Drug Use Research & Management Program
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Drug Use Evaluation: Lumateperone

Plain Language Summary: How is lumateperone prescribed for people on Oregon Medicaid compared to similar medicines?

- Lumateperone is a medicine that providers can recommend for schizophrenia. Studies do not show that lumateperone improves behavior or thought patterns more than other medicines in people with schizophrenia.
- Providers who live in rural counties are the ones who usually recommend lumateperone. People taking lumateperone had higher health costs than people who were taking similar medicines.
- The Drug Use Research Management program recommends reaching out to providers to identify why they recommend this medicine. Educate providers on the cost of lumateperone compared to other medicines that have similar benefits and risks.

Research Questions:

1. Which potential indications are present on or prior to initiation of lumateperone or MHCAG recommended first line, second generation antipsychotics for schizophrenia in Oregon Medicaid patients.
2. Which provider specialties initiate lumateperone or MHCAG recommended first line, second generation antipsychotics in Oregon Medicaid patients?
3. How are lumateperone and MHCAG recommended first line, second generation antipsychotics used in conjunction with other psychotropic medications in Oregon Medicaid patients?
4. What are the impacts on healthcare resource utilization (HRU) for Oregon Medicaid patients starting lumateperone or MHCAG recommended antipsychotics?

Conclusions:

1. Lumateperone had a significantly higher rate of patients with schizophrenia compared to MHCAG agents (56.86% vs. 19.83%; $p<0.0001$) and a significantly lower rate of bipolar disorder (29.41% vs. 49.16%; $p=0.0064$).
2. Prescribers in Douglas County accounted for 16.43% of patients receiving lumateperone compared to only 3.75% of patients in the MHCAG agent group. Several other rural counties had higher rates of lumateperone use (e.g., Lincoln 9.29% vs. 1.37%, Polk 6.43% vs. 2.93%, Columbia 2.86% vs. 0.68%). Prescriber specialties also varied significantly with “Nurse Practitioner – Psychiatric/Mental Health” accounting for 72.86% of lumateperone initial prescriptions vs. 33.23% of MHCAG initial prescriptions ($p<0.0001$).
3. Concurrent use of psychotherapeutic regimens was common, with lumateperone patients having a higher rate of other antipsychotic use compared to MHCAG patients (74.51% vs. 53.63%; $p=0.0038$). Concurrent antidepressant use was lower in the lumateperone group compared to the MHCAG group (50.98% vs. 64.80%; $p=0.0471$).
4. The time to discontinuation of the index antipsychotic was similar for lumateperone vs. MHCAG patients. Lumateperone patients had significant increases in costs for inpatient services, pharmacy services, and total cost of care. The lumateperone group had significantly lower baseline inpatient

HRU and significantly higher follow up HRU compared to the MHCAG group, suggestive of treatment patterns beyond the direct effects of lumateperone use.

Recommendations:

1. Consider outreach to providers and regions with higher use of lumateperone to identify reasons for practice differences.
2. Consider provider education programs to raise awareness of the similar outcomes and higher costs associated with lumateperone.
3. No changes to utilization controls for lumateperone are warranted at this time.

Background

In August 2020, the Drug Use Research and Management program reviewed lumateperone as part of the antipsychotic drug class update and new drug evaluation.[1] Low quality evidence shows that lumateperone 42mg once daily may reduce Positive and Negative Syndrome Scale (PANSS) scores compared to placebo in patients with schizophrenia who were treatment experienced, but not treatment resistant.[2–4] The failure to demonstrate a dose-response and a lack of consistent statistical differences between placebo and treatment arms for the primary study endpoints makes interpretation of the available evidence challenging. In December 2021, the FDA approved lumateperone for the treatment of bipolar depression.[5] Beginning in April of 2020, the Oregon Fee For Service (FFS) Medicaid program began seeing claims for lumateperone treatment.

The objective of this study was to determine how lumateperone is used compared to other antipsychotics medications used to treat schizophrenia in treatment-experienced patients. In particular, this study evaluated which indications were present and likely targets for lumateperone treatment, which prescribers initiated lumateperone treatment, how lumateperone was used in combination with other antipsychotics, and finally how the use of lumateperone impacted the overall cost of care.

