



Common Drug Review

Pharmacoeconomic Review Report

January 2014

Drug	lurasidone hydrochloride (Latuda)
Indication	Management of manifestations of schizophrenia
Listing request	Management of manifestations of schizophrenia
Manufacturer	Sunovion Pharmaceuticals

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TABLE OF CONTENTS

ABBREVIATIONS	ii
SUMMARY	iii
REVIEW OF THE PHARMACOECONOMIC SUBMISSION	1
1. Introduction.....	1
2. Summary of Pharmacoeconomic Submission	3
3. Key Limitations	5
4. Issues for Consideration	5
5. Conclusions.....	6
Tables	
Table 1: Cost Comparison Table of Oral Atypical Antipsychotics for Schizophrenia	1
Table 2: Annual Drug Costs for Lurasidone versus Metabolically Neutral AAPs (CDR Calculations)	4
Table 3: Annual Drug Costs for Lurasidone versus Other AAPs (CDR Calculations)	4

ABBREVIATIONS

AAP	atypical antipsychotic
AP	antipsychotic
ODB	Ontario Drug Benefit
ODT	oral disintegrating tablet
XR	extended release

SUMMARY

Lurasidone (Latuda) is available as 40 mg, 80 mg, and 120 mg tablets at a confidential flat price of [REDACTED] per tablet ([REDACTED] per day). The manufacturer submitted a cost-minimization analysis that compared lurasidone with other AAPs, and focused on the metabolically neutral agents, aripiprazole and ziprasidone.¹ At the submitted price of [REDACTED], lurasidone ([REDACTED] per year) is less expensive than aripiprazole (\$1,509 to \$1,746 per year) and ziprasidone (\$1,448 per year). Therefore, lurasidone would generate modest cost savings for public plans if it were used instead of aripiprazole or ziprasidone. By contrast, lurasidone is more expensive than quetiapine (\$352 to \$705) and risperidone (\$443 to \$665), regardless of dose. Therefore, lurasidone would incur additional costs to public plans were it to be used instead of quetiapine or risperidone. Whether lurasidone is more or less expensive than other AAPs (olanzapine, risperidone oral disintegrating tablet (ODT), quetiapine extended release (XR), paliperidone) depends on the dose considered and prices within individual public plans.

REVIEW OF THE PHARMACOECONOMIC SUBMISSION

1. INTRODUCTION

Lurasidone hydrochloride (Latuda) is an AAP indicated for the management of manifestations of schizophrenia.² It is available as a 40 mg, 80 mg, and 120 mg tablet at a confidential flat price of [REDACTED] per tablet, or [REDACTED] per day. The recommended starting dose of lurasidone is 40 mg daily. Patients should be treated with the lowest effective dose (anticipated to be 40 mg to 80 mg daily), and doses higher than 80 mg may be considered.² The manufacturer is seeking reimbursement for lurasidone for the management of the manifestations of schizophrenia.

This is a resubmission based on the submission of new clinical information and [REDACTED] ([REDACTED]). In addition, the Health Canada indication has been revised to reflect approval for the management of schizophrenia, rather than acute schizophrenia. Previously (January, 2013), the Canadian Drug Expert Committee (CDEC) recommended that lurasidone not be listed for the acute treatment of schizophrenia due to insufficient evidence that Latuda had comparable efficacy relative to other less costly antipsychotics (APs). [REDACTED]

1.1 Cost Comparison Table

The comparator treatments presented in the table below have been deemed the appropriate comparators by clinical experts. Comparators may be recommended (appropriate) practice, versus actual practice. Comparators are not restricted to drugs. They may also be devices or procedures. Costs are manufacturer list prices, unless otherwise specified.

