40, 80, and 120 mg/d, respectively, compared to +0.26 for placebo. The proportion of patients with at least a 7% increase in body weight from baseline to endpoint was 5.6% for lurasidone compared to 4.0% for placebo (NNH 63). Proportions of patients receiving placebo who shifted to the abnormal range for blood glucose, cholesterol, or triglyceride levels were 8.6, 6.6, and 12.5%, respectively. The corresponding rates for patients receiving lurasidone demonstrated an inconsistent pattern, with most of the values being either a little higher or a little lower than that for placebo (2).

Lurasidone can increase prolactin and this appears to be dose related and differed by gender (2, 6). Median changes in prolactin (ng/mL) from baseline among all patients (men and women) in the short-term trials were +0.3 (+0.5for men and -0.9 for women), +1.1 (+0.9 and +2.0), and +3.3 (+3.1 and +6.7) for lurasidone 40, 80, and 120 mg/d, respectively, compared with -0.6 (-0.5 and -1.5) for placebo (6). The proportions of all patients (and men and women) with prolactin elevations at least five times the upper limit of normal were 3.6% (1.9% and 8.3%) for lurasidone versus 0.7% (0.6% and 1%) for placebo, yielding a NNH of 35 (77and 14). Indirect comparisons with other antipsychotics on the basis of a threshold of five times the upper limit of normal is made difficult as there is no clear standard on what threshold should be used when reporting categorical results. Categorical outcomes for prolactin are infrequently reported in general. Data available from the registration program for asenapine used a lower threshold (four times the upper limit of normal), with this threshold exceeded in 6.2% of patients receiving asenapine, 27.6% receiving risperidone, 10.4% receiving haloperidol, 4.0% receiving olanzapine, and 1% receiving placebo, yielding NNHs versus placebo of 19, 4, 11, and 33 for asenapine, risperidone, haloperidol, and olanzapine, respectively (4).

Orthostatic hypotension as a spontaneously reported adverse event was uncommon, occurring in 4/1,004 of patients receiving lurasidone versus 1/455 receiving placebo. Orthostatic effects, as defined by a change of at least 20 mm Hg decrease in systolic blood pressure and at least 10 bpm increase in pulse from sitting to standing or supine to standing positions, occurred in short-term clinical trials, with a frequency of 0.9% with placebo and 0.8% with lurasidone 40 mg, 1.4% with 80 mg and 1.7% with 120 mg (2, 6).

Other uncommon events include seizures, occurring in 1/1,004 patients receiving lurasidone compared with 1/455 receiving placebo, and treatment-emergent suicidal ideation, occurring in 6/1,004 for patients receiving lurasidone compared with 2/455 receiving placebo. No suicide attempts or completed suicides were reported in these short-term, placebo-controlled trials (6).

The product label describes tolerability and safety outcomes from uncontrolled longer-term studies (primarily open-label extension studies) (6). These are summarized in Table 2 and provide evidence for a favorable long-term tolerability profile for lurasidone.

No clinically important differences were observed between lurasidone and placebo in changes in routine hematology, urinalysis, or serum chemistry (6). Elevations in creatinine were observed for patients receiving lurasidone or placebo in the short-term studies, with a mean change of 0.06 mg/dL for lurasidone-treated patients versus 0.03 mg/ dL for placebo. The proportion of patients experiencing a creatinine shift from normal to high ( $\geq 1.1$  to  $\geq 1.3$  mg/dL depending on the definition for each study) occurred in 3.1% of lurasidone-treated patients compared with 1.4% for placebo (NNH 59). Mean changes in the liver enzymes AST and ALT were similar for lurasidone and placebo, with proportions of patients with elevations at least three times the upper limit of normal being very low: 0.8% for lurasidone for each transaminase and 0.9% for AST and 1.1% for ALT in patients receiving placebo (2).