Methods:

The Oregon Medicaid Decision Support and Surveillance Utilization Review System (DSSURS) data warehouse was the data source for this retrospective observational study. DSSURS contains all medical and pharmacy administrative calls for all fee-for-service (FFS) and coordinated care organization (CCO) paid claims from the Oregon Medicaid Management Information System (MMIS).[7] The claim evaluation window was from 4/1/2019 to 12/31/2021. For patients with at least one claim for lumateperone, the index event was the first claim for lumateperone. For all other included patients, the index event was the first claim for any MHCAG antipsychotic. The Mental Health Clinical Advisory Group (MHCAG), a subcommittee of the Pharmacy and Therapeutics Committee, has developed treatment algorithms for patients with schizophrenia. [6] The MHCAG algorithm suggests the use of aripiprazole, risperidone, or paliperidone as starting antipsychotics for the treatment of schizophrenia. The index date was the date of service of the index event. The index antipsychotic was the antipsychotic associated with the index event. The baseline period was the 365 days prior to the index date (excluding the index date). The follow-up period was the 365 days following the index date (inclusive of the index date). SAS software version 9.4 was used to perform all data analysis and statistical operations. (Copyright ©2021 SAS Institute Inc.) Continuous outcomes were compared using Student T-Tests while categorical variables were compared using Chi Squared tests.

Inclusion Criteria:

1. At least one paid FFS claim for either lumateperone or a MHCAG antipsychotic (**Table 7**) during the claim evaluation window

Exclusion Criteria:

1. Patients under 18 years old
2. Patients with non-Medicaid primary insurance coverage (TPL) effective during either the baseline or follow up period

3. Heritage Native American All Inclusive Rate (HNA AIR) claims during the baseline or follow up period
4. Claims for benefit plans other than OHP Plus (BMH) during either the baseline or follow up period
5. Patient without a history of antipsychotic pharmacy claims
6. Less than 75% of days OHP Plus (BMH) benefit plan eligibility during the 365 day baseline period
7. Less than 75% of days OHP Plus (BMH) benefit plan eligibility during the 365 day follow up period

Cohorts:

Patients with an index antipsychotic of lumateperone were assigned to the lumateperone group. Patients with any other index antipsychotic were assigned to the MHCAG group.

Definitions:

Patients were considered antipsychotic experienced if there were any claims during the claims evaluation window for any antipsychotic medication for more than 42 days (**Table 7, Table 8**). Age was calculated based on the index date. Patients were categorized based on their enrollment in a CCO, FFS or both during both the baseline and follow up periods. Concurrent psychotropic regimens were defined by the presence of medications defined in **Table 7** and **Table 8**. The index medication was excluded from the concurrent psychotropic regimen definitions. Persistence to antipsychotic therapy was measured by the time from the index date to the last date covered by the index medication (time to discontinuation). Costs were calculated based on the amount paid and averaged over the entire study population. Inpatients days were cumulative across all hospitalizations.

Supplemental Analysis:

For the supplemental analysis, all patients meeting inclusion criteria and not meeting any exclusion criteria 1-4 were evaluated for geographic distribution and provider specialty.

Results:

Of the 12,452 patients meeting inclusion criteria, 767 were included in the final study population (**Table 1**). There were no statistically significant differences in baseline demographics of age, gender, or CCO enrollment (**Table 2**). **Table 3** shows lumateperone had a significantly higher rate of patients with schizophrenia compared to MHCAG agents (56.86% vs. 19.83%; p<0.0001) and a significantly lower rate of bipolar disorder (29.41% vs. 49.16%; p=0.0064). Concurrent use of psychotherapeutic regimens was common (**Table 4**), with lumateperone patients having a higher rate of other antipsychotic use compared to MHCAG patients (74.51% vs. 53.63%; p=0.0038). Concurrent antidepressant use was lower in the lumateperone group compared to the MHCAG group (50.98% vs. 64.80%; p=0.0471). As illustrated in **Figure 1**, the time to discontinuation of the index antipsychotic was similar between the groups. The lumateperone group had lower mean baseline HRU for emergency department ($414 vs. $728; p=0.0113) and inpatients services ($2,224 vs. $5,707; p=0.0004) and higher baseline pharmacy utilization ($6,969 vs. $2,879; p=0.0026), though baseline total costs were similar between the 2 groups (p=0.6518). The lumateperone group had an increase in inpatient HRU from baseline to follow up, while the MHCAG group had a reduction in inpatient HRU ($1,920 vs. -$2,031; p=0.0212). The lumateperone group

had a significantly larger increase in pharmacy costs as well ($3,681 vs. $726; p=0.0429). Lumateperone had an overall increase in costs of $8,081 compared to the reduction in overall costs in the MHCAG group of -$692 (p=0.0192).

