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Drug Use Evaluation: Antipsychotic Utilization in Schizophrenia Patients

Research Questions:

1. How many schizophrenia patients are prescribed recommended first-line second-generation treatments for schizophrenia?
2. How many schizophrenia patients switch to an injectable antipsychotic after stabilization on an oral antipsychotic?
3. How many schizophrenia patients are prescribed 2 or more concomitant antipsychotics?
4. Are claims for long-acting injectable antipsychotics primarily billed as pharmacy or physician administered claims?
5. Does adherence to antipsychotic therapy differ between patients with claims for different routes of administration (oral vs. long-acting injectable)?

Conclusions:

- In total, 4663 schizophrenia patients met inclusion criteria, and approximately 14% of patients (n=685) were identified as treatment naïve without claims for antipsychotics in the year before their first antipsychotic prescription. Approximately 45% of patients identified as treatment naïve had a history of remote antipsychotic use, but it is unclear if antipsychotics were historically prescribed for schizophrenia.
- Oral second-generation antipsychotics which are recommended as first-line treatment in the MHCAG schizophrenia algorithm were prescribed as initial treatment in 37% of treatment naive patients and 28% of all schizophrenia patients. Recommended agents include risperidone, paliperidone, and aripiprazole.
- Utilization of parenteral antipsychotics was limited in patients with schizophrenia. Overall only 8% of patients switched from an oral to an injectable therapy within 6 months of their first claim. Approximately, 60% of all schizophrenia patients (n=2512) had claims for a single antipsychotic for at least 12 continuous weeks and may be eligible to transition to a long-acting injectable antipsychotic. Only 710 of these patients were on continuous therapy with a recommended first-line therapy (aripiprazole, paliperidone, or risperidone) for which there is a recommended injectable formulation.
- Only 10% of treatment naïve schizophrenia patients were prescribed concomitant antipsychotics for more than 8 weeks. Utilization of concomitant medications was slightly higher in all schizophrenia patients with approximately 17% of patients prescribed combination antipsychotic therapy.
- The vast majority of claims for long-acting injectable antipsychotics are billed through pharmacy for members enrolled in a coordinated care organization (CCO) whereas approximately 72% of fee-for-service (FFS) claims are billed as medical claims by providers after administration to the patient.
- Adherence to therapy was similar in patients with schizophrenia and did not differ between oral and injectable antipsychotic formulations. In the 6 months following the first claims, approximately 9-11% of patients had less than 25% of days covered (corresponding to less than 45 days) and 62-64% of patient had more than 75% of days covered (corresponding to >135 days).

Recommendations:

- Explore opportunities to increase access to recommended therapies for schizophrenia patients through discussion of provider educational opportunities and retrospective drug use review.

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Background:
In order to improve care for patients with mental health conditions, the Mental Health Clinical Advisory Group (MHCAG), a subcommittee of the Pharmacy and Therapeutics Committee, has developed treatment algorithms for patients with schizophrenia. This is the first treatment algorithm developed by MHCAG, and full treatment algorithms are undergoing publication. Medication algorithms include the following recommendations:

- Initial treatment: In treatment naïve patients, recommend use of aripiprazole, risperidone, or paliperidone as a first-line treatment
    - If the patient has an inadequate response after dose optimization over 2-6 weeks, recommend trial of another first-line treatment
    - With adequate response after 2-4 weeks, recommend transition to a long-acting injectable formulation to promote adherence to treatment
    - If first-line treatment options are not successful, consider switching to clozapine as a second or third-line agent
- Alternative treatment: If patient has an inadequate response to clozapine or partial response to 2 oral antipsychotic monotherapies, consider obtaining a second opinion with referral to a specialist. Recommended options for treatment include 1) switching to a different second-generation antipsychotic or a first-generation antipsychotic with a cross-taper to avoid dual therapy OR 2) augmentation of antipsychotic therapy if patient has a partial response to monotherapy
    - If the patient has inadequate response to one of these treatment options, recommend trial of the second treatment option
    - If both regimens are unsuccessful, reassess patient for clozapine treatment
    - If clozapine treatment is unsuccessful, consider augmentation with a first-generation, second-generation antipsychotic or electroconvulsive therapy.

Currently in the Oregon Health Plan, antipsychotic medications are exempt from traditional preferred drug list (PDL) and prior authorization (PA) requirements. However, clinical PA criteria which address safety concerns or medically inappropriate use may be implemented. Currently, safety edits are implemented for low dose quetiapine and pimavanserin. The majority of antipsychotic use is for second generation antipsychotics. The goal of this analysis is to assess current utilization patterns and identify opportunities for provider education and retrospective drug use review.

Methods:
The patient population included current Medicaid patients (enrolled in FFS and CCOs) with an index event from 6/1/2017 to 5/31/2018. The index event was defined as the first paid FFS pharmacy claim for an oral first or second generation antipsychotic or paid pharmacy or medical claims for injectable antipsychotics. Patients were included if they had a diagnosis of schizophrenia identified based on ICD-10 diagnosis codes in the 1.5 years before or 6 months after the index event (ICD-10 codes F20.0-F20.9). Data in the most recent 6 months may not capture all patients with a diagnosis of schizophrenia as medical claims may be incomplete. Patients were excluded if they had Medicare part D coverage or had ≤75% eligibility in the year prior to the index event in order to ensure complete medical records for diagnoses.