TABLE 1: COST COMPARISON TABLE OF ORAL ATYPICAL ANTIPSYCHOTICS FOR SCHIZOPHRENIA

Drug / Comparator	Strength	Dosage Form	Price (\$)	Recommended Daily Dose	Average Daily Drug Cost (\$)	Annual Drug Cost (\$)
Lurasidone (Latuda)	40 mg 80 mg 120 mg	tab	[REDACTED] ^a	40 mg to 120 mg daily	[REDACTED]	[REDACTED]
Asenapine (Saphris)	5 mg 10 mg	tab	1.5516 ^b	5 mg twice daily	3.10	1,133
Aripiprazole (Abilify)	2 mg 5 mg 10 mg 15 mg 20 mg 30 mg	tab	3.0970 3.4867 4.1337 4.7827 5.4317 6.7277	10 mg to 15 mg daily	4.13 to 4.78	1,509 to 1,746
Clozapine (generic)	25 mg 100 mg	tab	0.6594 ^c 2.6446 ^c	150 mg to 600 mg daily	3.06 to 15.87	1,117 to 5,792
Olanzapine (generic)	2.5 mg 5 mg 7.5 mg 10 mg 15 mg	tab	0.4493 0.8986 1.3479 1.7972 2.6958	5 mg to 20 mg daily	0.90 to 3.59	328 to 1,312

CDR PHARMACOECONOMIC REVIEW REPORT FOR LATUDA

Drug / Comparator	Strength	Dosage Form	Price (\$)	Recommended Daily Dose	Average Daily Drug Cost (\$)	Annual Drug Cost (\$)
	5 mg 10 mg 15 mg	ODT	0.8937 1.7857 2.6778		0.89 to 3.57	326 to 1,304
Paliperidone (Invega)	3 mg 6 mg 9 mg	XR tab	3.7240 5.5700 7.4240	6 mg once daily	5.57	2,033
Quetiapine (generic)	25 mg 100 mg 200 mg 300 mg	tab	0.1235 0.3295 0.6617 0.9656	150 mg to 300 mg twice daily	0.97 to 1.93	352 to 705
	50 mg 150 mg 200 mg 300 mg 400 mg	XR tab ^d	0.3950 0.7780 1.0520 1.5440 2.0960	400 mg to 800 mg	2.10 to 4.19	765 to 1,530
Risperidone (generic)	0.25 mg 0.5 mg 1 mg 2 mg 3 mg 4 mg	tab	0.1314 0.2202 0.3041 0.6071 0.9108 1.2144	4 mg to 6 mg daily	1.21 to 1.82	443 to 665
	0.5 mg 1 mg 2 mg 3 mg 4 mg	ODT	0.7450 0.7725 1.5281 2.2913 3.0638	4 mg to 6 mg daily	3.06 to 4.58	1,118 to 1,673
Ziprasidone (Zeldox)	20 mg 40 mg 60 mg 80 mg	cap	1.7318 1.9836 1.9836 1.9836	40 mg to 80 mg twice daily	3.97	1,448

cap = capsule; ODT = oral disintegrating tablet; tab = tablet; XR = extended release.

All prices are from the Ontario Drug Benefit Formulary (accessed August 2013) unless otherwise indicated and do not include dispensing fees.

^a Manufacturer's confidential submitted price.

^b Asenapine is indicated for schizophrenia, but is only reimbursed by public plans for bipolar disorder. Therefore, the McKesson Canada pricing (including markup) is provided in the table, rather than public formulary prices.

^c Manitoba formulary (Aug 2013).

^d The manufacturer's submission used the cost of brand name quetiapine, Seroquel XR, rather than generic quetiapine.

2. SUMMARY OF PHARMACOECONOMIC SUBMISSION

The manufacturer submitted a cost-minimization analysis comparing lurasidone 40 mg, 80 mg, and 120 mg tablets with other AAPs available on the Canadian market. The manufacturer focused on the metabolically neutral AAPs aripiprazole and ziprasidone, based on an assumption that the efficacy and metabolic effects of lurasidone are similar to these drugs. The perspective was that of the public health care system, with time horizons of one day and one year.

