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Drug Use Evaluation: Low Dose Quetiapine

Research Questions:

- Does the current safety edit appropriately prevent prescribing in at risk populations (very old or very young) for off-label uses?

Conclusions:

- The majority of low-dose quetiapine claims (85%, n=3482) were for adult patients 18-59 years of age. There were 324 patients (7.9%) with claims for low-dose quetiapine who were less than 18 years of age and 292 patients (7.1%) over 60 years of age with low-dose quetiapine claims.
- Eighty-five percent of patients who met criteria for the safety edit had a paid claim for low-dose quetiapine within 90 days. Fifteen percent of patients (n=621) had an initial denied claim without subsequent follow-up.
- The majority of patients without a paid low-dose quetiapine claim had denied claims with a daily dose less than 50 mg (68%) or did not have an FDA-indicated diagnosis (65%).

Recommendations:

- Recommend modification of safety edit to apply to only patients with a daily dose less than or equal to 50 mg (see **Appendix 1**).

Background:

Quetiapine is a second generation antipsychotic which is been approved by the Food and Drug Administration (FDA) for bipolar disorder, schizophrenia and as adjunct treatment for depression.[1] Doses for these conditions typically range from 300 mg to 800 mg daily. Low-dose quetiapine (<150 mg) may be used off-label for a variety of conditions including insomnia, anxiety, obsessive compulsive disorder and dementia.[1] However, quetiapine has been associated with significant safety concerns including increased mortality in elderly patients with dementia-related psychosis and suicidal thoughts and behaviors in children and adolescents.[1]

A drug use evaluation in 2010 demonstrated that a significant proportion of the Oregon Health Plan (OHP) population (~56%) had claims for low-dose quetiapine without an FDA approved diagnosis.[2] In January 2011, a safety edit for any claims less than 150 mg was implemented to discourage off-label use.[2] Patients with diagnoses of schizophrenia, bipolar disorder, history for use for a second generation antipsychotic, or prescriptions written by a mental health specialist could be automatically approved. In the past few years, the majority of requests submitted for low-dose quetiapine have been subsequently approved. This brief drug use evaluation reassesses need for the low-dose quetiapine safety edit and explores how criteria can be modified to more appropriately target at risk populations.

Methods:

The patient population included current Medicaid patients with a fee for service (FFS) claim for quetiapine in one year period from 7/1/2016 to 06/30/2017. The index event was defined as the first paid or denied claim for quetiapine in the reporting period prescribed at a daily dose of 150 mg or less. Patients were stratified by age, quetiapine dose, and diagnosis. Patients with diagnoses for schizophrenia, bipolar disorders, and major depressive disorder within the last year

were identified based on ICD-10 diagnosis codes (**Appendix 2**). Denied claim were defined as claims with Explanation of Benefit (EOB) codes of 1056 "PA required", 4506 "non-preferred drug", 0030 "Quantity per day limit exceeded" or 0148 "Quantity dispensed exceed max allowed" without any of the following EOB codes: 0154 "Bill part D plan", 1109 "drug covered by Medicare Part D", 0003 "recipient not eligible", 91 "non-covered service", 1048 "prescribing provider not on file. Patients with claims for concurrent antidepressants, mood stabilizers (lithium or divalproex), or history of claims for other second generation antipsychotics were also identified. Patients were excluded if they had Medicare part D coverage or had Medicaid eligibility for less than 75% of time in the year prior to the index event.

Results:

Results for patients with paid and denied claims are reported in **Table 1**. Over the course of the year, approximately 4100 patients had claims for low-dose quetiapine. The majority of these claims (85%, n=3482) were for patients 18-59 years of age. Eighty-five percent of patients who met criteria for the safety edit had a paid claim within 90 days. Only 1 patient had a request which was submitted and denied, but 15% of patients (n=621) had an initial denied claim without subsequent follow-up. Of these patients without follow-up, the majority were for a daily dose of 50 mg or less (68% of patients) or for patients without an FDA indicated diagnosis (65% of patients). Because data are based on a retrospective analysis of claims history, diagnoses may not accurately reflect true patient diagnoses or correlate with actual medication adherence. Of the patients with no subsequent claim within 90 days, 45 patients (7%) had other insurance on file, which may explain the lack of follow-up for these particular patients.