Lurasidone does not have an impact on the ECG QT interval (6). In a dedicated QT study involving 87 clinically stable patients with schizophrenia or schizoaffective disor-

Table 2 Toler from Studi exte	ability and Uncontrol ies (primar nsion stud	bility and Safety Outcomes Incontrolled Longer-Term es (primarily open-label sion studies)*			
Variable	Week 24	Week 36	Week 52		
Weight (kg), mean change	-0.38	-0.47	-0.71		
Glucose (mg/dL), mean change	+1.6	+0.3	+1.2		
Total cholesterol (mg/dL) mean change	-4.2	-1.9	-3.6		
Triglycerides (mg/dL), mean change	-13.6	-3.5	-6.5		
Prolactin (ng/mL),					

\*Source data from reference #6.

median change

der given lurasidone 120 or 600 mg/d, or ziprasidone 160 mg daily, no patients receiving lurasidone experienced a QTc increase greater than 60 msec from baseline, nor did any patient experience a QTc greater than 500 msec (6).

-1.9

-5.4

-3.3

#### **Potential Drug-Drug Interactions**

Table 3 summarizes the potential drug-drug interactions involving lurasidone.

#### Dosing

Lurasidone tablets are available in 40 and 80 mg strengths. The product label recommends a starting dose of 40 mg/d administered once daily with food ( $\geq$ 350 calories),

with a maximum recommended dose of 80 mg/d (6). Maximum tolerated dose (MTD) for lurasidone was determined using two linked studies that enrolled patients with stable schizophrenia and results were presented in a poster (21). The MTD was defined as the dose where at least four patients at a given dosage level reported more than one moderate or severe adverse event related to lurasidone, or the dose at which greater than one patient reported a serious adverse event at least possibly related to lurasidone. Doses tested ranged from 120 mg to 600 mg/d across the studies. The MTD was determined to be 400 mg/d, with moderate to severe adverse events most frequently encountered at 520 mg/d being akathisia (5 patients), sedation (3 patients) and restlessness (2 patients). No clinically relevant ECG findings with lurasidone were encountered, nor were clinically significant abnormalities observed in laboratory measures, vital signs, or physical examination.

## **Discussion and Conclusions**

The registration trials have demonstrated efficacy and tolerability, particularly at a dose of 40 or 80 mg/d. A limitation is that subjects in registration studies may be dissimilar to patients routinely encountered in clinical practice in terms of comorbid psychiatric and somatic conditions, including substance use disorders. Known nonresponders to antipsychotics are also usually excluded from registration trials. Additional clinical trials (and clinical experience) with a broader population of patients with schizophrenia would be useful. Longer-term studies would also be helpful to understand how lurasidone will perform in the maintenance phase of schizophrenia treatment.

Table 3 Pote	tial Drug-Drug Interactions and Recommendations for Dosing*						
	Effect on Lurasidone Pharmacokinetics						
Coadministered Drug	Property	Cmax	AUC	Recommendation for Lurasidone			
Ketoconazole	Strong CYP3A4 inhibitor	<b>▲</b> 7x	<b>▲</b> 9x	Contraindicated			
Diltiazem	Moderate CYP3A4 inhibitor	▲2x	▲2x	Maximum dose 40 mg/d			
Rifampin	Strong CYP3A4 inducer	▼to 1/7th	▼to 1/5th	Contraindicated			
Lithium	-	Minimal (▼to 9/10th) Minimal (▲1.1x)		No adjustment required			
		Effect on Pharmacokinetics of Coadministered Drug					
Coadministered Drug	Property	Cmax	AUC	Recommendation for Coadministered Drug			
Digoxin P-glycoprotein substr		Minimal (▲1.09x)	Minimal (▲113x)	No adjustment required			
		()		No adjustment required			
Midazolam	CYP3A4 substrate	Minimal (▲1.21x)	Minimal (▲1.44x)	No adjustment required			

Cmax=maximum concentration; AUC=Area under the plasma concentration curve. \*Source data from references #6, 11, 24.

To date, there has been only one published, peer-reviewed study report (22); the remainder of the information available has come from the product label (6), and from other sources such as posters presented at scientific meetings. These other sources are not subject to peer review and their content may undergo further quality review and subsequent revision prior to final publication.