Treatment naïve patients were defined as patients without any claims for antipsychotics within the prior year based on medical and pharmacy claims. In some cases, patients may have a remote history of antipsychotic use and are not truly treatment naïve for their condition. A remote history of antipsychotic use was defined as patients with paid claims for antipsychotics at greater than 12 months before the index event. This data may be incomplete as many patients may not have a history of Medicaid eligibility. In addition, these patients may have been prescribed antipsychotics for conditions other than schizophrenia.

If patients had not transitioned to a parenteral antipsychotic within 6 months of an initial paid index event, they were categorized based on duration of treatment. Current treatment algorithms recommend transition of patients to a parenteral antipsychotic if patients have an adequate response after 2-4 weeks. Assessment of treatment response is difficult based on claims data, but patients would likely be eligible for transition to a parenteral antipsychotic if they are on

the same medication for ≥ 12 continuous weeks. Continuous therapy was defined as claims for the same drug (based on HICL sequence number [HSN]) for at least 12 weeks with a gap in therapy of no more than 2 weeks. If patients had claims for more than one antipsychotic and discontinued or started another antipsychotic drug (based on HSN) during this timeframe, patients were considered to be on non-optimal therapy and were excluded from this subgroup.

The number of patients prescribed at least 2 concomitant antipsychotics was evaluated in the 6 months following the index event. Utilization of concomitant antipsychotic therapy was defined as paid claims for at least 2 distinct drugs (based on HSN) with a duration of ≥ 8 weeks continuous treatment, ≥ 8 weeks of overlapping therapy, and no more than a 1 week gap in concomitant therapy.

Utilization of long-acting injectable antipsychotics in all patients with a diagnosis of schizophrenia was also evaluated. Claims were classified based on patient enrollment (either FFS or CCO) at the time of the pharmacy or medical claim for a long-acting injectable antipsychotic. A single member may have claims paid by multiple CCOs or FFS and a CCO if their enrollment status changed over the course of the assessment period.

Adherence to long-acting injectable formulations compared to oral formulations was assessed for all patients with a schizophrenia diagnosis. All adherence data was assessed in the 6 months following the index event. Days of coverage were defined according to **Table A3** for medical claims and defined based on days' supply submitted on pharmacy claims. If submitted days' supply for pharmacy claims of an injectable antipsychotic was less than 7 days, then **Table A3** was used to approximate days of coverage. In some cases (e.g., aripiprazole lauroxil or paliperidone palmitate) duration of coverage is dependent on the units given or dose administered. The proportion of days covered (PDC) may give an estimate of the number of patients who are adherent to their antipsychotic therapy. As defined here, short-term therapy over a period of 6 months would correspond to a PDC of up to 25% (≤45 days), intermittent therapy corresponds to PDC of 25-75%, and long-term therapy corresponds to a PDC of 75% or more (>135 days). The number of subsequent paid claims for injectable vs. oral antipsychotic therapy was also used as a measure of patient adherence.

Results:

In total, over 4,600 schizophrenia patients met inclusion criteria, and approximately 14% of patients were identified as treatment naïve without claims for antipsychotics in the year prior to the index event. Baseline characteristics for this population are shown in **Table 1**. Patients were most commonly adult males with a diagnosis of unspecified schizophrenia. Only a few patients had a history of schizophrenia diagnosis for more than one year and the majority of schizophrenia diagnoses were noted in the 6 month before or after the first claim for an antipsychotic. However, because diagnoses are based on medical claims, the patient's history of diagnoses may be incomplete, and Medicaid enrollment status may account for the limited number of patients with diagnoses prior to 1 year.

Table 1. Baseline demographics for schizophrenia patients

	All Schizophrenia		Treatment Naïve	
N=	**4,663**	**%**	**653**	**%**
Age				
Average (min - max)	40.5	(7-77)	34.4	(8-73)
<13	13	0.3%	2	0.3%
13-18	169	3.6%	50	7.7%
18-59	4,067	87.2%	575	88.1%
≥ 60	414	8.9%	26	4.0%

Female	1,784	38.3%	215	32.9%
White	3,008	64.5%	318	48.7%
Native American	269	5.8%	40	6.1%
Average time between first diagnosis and index event				
≥1 year	284	6.1%	34	5.2%
≥6 months	405	8.7%	30	4.6%
<6 months	3,974	85.2%	589	90.2%
Type of schizophrenia				
Paranoid (F20.0)	827	17.7%	93	14.2%
Disorganized (F20.1)	87	1.9%	17	2.6%
Catatonic (F20.2)	36	0.8%	13	2.0%
Undifferentiated (F20.3)	244	5.2%	37	5.7%
Residual (F20.5)	32	0.7%	2	0.3%
Other (F20.8)	366	7.8%	69	10.6%
Unspecified (F20.9)	3,071	65.9%	422	64.6%

Antipsychotic utilization by drug is shown in **Table 2** for all schizophrenia patients and treatment naïve patients. Approximately half of the patients defined as treatment naïve also had a remote history of antipsychotic use at least 1 year before their first antipsychotic claim. Because diagnoses are not available on prescriptions, it is unclear if patients with a remote history of antipsychotic use were prescribed these medications for schizophrenia or for other mental health conditions. Overall, there was no difference in prescribing patterns for patients with a remote history of antipsychotic use and those without prior antipsychotic use.