The manufacturer assumed that lurasidone had similar efficacy and safety to other AAPs, based on clinical trials ranging from six weeks to 12 months long and an indirect comparison of lurasidone versus aripiprazole and ziprasidone.² Only drug acquisition costs were considered, as other health care costs were assumed to be equivalent. Drug costs were derived from the Ontario Drug Benefit Formulary where available, with the remainder from the BC PharmaCare Formulary. Although included in Table 1 due to its Health Canada-approved indication for the treatment of schizophrenia, drug plans that reimburse asenapine only do so for bipolar disorder. Therefore, asenapine was not considered in the manufacturer's submission. Clozapine was not considered due to the unlikelihood of patients taking clozapine being switched to lurasidone. Paliperidone was also not considered in the manufacturer's submission, although the reason for this is unclear.

At the submitted price, lurasidone (██████████) is less expensive than aripiprazole (\$1,509 to \$1,746 per year) and ziprasidone (\$1,448 per year) (Table 2), regardless of dose. Therefore, lurasidone would likely generate modest cost savings were it to be used instead of aripiprazole or ziprasidone. By contrast, lurasidone is more expensive than quetiapine (\$352 to \$705) and risperidone (\$443 to \$665), regardless of dose (Table 3). Therefore, lurasidone would result in increased costs were it to be used instead of quetiapine or risperidone. When compared with the remaining AAPs in Table 3, whether lurasidone is less or more expensive depends on dosing. Specifically, at lower recommended doses, standard and ODT olanzapine, risperidone ODT, and quetiapine XR are less expensive than lurasidone, while paliperidone is more expensive than lurasidone (Table 3). However, at higher doses, standard and ODT olanzapine, quetiapine XR, risperidone ODT, and paliperidone are more expensive (Table 3).

It should be noted that the incremental costs of lurasidone presented in Table 2 and Table 3 reflect differences in cost relative to comparators based on Ontario Drug Benefit Formulary prices; however, the magnitude but not the direction of price differences for individual public plans will vary in accordance with the prices of the various comparators within individual plans.

TABLE 2: ANNUAL DRUG COSTS FOR LURASIDONE VERSUS METABOLICALLY NEUTRAL AAPs (CDR CALCULATIONS)

AAPs	Range ^a of Annual Costs (\$)	Incremental Annual Cost ^b (\$)	
		Lower Recommended Dose	Upper Recommended Dose
Lurasidone (Latuda)	██████	Reference	Reference
Ziprasidone (Zeldox)	1,448	██████	██████
Aripiprazole (Abilify)	1,509 to 1,746	██████	██████

AAPs = atypical antipsychotics; CDR = Common Drug Review.

^a Based on recommended doses.

^b Positive numbers indicate the comparator costs more than lurasidone. All prices are from the Ontario Drug Benefit Formulary (accessed August 2013).

TABLE 3: ANNUAL DRUG COSTS FOR LURASIDONE VERSUS OTHER AAPs (CDR CALCULATIONS)

AAPs	Range ^a of Annual Costs (\$)	Incremental Annual Cost ^b (\$)	
		Lower Recommended Dose	Upper Recommended Dose
Olanzapine ODT (generic)	326 to 1,304	██████	██████
Olanzapine (generic)	328 to 1,312	██████	██████
Quetiapine (generic)	352 to 705	██████	██████
Risperidone (generic)	443 to 665	██████	██████
Quetiapine XR (generic)	765 to 1,530	██████	██████
Lurasidone (Latuda)	██████	Reference	Reference
Risperidone ODT (generic)	1,118 to 1,673	██████	██████
Paliperidone XR (Invega)	2,033	██████	██████

AAPs = atypical antipsychotics; CDR = Common Drug Review; ODT = oral disintegrating tablet; XR = extended release.

^a Based on recommended doses.

^b Positive numbers indicate the comparator costs more than lurasidone. All prices are from the Ontario Drug Benefit Formulary (accessed August 2013).