Lurasidone joins a group of second-generation antipsychotics that have a lower propensity for weight gain and adverse metabolic effects than some others. Table 4 provides a broad overview of similarities and differences between lurasidone and ziprasidone, aripiprazole, iloperidone, and asenapine. This table is not exhaustive and, with the exception of lurasidone versus ziprasidone, there is no data available from clinical trials that directly compare lurasidone with these other agents.

Switching from one antipsychotic to another requires careful consideration of a medication's pharmacodynamic profile in order to avoid unintended consequences. For example, switching to lurasidone from a medication that has potent histamine H1 activity may theoretically lead to problems with sleep or anxiety. Switch studies can help provide additional information that will inform clinical practice.

Lurasidone's relative efficacy ranking is currently

unknown. Cost may also impact decision making, particularly since inexpensive generic versions of risperidone are currently available and other second-generation generics are soon to follow.

For an extended review of lurasidone that includes additional information on all the registered clinical studies of lurasidone and a comprehensive examination of number needed to treat, number needed to harm, and likelihood to be helped or harmed, the reader is referred to the author's paper in the *International Journal of Clinical Practice* (2). Additional information can also be found in the Drug Approval Package posted on the FDA's website (27).

#### Disclosures

No writing assistance or external financial support was utilized in the production of this article. Leslie Citrome is a consultant for, has received honoraria from, or has conducted clinical research supported by, the following: Abbott Laboratories, AstraZeneca Pharmaceuticals, Avanir Pharmaceuticals, Azur Pharma, Barr Laboratories, Bristol-Myers Squibb, Eli Lilly and Company, Forest Research Institute, GlaxoSmithKline, Janssen Pharmaceuticals, Jazz Pharmaceuticals, Merck, Novartis, Pfizer Inc., Sunovion, and Vanda Pharmaceuticals.

and	ind Asenapine*					
Comparator (Ref #)	Shared Properties	Advantages of Lurasidone	Advantages of Comparator			
Ziprasidone (25)	• Food effect	<ul> <li>Once daily dosing</li> <li>Starting dose as per product labeling may be therapeutic</li> <li>Lower caloric requirement (350 calories) when administering</li> <li>No effect on ECG QT interval</li> </ul>	<ul> <li>More extensive evidence base for multiple indications</li> <li>Available as a short-acting intramuscular formulation</li> </ul>			
Aripiprazole (26)	• Once daily dosing • Starting dose may be therapeutic	<ul> <li>Aripiprazole's partial agonism at the dopamine D2 receptor may make switching from other antipsychotics to aripiprazole more unpredictable</li> </ul>	<ul> <li>No food effect</li> <li>More extensive evidence base for multiple indications</li> <li>Available as a short-acting intramuscular and as an orally disintegrating tablet formulation</li> </ul>			
lloperidone (3)	<ul> <li>At present, regulatory approval for schizophrenia only</li> <li>Limited "real world" experience</li> </ul>	<ul> <li>Once daily dosing</li> <li>Starting dose as per product labeling may be therapeutic</li> <li>No effect on ECG QT interval</li> <li>Minimal alpha 1 noradrenergic receptor effects</li> </ul>	<ul> <li>No food effect</li> <li>Extrapyramidal symptoms and akathisia on par with placebo</li> </ul>			
Asenapine (4)	Starting dose may be therapeutic     Dose-related sedation/somnolence     Limited "real world" experience	Once daily dosing     No requirement to not eat or drink     for 10 minutes post administration	<ul> <li>No food effect</li> <li>Covert noncompliance not possible with sublingual administration</li> </ul>			

## Table 4 Lurasidone's Similarities and Differences with Ziprasidone, Aripiprazole, Iloperidone, and Asenapine\*

\*This table is not exhaustive and, with the exception of lurasidone versus ziprasidone, there is no data available from clinical trials that directly compare lurasidone with these other agents.

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