	Claim initially paid OR paid within 1 day of denial		**Claim paid within 2-30 days of the initial denial**		**Claim paid within 31-90 days of the initial denial**		**Request submitted and denied**		**No request submitted AND no paid claim within 90 days of the initial denial***		**Total**
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**	**%**	**N**
Total	**2,777**	**68%**	**548**	**13%**	**151**	**4%**	**1**	**0%**	**621**	**15%**	**4,098**
Age											
0-9	31	70%	5	11%	3	7%			5	11%	44
10-17	207	74%	35	13%	11	4%			27	10%	280
18-59	2,344	67%	475	14%	135	4%	1	0%	527	15%	3,482
≥60	195	67%	33	11%	2	1%			62	21%	292
Dose											
≤50 mg/day	971	54%	322	18%	82	5%			**422**	**23%**	1,797
51-100 mg/day	1,056	73%	158	11%	52	4%	1	0%	171	12%	1,438
101-150 mg/day	750	87%	68	8%	17	2%			28	3%	863
Diagnoses											
Schizophrenia	189	88%	13	6%	4	2%			9	4%	215
Bipolar Disorder	830	79%	111	11%	30	3%			84	8%	1,055
MDD diagnoses AND a claim for an antidepressant within 45 days before the index event	993	73%	192	14%	52	4%			130	10%	1,367
Pts with a claim for lithium or divalproex (HSNs 001669, 001670, or 001884) within 45 days before the index event	302	78%	47	12%	10	3%			29	7%	388
Pts with a claim for a second generation antipsychotic the 6 months prior to the index event	2,702	99%	18	1%	4	0%			7	0%	2,731

None of the above	37	5%	240	32%	69	9%	1	0%	**403**	**54%**	750

*Patients are only included in this category if they had continuous enrollment 90 days post index event.

Table 1. Status for patients with an index event in the last year. Diagnoses are not mutually exclusive.

References:

1. Micromedex Healthcare Series [internet database]. Greenwood Village, CO: Truven Health Analytics, Inc. Updated periodically. Accessed October 23, 2017.
2. Meeker A. Oregon Medicaid FFS Drug Class List. Policy Evaluation: Low Dose Quetiapine Safety Edit. September 2015; http://www.orpdl.org/durm/meetings/meetingdocs/2015_09_24/archives/2015_09_24_LowDoseQuetiapinePolicyEvaluationARCHIVED.pdf. Accessed October 23, 2017.

Appendix 1. Proposed Safety Edit

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; F3130	For Seroquel XR® only, 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: *11/17 (SS); 9/15; 9/10; 5/10*

Implementation: *1/1/18; 10/15; 1/1/11*

Appendix 2. Quetiapine GSN codes and diagnosis codes

GSN	Generic
034187	QUETIAPINE FUMARATE
034188	QUETIAPINE FUMARATE
034189	QUETIAPINE FUMARATE
047198	QUETIAPINE FUMARATE
060292	QUETIAPINE FUMARATE
060293	QUETIAPINE FUMARATE
062748	QUETIAPINE FUMARATE
062749	QUETIAPINE FUMARATE
062750	QUETIAPINE FUMARATE

063240	QUETIAPINE FUMARATE
064725	QUETIAPINE FUMARATE
074076	QUETIAPINE FUMARATE

Condition	ICD-10 Diagnosis Code
Schizophrenia	F205; F209; F2081; F2089
Bipolar Disorders	F3010; F302; F3160-F3164; F3177-3178; F319; F3110-F3113; F312; F3130
MDD	F314-315; F322-323; F329; F332-333; F339