A sensitivity analysis was also provided by the manufacturer that compared the weighted average daily cost of lurasidone with other AAPs, excluding titration and the below-recommended dosing strengths of the comparators. In line with the results of the primary analysis (above), the results of the sensitivity analysis indicated that the weighted average daily cost of lurasidone is higher than that of risperidone, non-XR quetiapine, and olanzapine, but lower than the cost of ziprasidone, aripiprazole, and brand name quetiapine XR (Seroquel XR).

3. KEY LIMITATIONS

3.1 Indirect Comparison

While no differences in efficacy between lurasidone and all other oral AAPs were observed in a network meta-analysis, the absence of head-to-head trials and limitations with the indirect comparison make the assumption of equivalent efficacy uncertain. This applies both to the assumption of equivalent efficacy and safety for lurasidone versus other AAPs, as well as the assumption that lurasidone has a metabolic profile similar to the metabolically neutral agents, aripiprazole and ziprasidone.

3.2 Quetiapine XR Available as Generic

The manufacturer's analyses included pricing for Seroquel XR (i.e., brand name quetiapine XR). However, lower-priced generic quetiapine XR is now reimbursed in most jurisdictions. The generic pricing of \$2.10 to \$4.19 per day (Table 1) is less than the previously reimbursed daily cost of Seroquel XR (\$5.24 to \$10.48). When considering the cost of generic quetiapine, the daily cost of lurasidone is [REDACTED] more expensive than 400 mg quetiapine XR, but [REDACTED] less expensive than 800 mg quetiapine XR.

4. ISSUES FOR CONSIDERATION

4.1 Higher Doses of Lurasidone

While lurasidone is available in 40mg, 80mg and 120mg tablets, a daily dose of 160 mg was also shown to be effective relative to placebo in a randomized trial.³ As this dose would require taking at least two tablets daily, the daily and annual costs would be doubled. The manufacturer has proposed a mechanism to mitigate this by capping the daily cost of 160 mg lurasidone at [REDACTED]. However, it is not clear whether this could be operationalized by all public plans.

4.2 Lack of Titration

Lurasidone does not require complex initial titration, which may reduce initial prescription expenses (especially dispensing fees), in patients starting on or switching to lurasidone relative to some of its comparators (e.g., ziprasidone).

4.3 Variations in Comparator Pricing Between Drug Plans

Table 1 compares the confidential submitted price of lurasidone with comparator pricing as listed in the ODB Formulary (except for asenapine and clozapine, for which alternative price sources were used). While the pricing of AAPs varies among public drug plans, the use of ODB list prices for comparison is conservative because the ODB prices for all AAPs are the least expensive (or within a few cents of being the least expensive) among all drug plans. One exception is aripiprazole; nevertheless, at the confidential submitted daily price of [REDACTED] per day, lurasidone is still [REDACTED] less expensive than the lowest public plan price for aripiprazole (\$3.84, Alberta Health Drug Benefit List, accessed August 2013). Similarly, lurasidone is consistently less expensive than ziprasidone. Whether lurasidone is more or less expensive than other (non-metabolically neutral) AAPs depends on the dose considered (see above) and the prices within individual public plans.

5. CONCLUSIONS

At the submitted price of [REDACTED], lurasidone ([REDACTED] per year) is less expensive than aripiprazole (\$1,509 to \$1,746 per year) and ziprasidone (\$1,448 per year). Therefore, lurasidone would generate modest cost savings for public plans if it were used instead of aripiprazole or ziprasidone. By contrast, lurasidone is more expensive than quetiapine (\$352 to \$705) and risperidone (\$443 to \$665), regardless of dose. Therefore, lurasidone would incur additional costs to public plans if it were used instead of quetiapine or risperidone. Whether lurasidone is more or less expensive than other AAPs (olanzapine, risperidone ODT, quetiapine XR, paliperidone) depends on the dose considered and prices within individual public plans.

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