Oral second-generation antipsychotics which are recommended as first-line treatment in the MHCAG schizophrenia algorithm (aripiprazole, risperidone, or paliperidone) were prescribed as initial treatment in only 38% of treatment naïve patients. Approximately 4-6% of the treatment naive were initially prescribed parenteral antipsychotics and 6-7% were prescribed a first-generation antipsychotic. Parenteral antipsychotics may be initially prescribed for patients who transition from inpatient treatment. Of the second generation antipsychotics which are not recommended as first-line treatments, olanzapine and quetiapine were most commonly prescribed. Utilization of first generation antipsychotics, parenteral antipsychotics, and other second generation antipsychotics which are not recommended as first-line treatment were slightly more common in all patients with schizophrenia. Increased use of these medications in a broader population including treatment-experienced schizophrenia patients is not unexpected, as these treatments are more likely to be used for patients who have tried and failed other therapies.

Table 2. Antipsychotic utilization based on treatment regimen. Utilization presented for all patients, treatment naïve patients, and treatment naïve patients with remote history of antipsychotic use. Treatment naïve was defined as patients with no antipsychotic use in the 12 months before the index event. Remote antipsychotic use was defined as patients with a history of any antipsychotic use at >12 months before the index event.

	All Schizophrenia		**Treatment Naïve**			
			All treatment naïve		History of remote antipsychotic use	
Index Drug Event	**4,663**	**%**	**653**	**%**	**300**	**%**
1st generation antipsychotic	**514**	**11.0%**	**39**	**6.0%**	**22**	**7.3%**
2nd generation antipsychotic	**3,685**	**79.0%**	**585**	**89.6%**	**259**	**86.3%**
Recommended 1st line regimen	*1,307*	*28.0%*	*248*	*38.0%*	*101*	*33.7%*
aripiprazole	572	12.3%	119	18.2%	43	14.3%
paliperidone	153	3.3%	20	3.1%	7	2.3%
risperidone	582	12.5%	109	16.7%	51	17.0%
Other regimens	*2,378*	*51.0%*	*337*	*51.6%*	*158*	*52.7%*
asenapine	41	0.9%	5	0.8%	2	0.7%
clozapine	309	6.6%	8	1.2%	3	1.0%
olanzapine	967	20.7%	159	24.3%	73	24.3%
quetiapine	628	13.5%	117	17.9%	57	19.0%
IE dose =< 50 mg/day	76	1.6%	33	5.1%	18	6.0%
ziprasidone	177	3.8%	8	1.2%	6	2.0%
lurasidone	187	4.0%	25	3.8%	11	3.7%
brexpiprazole	29	0.6%	11	1.7%	4	1.3%
cariprazine	32	0.7%	2	0.3%	1	0.3%
iloperidone	7	0.2%	2	0.3%	1	0.3%
pimavanserin	1	0.0%	0	0.0%	0	0.0%
Parenteral antipsychotic	**464**	**10.0%**	**29**	**4.4%**	**19**	**6.3%**
Recommended regimens	*350*	*7.5%*	*11*	*1.7%*	*8*	*2.7%*
aripiprazole (all formulations)	89	1.9%	2	0.3%	0	0.0%
paliperidone palmitate	211	4.5%	9	1.4%	8	2.7%
risperidone (all formulations)	50	1.1%	0	0.0%	0	0.0%
Non-recommended regimens (all other parenteral)	*114*	*2.4%*	*18*	*2.8%*	*11*	*3.7%*

Current MCHAG algorithms for patients with schizophrenia recommend transition to an injectable antipsychotic if the patient has an adequate response after 2-4 weeks. Only 58 patients (9.3% of all treatment naïve patients) had a claim for a long-acting injectable antipsychotic within the 6 months following the index

event. Approximately, 25% of treatment naïve patients prescribed oral therapy (n=155) had claims for a single antipsychotic for at least 12 weeks and would likely be eligible to transition to a long-acting injectable antipsychotic. Similar trends were observed in all schizophrenia patients. Overall, only 8% of patients transition to a long-acting injectable antipsychotic within 6 months, but approximately 60% of patients have claims for continuous treatment for at least 12 weeks and may be eligible for LAI therapy. More patients who were prescribed a recommended first-line treatment option transitioned to a long-acting injectable antipsychotic in the 6 months following the index event (84% vs. 46% for all schizophrenia patients).