The supplemental analysis revealed significant differences in prescriber location between the groups (p<0.0001). In particular, prescribers in Douglas County accounted for 16.43% of patients receiving lumateperone compared to only 3.75% of patients in the MHCAG group. Several other rural counties had similarly higher rates of lumateperone use (e.g., Lincoln 9.29% vs. 1.37%, Polk 6.43% vs. 2.93%, Columbia 2.86% vs. 0.68%). Prescriber specialties also varied significantly with "Nurse Practitioner – Psychiatric/Mental Health" accounting for 72.86% of lumateperone initial prescriptions vs. 33.23% of MHCAG initial prescriptions (p<0.0001).

Table 1. Attrition Table

Exclusion Criteria	Lumateperone		MHCAG	
00-Available patients	147		12,305	
01-Patients under 18 years old	0	0%	1,752	14%
02-Baseline TPL Coverage	4	3%	681	5%
03-Followup TPL Coverage	3	2%	85	1%
04-Has Baseline or Follow up HNA Air Claims	0	0%	46	0%
05-Has claims Benefit Plan other than BMH during baseline	0	0%	15	0%
06-Has claims Benefit Plan other than BMH during followup	0	0%	44	0%
07-Not treatment experienced	25	17%	8,020	64%
08-Less than 25% baseline eligibility	0	0%	25	0%
09-Less than 25% follow up eligibility	25	17%	328	3%
10-Less than 50% baseline eligibility	4	3%	65	1%
11-Less than 50% follow up eligibility	13	9%	237	2%
12-Less than 75% baseline eligibility	3	2%	72	1%
13-Less than 75% follow up eligibility	19	13%	219	2%
Patient Remaining	**51**	**35%**	**716**	**6%**

Abbreviations: BMH: Oregon Health Plan plus benefit package; HNA AIR = Heritage Native American All Inclusive Rate; TPL = third party liability (e.g., other primary insurance)

Table 2. Baseline Demographics

		Lumateperone (n=51)	MHCAG (n=716)	
		n(%)	n(%)	p
Age (Years)	Mean (Median)[Standard Deviation]	39.4 (36.0) [12.1]	37.4 (36.0) [11.5]	0.2408
	18-29	12 (23.53%)	207 (28.91%)	0.6653
	30-39	15 (29.41%)	224 (31.28%)	
	40-49	12 (23.53%)	156 (21.79%)	
	50-59	11 (21.57%)	105 (14.66%)	
	60 and over	1 (1.96%)	24 (3.35%)	
Gender	Female	26 (50.98%)	447 (62.43%)	0.1042
	Male	25 (49.02%)	269 (37.57%)	
Plan	CCO	45 (88.24%)	530 (74.02%)	0.0552
	CCO+FFS	5 (9.80%)	176 (24.58%)	
	FFS	1 (1.96%)	10 (1.40%)	