Table 3. Number and proportion of schizophrenia patients who switch to a parenteral or long-acting injectable (LAI) antipsychotic within 6 months after the index event (based on pharmacy and medical claims).

	Treatment Naïve				**All Schizophrenia**			
	Patients with LAI use		Patients without LAI use AND with ≥ 12 weeks of continuous therapy		Patients with LAI use		Patients without LAI use AND with ≥ 12 weeks of continuous therapy	
Index Drug Event	**58**		**155**		**342**		**2,512**	
1st generation antipsychotic	**2**	**3.4%**	**7**	**4.5%**	**56**	**16.4%**	**305**	**12.1%**
2nd generation antipsychotic	**56**	**96.6%**	**148**	**95.5%**	**286**	**83.6%**	**2,206**	**87.8%**
Recommended 1st line regimen	*31*	*53.4%*	*60*	*38.7%*	*129*	*37.7%*	*710*	*28.3%*
aripiprazole	11	19.0%	33	21.3%	50	14.6%	302	12.0%
paliperidone	7	12.1%	1	0.6%	33	9.6%	73	2.9%
risperidone	13	22.4%	26	16.8%	46	13.5%	335	13.3%
Other regimens	*25*	*43.1%*	*88*	*56.8%*	*157*	*45.9%*	*1,496*	*59.6%*
asenapine		0.0%	1	0.6%	2	0.6%	21	0.8%
clozapine		0.0%	4	2.6%	5	1.5%	287	11.4%
olanzapine	12	20.7%	34	21.9%	78	22.8%	552	22.0%
quetiapine	8	13.8%	33	21.3%	47	13.7%	359	14.3%
ziprasidone		0.0%	1	0.6%	8	2.3%	123	4.9%
lurasidone	4	6.9%	7	4.5%	11	3.2%	114	4.5%
brexpiprazole	1	1.7%	5	3.2%	3	0.9%	12	0.5%
cariprazine		0.0%	1	0.6%	2	0.6%	22	0.9%
iloperidone		0.0%	2	1.3%	1	0.3%	6	0.2%
pimavanserin		0.0%		0.0%		0.0%	1	0.0%

Overall, 795 schizophrenia patients (17% of the entire population) had claims for 2 or more concomitant antipsychotic medications in the 6 months following the index event**.** Of the patients with dual antipsychotic therapy, few patients (10%) had claims for more than 2 antipsychotics at a time and dual antipsychotic use was infrequent in treatment naïve patients. The most commonly prescribed combinations of antipsychotic medications are listed in **Table 4** and commonly included olanzapine, quetiapine, aripiprazole, and risperidone.

Table 4. Concomitant antipsychotic therapy in patients with ≥ 2 antipsychotic medications (duration of overlap ≥ 8 weeks) in the 6 months after the index event.

			All Schizophrenia		Treatment Naïve	
N=			**795**	**%**	**24**	**%**
Duration of overlap						
8-12 weeks			295	37.1%	13	54.2%
13-24 weeks			350	44.0%	9	37.5%
>24 weeks			264	33.2%	3	12.5%
Number of drugs						
2			719	90.4%	24	100.0%
3			71	8.9%	0	0.0%
4			4	0.5%	0	0.0%
5			1	0.1%	0	0.0%
Most commonly prescribed concomitant antipsychotics						
1	risperidone	quetiapine fumarate	45	5.7%	1	4.2%
2	haloperidol	olanzapine	43	5.4%	3	12.5%
3	aripiprazole	quetiapine fumarate	40	5.0%	2	8.3%
4	aripiprazole	olanzapine	36	4.5%	2	8.3%
5	risperidone	olanzapine	31	3.9%	1	4.2%
6	clozapine	haloperidol	30	3.8%	1	4.2%
7	olanzapine	quetiapine fumarate	28	3.5%		0.0%
8	paliperidone palmitate	olanzapine	25	3.1%	1	4.2%
9	clozapine	olanzapine	24	3.0%		0.0%
10	risperidone	aripiprazole	23	2.9%	1	4.2%
11	paliperidone	olanzapine	21	2.6%	2	8.3%
12	clozapine	aripiprazole	20	2.5%		0.0%
13	aripiprazole	haloperidol	20	2.5%		0.0%
14	perphenazine	olanzapine	18	2.3%	2	8.3%
15	olanzapine	lurasidone HCl	17	2.1%		0.0%
16	clozapine	risperidone	17	2.1%	1	4.2%
17	paliperidone palmitate	quetiapine fumarate	16	2.0%		0.0%
18	paliperidone	quetiapine fumarate	16	2.0%	1	4.2%
19	haloperidol	quetiapine fumarate	16	2.0%		0.0%
20	clozapine	quetiapine fumarate	15	1.9%	1	4.2%

Table 5 describes how claims for injectable antipsychotics are billed for FFS and CCO members. Mental health medications, including antipsychotics, are carved out of the CCO budget and paid for by FFS when they are billed as a pharmacy claim. However, these medications are administered by providers and may be billed by as provider administered medical claims. Any medical claims for injectable antipsychotics administered to members enrolled in a CCO are billed to the

CCO. As a result, the vast majority of claims for CCO members are billed through pharmacy whereas approximately 72% of FFS claims are billed by providers after administration rather than through a pharmacy.

Table 5. Evaluation of long-acting injectable antipsychotic use by billing method (pharmacy vs. medical claims) in all schizophrenia patients. Claims are categorized based on CCO or FFS member enrollment at the time of the claim.

	Pharmacy claims		Medical claims		Total paid claims
	#	%	#	%	#
FFS enrollment	11	27.5%	29	72.5%	40
CCO enrollment	221	98.7%	3	1.3%	224
HEALTH SHARE OF OREGON	62	100.0%		0.0%	62
EASTERN OREGON CCO, LLC	41	100.0%		0.0%	41
WILLAMETTE VALLEY COMM. HEALTH	34	100.0%		0.0%	34
TRILLIUM COMMUNITY HEALTH PLAN	30	100.0%		0.0%	30
PACIFICSOURCE COMMUNITY SOL INC	11	100.0%		0.0%	11
ALLCARE CCO, INC.	9	100.0%		0.0%	9
COLUMBIA PACIFIC CCO LLC	8	80.0%	2	20.0%	10
FAMILYCARE, CCO	5	100.0%		0.0%	5
JACKSON CARE CONNECT	5	100.0%		0.0%	5
CAPITOL DENTAL CARE INC	4	100.0%		0.0%	4
INTERCOMMUNITY HEALTH NETWORK	4	100.0%		0.0%	4
ADVANTAGE DENTAL	3	75.0%	1	25.0%	4
PRIMARYHEALTH JOSEPHINE CO CCO	2	100.0%		0.0%	2
UMPQUA HEALTH ALLIANCE, DCIPA	2	100.0%		0.0%	2
OREGON DENTAL SERVICES	1	100.0%		0.0%	1

Adherence was evaluated for all schizophrenia patients using the proportion of covered days in the 6 months following the index event for patients prescribed oral or injectable therapy (**Table 6**). Overall there were no large differences in days of coverage for patients prescribed injectable versus oral therapy or in the numbers of subsequent prescriptions filled in the 6 months after the first claim (**Table 6**). In the 6 months following the first claims, approximately 9-11% of patients had less than 25% of days covered (corresponding to less than 45 days) and 62-64% of patient had more than 75% of days covered (corresponding to >135 days). Because covered days may be inaccurate, particularly for injectable claims, the number of subsequent filled claims was also evaluated for each patient. Overall, results were similar to the proportion of covered days, assuming the majority of patients received claims for 30 days' supply. Approximately 8% of patients in each group never receive another prescription for an antipsychotic and 55-65% of patients had at least 5 claims paid over 6 months.

A significant proportion of patients (46%) who were on injectable antipsychotics, transition back to oral therapy and only 8% of patients initially prescribed oral therapy had a subsequent claim for a long-acting injectable antipsychotic. There are multiple reasons patients may transition between therapies. For example, if patients are late receiving a routine antipsychotic injection they may briefly need oral therapy until they achieve therapeutic levels with an injectable formulation.

Table 6. Adherence information for patients with injectable or oral therapy in the 6 months following the Index Event (IE) for all schizophrenia patients.

	Patients with IE for a long-acting injectable antipsychotic		Patients with IE for oral therapy	
N=	**464**	**%**	**4,199**	**%**
Days of coverage				
<= 30 days	31	6.7%	384	9.1%
31-90 days	53	11.4%	664	15.8%
91-180 days	294	63.4%	2,349	55.9%
>= 181 days	86	18.5%	802	19.1%
Proportion of days covered				
<=25%	41	8.8%	482	11.5%
26-75%	122	26.3%	1,096	26.1%
>75%	301	64.9%	2,621	62.4%
Number of paid claims with the same route of administration (oral vs. injectable)				
0 (only the IE)	39	8.4%	343	8.2%
1-4	168	36.2%	1121	26.7%
5-6	169	36.4%	1150	27.4%
>6	88	19.0%	1585	37.8%
Number of patients with claims for the alternative route of administration (oral or injectable)				
	212	45.7%	342	8.1%

The most common prescribers of antipsychotics in schizophrenia patients are shown in **Table 7**. Physician and nurse practitioner psychiatric and mental health specialists account for the majority of prescribing in both treatment naïve patients and the general schizophrenia population (55% for treatment naïve and 66% for all schizophrenia patients). Family physicians and nurse practitioners prescribe antipsychotic medications in approximately 13% of patients with schizophrenia.