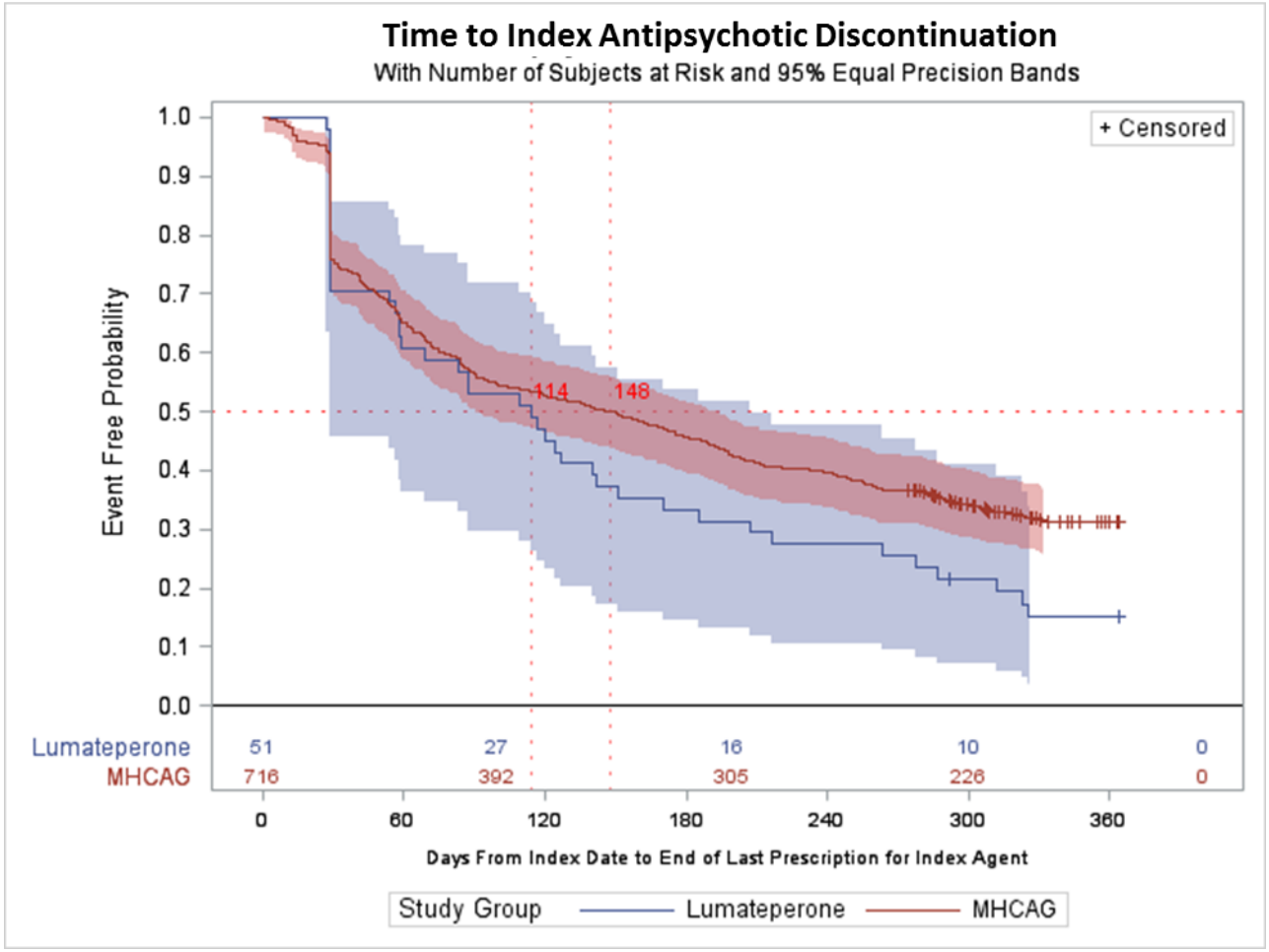
Table 3. Baseline Comorbidities

	Lumateperone (n=51)	MHCAG (n=716)	
	n(%)	n(%)	p
Bipolar	**15 (29.41%)**	**352 (49.16%)**	**0.0064**
Schizophrenia	**29 (56.86%)**	**142 (19.83%)**	**<0.0001**

Table 4. Concurrent Psychotherapeutic Regimens

	Lumateperone (n=51)	MHCAG (n=716)	
	n(%)	n(%)	p
Antidepressants	**26 (50.98%)**	**464 (64.80%)**	**0.0471**
Anxiolytics	12 (23.53%)	113 (15.78%)	0.1478
Mood Stabilizer	10 (19.61%)	192 (26.82%)	0.2588
Other Antipsychotics	**38 (74.51%)**	**384 (53.63%)**	**0.0038**

Figure 1. Time to Index Antipsychotic Discontinuation



Author: Williams

Date: Oct 2022

Table 5. Health Resource Utilization (US Dollars)

		Lumateperone (n=51)	MHCAG (n=716)	
		Mean(Median)[SD]	Mean(Median)[SD]	p
Baseline	**Emergency Department**	**414 (87) [776]**	**728 (246) [1,436]**	**0.0113**
	Inpatient	**2,224 (0) [4,983]**	**5,707 (0) [17,921]**	**0.0004**
	Outpatient	7,738 (3,641) [14,273]	9,281 (5,349) [14,285]	0.4564
	Pharmacy	**6,969 (3,091) [9,112]**	**2,879 (471) [5,377]**	**0.0026**
	Total	17,346 (13,970) [18,414]	18,595 (11,025) [26,050]	0.6518
Follow up	**Emergency Department**	**357 (0) [769]**	**711 (134) [1,806]**	**0.0065**
	Inpatient	4,144 (0) [12,769]	3,676 (0) [12,606]	0.7978
	Outpatient	10,275 (3,722) [20,747]	9,912 (4,938) [17,207]	0.9032
	Pharmacy	**10,650 (8,164) [9,027]**	**3,605 (549) [7,500]**	**<0.0001**
	Total	25,427 (16,255) [30,702]	17,903 (8,870) [26,675]	0.0545
Change From Baseline to Follow up	Emergency Department	-56.2 (0.0) [404.8]	-17.6 (0.0) [1,471.2]	0.6256
	Inpatient	**1,920 (0) [10,787]**	**-2,031 (0) [19,659]**	**0.0212**
	Outpatient	2,537 (315) [18,135]	631 (-74) [13,514]	0.4647
	Pharmacy	**3,681 (3,439) [9,992]**	**726 (41) [7,241]**	**0.0429**
	Total	**8,081 (4,198) [25,330]**	**-692 (-592) [25,829]**	**0.0192**

Table 6. Inpatient Days

	Lumateperone (n=51)	MHCAG (n=716)	
Inpatient Days	**Mean(Median)[SD]**	**Mean(Median)[SD]**	**p**
Baseline	**1.86 (0.00) [4.50]**	**4.84 (0.00) [15.14]**	**0.0006**
Follow up	4.14 (0.00) [12.71]	2.58 (0.00) [8.04]	0.3915
Change from Baseline to Follow up	**2.27 (0.00) [10.06]**	**-2.26 (0.00) [15.32]**	**0.0039**

Discussion:

Patients receiving lumateperone had significantly higher increases in total costs, pharmacy costs, and inpatient costs compared to MHCAG patients. The difference in pharmacy cost was not unexpected, given that most MHCAG formulations have generic versions. The differences in inpatient costs raises a number of questions. The higher baseline inpatient costs in the MHCAG group suggests the possibility that the initiation of MHCAG prescriptions may be triggered by an inpatient encounter. The higher follow up inpatient costs may suggest that lumateperone may have been initiated in an attempt to prevent inpatient hospitalizations. These inpatient findings, combined with generally higher rates of lumateperone use in more rural counties (e.g., Douglas, Lincoln, Polk, and Columbia) also raise questions about access to acute mental health services.

Limitations:
All retrospective administrative claims studies have inherent limitations. Such studies cannot determine causality and results should be interpreted with caution. Study groups were selected based on the initiation of either lumateperone or an MHCAG antipsychotic. Antipsychotic in general, and MHCAG recommended agents in particular, have indications beyond schizophrenia, which may affect the presence of other psychotropic agents (**Table 4**).Although there were no significant differences in baseline demographics between the groups, no propensity matching was performed, so there may be undetected differences between the groups. The geographical distribution of patients receiving lumateperone was significantly different compared to the MHCAG group. These geographic differences may contribute to differences in access to mental health services, further complicating interpretation of the results. The exclusion of patients with incomplete or peculiar administrative claims data (i.e., TPL coverage, less than 75% eligibility, HNA AIR) reduced the sample size substantially and therefore may not represent utilization across the entire Medicaid population.

References:

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Appendix 1: Drug Coding

Table 7 Included Antipsychotics

HSN	Drug Name
008721	Risperidone
025509	Risperidone microspheres
024551	Aripiprazole
042595	Aripiprazole lauroxil
045050	Aripiprazole lauroxil, submicr
034343	Paliperidone
036479	Paliperidone
046280	Lumateperone

Table 8 Other Drug Codes

Code Type	Code Value	Drug Name	Route
HIC	H7O, H7P, H7T, H7U, H7X (Excluding drugs in Table 1)	Other antipsychotics	Any
HSN	001669, 001670, 007378	Mood stabilizers	Any
HIC	H24, H2H, H2S, H2U, H7B, H7C, H7D, H7E, H7J, H7Z, H8P, H8T, H8Z	Antidepressants	Any
HIC	J2B, H20, H8K, H2X, H4A	Anxiolytics	Any

Table 9 Diagnosis Codes

ICD 10 codes	Description
F20.x	Schizophrenia
F31.x	Bipolar Disorder