Table 7. Prescribing rates stratified by primary provider taxonomy for the top 20 providers prescribing antipsychotics to schizophrenia patients

		All Schizophrenia		Treatment Naïve	
	N=	4,663		653	
1	PHYSICIAN-PSYCHIATRY&NEUROLOGY-PSYCHIATRY	1,594	34.2%	217	33.2%
2	NURSE PRACTITIONER - PSYCHIATRIC/MENTAL HEALTH	1,510	32.4%	144	22.1%
3	PHYSICIAN-FAMILY MEDICINE	340	7.3%	61	9.3%
4	NURSE PRACTITIONER - FAMILY	305	6.5%	49	7.5%
5	PHYSICIAN-INTERNAL MEDICINE	140	3.0%	25	3.8%
6	PHYSICIAN ASSISTANT	118	2.5%	18	2.8%
7	PHYSICIAN-PSYCHIATRY&NEUROLGY-CHILD&ADOLESCENT PSYCHIATRY	98	2.1%	21	3.2%
8	PHYSICIAN ASSISTANT - MEDICAL	96	2.1%	15	2.3%
9	PHYSICIAN-EMERGENCY MEDICINE	60	1.3%	23	3.5%
10	REGISTERED NURSE - PSYCHIATRIC/MENTAL HEALTH	56	1.2%	4	0.6%
11	PHYSICIAN-PSYCHIATRY&NEUROLGY-GERIATRIC PSYCHIATRY	41	0.9%	4	0.6%
12	CLINICAL NURSE SPECIALIST - PSYCHIATRIC/MENTAL HEALTH	40	0.9%	4	0.6%
13	STUDENT IN AN ORGANIZED HEALTH CARE EDUCATION/TRAINING PROGRAM	33	0.7%	8	1.2%
14	NURSE PRACTITIONER	31	0.7%	7	1.1%
15	PHYSICIAN-HOSPITALIST	20	0.4%	9	1.4%
16	HOSPITALS: GENERAL ACUTE CARE HOSPITAL	19	0.4%	12	1.8%
17	NATUROPATH	16	0.3%	3	0.5%
18	PHYSICIAN-GENERAL PRACTICE	16	0.3%	0	0.0%
19	BEHAVIORAL NEUROLOGY & NEUROPSYCHIATRY	15	0.3%	3	0.5%
20	PHYSICIAN-PSYCHIATRY&NEUROLOGY-NEUROLOGY	14	0.3%	6	0.9%

Discussion and Limitations:

Data presented in this report is based on Medicaid claims history and has several inherent limitations. For example, we depend on providers to submit accurate diagnostic information for their patients, though it may not be accurate in all circumstances and it is likely that delays in billing for medical claims resulted in some patients who have schizophrenia being excluded from this analysis since they did not have a recent schizophrenia diagnosis based on medical claims. Similarly, information on provider specialty may be inaccurate, out-of-date, or incomplete for some providers, and prescribers with multiple specialties or designations may not be identified. In addition, use of proportion of days covered attempts to estimate the frequency which a patient takes a prescription, but accuracy of this method has not been validated and patients may not always be categorized appropriately. We rely on pharmacies to submit accurate duration of therapy, but duration is likely to vary (especially for injectable medications) making estimates of PDC less reliable. Medical claims are not submitted with a days' supply and while attempts were made to estimate the duration of coverage for medical claims based on standard dosing regimens, these estimates may not reflect the true duration of coverage.

In the Oregon Health Plan, antipsychotic medications are primarily carved-out of CCOs and are paid for by FFS. However, billing mechanisms should be taken into account for any educational initiatives or proposed projects. For patients enrolled in a CCO, injectable antipsychotics are primarily only covered through the pharmacy and paid for by FFS. Comparatively, for FFS patients, injectable antipsychotics can be billed as either a pharmacy or medical claim if the injectable antipsychotics is bought by and administered in a provider's office. When physician administered medications (i.e., long-acting injectable antipsychotics) are

billed through the pharmacy rather than a medical facility, there are several factors to consider. First, paying for injectable antipsychotics through the pharmacy may be associated with a significant amount of waste if the drug is never administered to the patient. Medical claims may only be billed after administered to the patient, and in this circumstance, we are certain the patient actually received the drug. When injectable antipsychotics are billed as a pharmacy claim, in some circumstances, they may never be administered to the patient if, for example, the patient misses their appointment with their provider.

When claims were evaluated for administration of an intramuscular or subcutaneous injection following a paid pharmacy claim for an injectable antipsychotic, there were no patients who had claims associated with medication administration. There could be several possible explanations for this:

1) Providers are not billing for costs associated with administering the antipsychotic
2) Providers are not billing *correctly* for costs associated with administration of the antipsychotic
3) There is no easy way to distinguish administration of medication from other medical claims
4) There is a significant time difference between a paid antipsychotic pharmacy claim and patient administration (> 3 weeks)
5) Patients are not being administered the long-acting injectable antipsychotic even though it was paid for by Medicaid

In the Oregon Health Plan (OHP), antipsychotic medications are exempt from traditional preferred drug list (PDL) and PA requirements. While OHP uses a voluntary preferred drug list, non-preferred medications do not currently stop for prior authorization. However, clinical PA criteria which address safety concerns or medically inappropriate use may be implemented. Historical initiatives for mental health medications have focused on provider education surrounding monitoring recommendations for antipsychotics and dose consolidation initiatives. For example, a target population of patients is identified and faxes are sent to providers which include a summary of the initiative and request for a voluntary change to the less expensive agent or consolidated dose. Depending on the initiative, initiatives have had limited success in changing prescriber behavior. The following are a few examples of provider educational opportunities and retrospective drug use review initiatives which may be worth considering to increase awareness of MHCAG recommendations for patients with schizophrenia:

1) Broad educational initiative (e.g., newsletter) on MHCAG schizophrenia recommendations
2) Targeted intervention identifying patients who are non-adherent to current therapy or patients with a history of previous emergency room admissions or hospitalizations. Notify these prescribers of the MHCAG algorithm for schizophrenia and request they consider trial of a preferred product or long-acting injectable.
3) Targeted intervention identifying treatment naïve schizophrenia patients and patients with no recent use of recommended regimens for schizophrenia (paliperidone, risperidone, or aripiprazole). Notify these prescribers of the MHCAG algorithm for schizophrenia and request they consider trial of a product recommended by the OHA and MHCAG.
4) Targeted intervention identifying patients on combination antipsychotic treatment and provide education to these prescribers on the MHCAG algorithm and resources available in Oregon for additional provider consultation services.
5) Explore opportunities to increase access to injectable antipsychotic medication in provider offices through replenishment models.

Low Dose Quetiapine

Goal(s):

- To promote and ensure use of quetiapine that is supported by the medical literature.
- To discourage off-label use for insomnia.
- Promote the use of non-pharmacologic alternatives for chronic insomnia.

Initiative:

- Low dose quetiapine (Seroquel® and Seroquel XR®)

Length of Authorization:

- Up to 12 months (criteria-specific)

Requires PA:

- Quetiapine (HSN = 14015) doses ≤50 mg/day
- Auto PA approvals for :
    - Patients with a claim for a second generation antipsychotic in the last 6 months
    - Patients with prior claims evidence of schizophrenia or bipolar disorder
    - Prescriptions identified as being written by a mental health provider

Covered Alternatives:

- Preferred alternatives listed at www.orpdl.org/drugs/
- Zolpidem is available for short-term use (15 doses/30 days) without PA.

Table 1. Adult (age ≥18 years) FDA-approved Indications for Quetiapine

Bipolar Disorder	F3010; F302; F3160-F3164; F3177-3178; F319	
Major Depressive Disorder	F314-315; F322-323; F329; F332-333; F339	Adjunctive therapy with antidepressants for Major Depressive Disorder
Schizophrenia	F205; F209; F2081; F2089	
Bipolar Mania	F3010; F339; F3110-F3113; F312	
Bipolar Depression	F3130	

Table 2. Pediatric FDA-approved indications

Schizophrenia	Adolescents (13-17 years)	
Bipolar Mania	Children and Adolescents (10 to 17 years)	Monotherapy

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code. Do not proceed and deny if diagnosis is not listed in Table 1 or Table 2 above (medical appropriateness)	
2. Is the prescription for quetiapine less than or equal to 50 mg/day? (verify days' supply is accurate)	**Yes**: Go to #3	**No:** Trouble-shoot claim processing with the pharmacy.
3. Is planned duration of therapy longer than 90 days?	**Yes:** Go to #4	**No:** Approve for titration up to maintenance dose (60 days).
4. Is reason for dose ≤50 mg/day due to any of the following: • low dose needed due to debilitation from a medical condition or age; • unable to tolerate higher doses; • stable on current dose; or • impaired drug clearance? • any diagnosis in table 1 or 2 above?	**Yes:** Approve for up to 12 months	**No:** Pass to RPh. Deny for medical appropriateness. Note: may approve up to 6 months to allow taper.

P&T/DUR Review: *3/19 (DM); 9/18; 11/17; 9/15; 9/10; 5/10*
Implementation: *1/1/18; 10/15; 1/1/11*

Pimavanserin (Nuplazid™) Safety Edit

Goals:

- Promote safe use of pimavanserin in patients with psychosis associated with Parkinson's disease.

Length of Authorization:

- Up to 6 months

Requires PA:

- Pimavanserin

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
5. What diagnosis is being treated?	Record ICD10 code	
6. Is the treatment for hallucinations and/or delusions associated with Parkinson's disease?	**Yes:** Go to #3	**No:** Pass to RPh. Deny; medical appropriateness
7. Are the symptoms likely related to a change in the patient's anti-Parkinson's medication regimen?	**Yes:** Go to #4 Consider slowly withdrawing medication which may have triggered psychosis.	**No:** Go to #5
8. Has withdrawal or reduction of the triggering medication resolved symptoms?	**Yes:** Pass to RPh; Deny; medical appropriateness	**No:** Go to #5
9. Is the patient on a concomitant first- or second-generation antipsychotic drug?	**Yes:** Pass to RPh; Deny; medical appropriateness	**No:** Go to #6
10. Has the patient been recently evaluated for a prolonged QTc interval?	**Yes:** Approve for up to 6 months	**No:** Pass to RPh; Deny; medical appropriateness

Appendix 2. Coding Information

Table A1. Drug codes

Class	HSN	Generic
Antipsychotics, 2nd Gen	024551	aripiprazole
Antipsychotics, 2nd Gen	036576	asenapine maleate
Antipsychotics, 2nd Gen	042283	brexpiprazole
Antipsychotics, 2nd Gen	042552	cariprazine HCl
Antipsychotics, 2nd Gen	004834	clozapine
Antipsychotics, 2nd Gen	037321	lurasidone HCl
Antipsychotics, 2nd Gen	011814	olanzapine
Antipsychotics, 2nd Gen	034343	paliperidone
Antipsychotics, 2nd Gen	043373	pimavanserin tartrate
Antipsychotics, 2nd Gen	014015	quetiapine fumarate
Antipsychotics, 2nd Gen	008721	risperidone
Antipsychotics, 2nd Gen	021974	ziprasidone HCl
Antipsychotics, Parenteral	024551	aripiprazole
Antipsychotics, Parenteral	042595	aripiprazole lauroxil
Antipsychotics, Parenteral	045050	aripiprazole lauroxil,submicr.
Antipsychotics, Parenteral	001621	chlorpromazine HCl
Antipsychotics, Parenteral	001624	fluphenazine decanoate
Antipsychotics, Parenteral	001626	fluphenazine HCl
Antipsychotics, Parenteral	001660	haloperidol decanoate
Antipsychotics, Parenteral	001661	haloperidol lactate
Antipsychotics, Parenteral	011814	olanzapine
Antipsychotics, Parenteral	036716	olanzapine pamoate
Antipsychotics, Parenteral	036479	paliperidone palmitate
Antipsychotics, Parenteral	008721	risperidone
Antipsychotics, Parenteral	025509	risperidone microspheres
Antipsychotics, Parenteral	001630	trifluoperazine HCl
Antipsychotics, Parenteral	023379	ziprasidone mesylate
Antipsychotics, 1st Gen	001621	chlorpromazine HCl
Antipsychotics, 1st Gen	001626	fluphenazine HCl
Antipsychotics, 1st Gen	001627	perphenazine
Antipsychotics, 1st Gen	001630	trifluoperazine HCl
Antipsychotics, 1st Gen	001631	thioridazine HCl
Antipsychotics, 1st Gen	001661	haloperidol lactate

Antipsychotics, 1st Gen	001662	haloperidol
Antipsychotics, 1st Gen	001667	thiothixene HCl
Antipsychotics, 1st Gen	001668	thiothixene
Antipsychotics, 1st Gen	001637	pimozide
Antipsychotics, 1st Gen	001664	loxapine succinate
Antipsychotics, 1st Gen	039886	loxapine

Table A2. Administration Codes for Long-acting Injectables

Code	Short Description	Long Description
G0351	Therapeutic/Diagnostic Injec	Therapeutic Or Diagnostic Injection (Specify Substance Or Drug); Subcutaneous Or Intramuscular
T1502	Medication Admin Visit	Administration of oral, intramuscular and/or subcutaneous medication by health care agency/professional, per visit
90772	Ther/proph/diag inj, sc/im	Therapeutic, prophylactic or diagnostic injection (specify substance or drug); subcutaneous or intramuscular

Table A3. Days of coverage associated with injectable antipsychotic prescriptions

Procedure Code	Generic Drug Name	Long Procedure Description	Days of coverage
C9035	aripiprazole lauroxil,submicr.	Injection, Aripiprazole Lauroxil (Aristada Initio), 1 Mg	10 days
C9037	risperidone	Injection, Risperidone (Perseris), 0.5 Mg	28 days
C9470 J1942	aripiprazole lauroxil aripiprazole lauroxil,submicr.	Injection, Aripiprazole Lauroxil, 1 Mg	28 days (<700 mg or units) 42 days (700-900 mg or units) 56 days (>900 mg or units)
J0400	aripiprazole	Injection, Aripiprazole, Intramuscular, 0.25 Mg	28 days
J0401	aripiprazole	Injection, Aripiprazole, Extended Release, 1 Mg	28 days
J1630	haloperidol lactate	Injection, Haloperidol, Up To 5 Mg	1 day (acute use)
J1631	haloperidol decanoate	Injection, Haloperidol Decanoate, Per 50 Mg	28 days
J2358	olanzapine pamoate	Injection, Olanzapine, Long-Acting, 1 Mg	28 days
J2426	paliperidone palmitate	Injection, Paliperidone Palmitate Extended Release, 1 Mg	28 days (<250 mg or units) 84 days (>=250 mg or units)
J2680	fluphenazine decanoate	Injection, Fluphenazine Decanoate, Up To 25 Mg	28 days
J2794	risperidone microspheres	Injection, Risperidone, Long Acting, 0.5 Mg	14 days
J3230	chlorpromazine HCl	Injection, Chlorpromazine Hcl, Up To 50 Mg	1 day (daily injection)
J3486	ziprasidone mesylate	Injection, Ziprasidone Mesylate, 10 Mg	1 day (acute use)
S0166	olanzapine	Injection, Olanzapine, 2.5 Mg	28 days