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Abbreviated Policy Evaluation: Zuranolone for Post-Partum Depression

Plain Language Summary:

- Zuranolone is a medicine approved by the Food and Drug Administration (FDA) to treat post-partum depression (mood changes that occur 4 weeks or less after having a baby).
- Zuranolone helps improve symptoms in people with severe depression who have recently given birth. Zuranolone does not improve symptoms for other types of depression.
- A full treatment course of zuranolone is 14 days.
- An evaluation of Oregon Medicaid claims data shows that zuranolone is being used for post-partum depression.
- We recommend removal of the safety edit for zuranolone unless it is prescribed for longer than 14 days.

Research Questions:

- What proportion of members have approved prior authorization (PA) requests for zuranolone?
- What are common denial reasons for zuranolone?

Conclusions:

- Utilization of zuranolone has increased since implementation of the safety edit on 1/1/2024 from 16 members in 2024, to 28 members in 2025, and 21 members in the first half of 2026.
- Current utilization data do not show substantial off-label prescribing. Most members had approved PAs (91%) and initial paid claims (87%). Four PA requests (5%) were denied because there was no documentation of moderate to severe depression symptoms. Three PA requests were denied for off-label durations, ages, or indications.

Recommendations:

- Update PA criteria to remove disease severity and age assessments. The current quantity limit of 14 days per year will remain.
- Evaluate costs in executive session.

Background:

Zuranolone is approved by the FDA for treatment of postpartum depression (PPD) in adults.[1] Zuranolone is the only drug currently approved by the FDA specifically for post-partum depression. Other oral antidepressants are indicated for major depressive disorder and are commonly used off-label for post-partum depression. Zuranolone is dosed once daily for 14 days, and efficacy or safety beyond a single treatment course has not been established.[1] Zuranolone can be used as monotherapy or as an adjunct to oral antidepressant treatment.[1]

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Evidence for zuranolone was initially reviewed by the Pharmacy and Therapeutics Committee in December 2023 and last reviewed in February 2026.[2,3] In two phase 3 trials, patients treated with zuranolone had an average reduction in the 17-point Hamilton Depression Rating Scale (HAM-D-17) of 4.0 (95% confidence interval [CI] -6.3, -1.7) and 4.2 (95% CI -6.9, -1.5) points more than placebo in patients with severe PPD (baseline HAM-D ≥26) lasting longer than 15 days, which was both statistically and clinically significant.[1] Response to the 14-day course of therapy was maintained through 45 days.[4] The HAM-D-17 is a clinician-rated, 17-item scale to assess symptoms (range 0 to 52) with higher scores indicating more severe depression.[4] The HAM-D is a validated tool in the study of depressive symptoms but may be associated with a higher representation of evaluation of somatic symptoms (e.g., insomnia and somatic anxiety) compared to other tools.[4] Remission is typically defined as a person free from depressive symptoms for several months after two or more depressive episodes.[5] A 50% improvement in symptom score from baseline is typically used to evaluate response to therapy.[5] Minimum clinically significant differences referenced in the literature for HAM-D generally range between 2 to 10 points.[6,7] Zuranolone has also been evaluated for treatment of major depressive disorder in several large phase 2 and 3 trials.[8-13] In 2023, the FDA declined to approve zuranolone for treatment of major depressive disorder because there was not substantial evidence of effectiveness for this population.

The most common adverse events associated with zuranolone were somnolence, dizziness, diarrhea, fatigue, nasopharyngitis, and urinary tract infections.[1] Zuranolone contains a box warning related to impaired ability to drive, and has additional warnings for central nervous system depressant effects, suicidal thoughts and behavior, and embryo-fetal toxicity.[1] Driving is not recommended for at least 12 hours after administration. Patients may not be able to assess their own driving competency or the degree of impairment caused by zuranolone.[1]

Zuranolone is currently designated as voluntary non-preferred on the "Open Card" or fee-for-service (FFS) preferred drug list (PDL) with a PA safety edit to ensure it is used in populations with established safety and efficacy data. The goal of this analysis is to evaluate utilization of zuranolone in the FFS Medicaid program and evaluate ongoing need for the current zuranolone PA safety edit.

Policy Evaluation Methods:
This review evaluated paid and denied FFS pharmacy claims and PA requests for zuranolone submitted after implementation of the safety edit from 1/1/24 to 6/30/26. Members were categorized according to the first paid or denied claim in the reporting period (defined as the index event). Denied claims were included if they had an error code indicating PA was required (errors 3000 and 3002) and were not associated with any codes indicating errors in billing (**Appendix 1; Table A1**). If members had paid and denied claims on the same day, the index event was classified as paid.

All PA requests for zuranolone submitted from 1/1/24 to 6/30/26 were identified. Requests were categorized as either approved or denied, and denied requests were manually reviewed to identify the reason for denial.

Policy Evaluation Results:
Since implementation of the PA safety edit on 1/1/2024, utilization of zuranolone has increased. There were 28 members with paid or denied claims in 2025 and 21 members with paid or denied claims from 1/1/26 to 6/30/26. In 2025 and the first half of 2026, most members (n=43, 88%) had initial paid claims for zuranolone, and most PA requests were approved (n=62, 91%). Eight percent of PA requests (n=7) were denied. Three PA requests were for off-label ages, indications, or doses. Four PA requests (5%) were denied because there was no documentation of moderate to severe depression symptoms.

The total number of approved PA requests for zuranolone was larger than the number of members with paid claims. This analysis did not specifically evaluate members who had approved PAs but no claims paid by Medicaid, and the potential reasons for this discrepancy are unknown. This analysis did not exclude members with other primary insurance or members who lost eligibility in the reporting period so there may be claims that were not billed to Medicaid.

Table 1. Members with initial paid or denied FFS claims for zuranolone by year.

	Member Count by Year		
Initial Claim Type	2024	2025	2026
Paid	6	23	20
Denied	10	5	1
Total	16	28	21

Table 2 Members with approved and denied PA requests. Members with more than one PA request will be counted more than once.

	PA Count by Year		
	2024	**2025**	**2026**
Approved PA	13	30	32
Denied PA		5	2
Severity criteria not met (mild depression symptoms or no documentation of severity)		2	2
Off-label duration (>14 days)		1	
Off-label age (<18 years)		1	
Off-label diagnosis (not post-partum depression)		1	
Total	13	35	34

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Appendix 1: Coding

Table A1. Error codes associated with denied claims

Error Status Code	Error Status Description	Criteria
5001	EXACT DUPLICATE	Exclude
4891	Not covered drug class	Exclude
4890	Non covered drug class	Exclude
4025	AGE IS NOT ALLOWED FOR NDC	Exclude
4002	Non-Covered Drug	Exclude
2508	RECIPIENT COVERED BY PRIVATE INSURANCE (PHARMACY)	Exclude
2507	RECIPIENT HAS MORE THAN ONE INSURANCE CARRIER	Exclude
2017	RECIPIENT SERVICES COVERED BY HMO PLAN	Exclude
2002	RECIPIENT NOT ELIGIBLE FOR HEADER DATE OF SERVICE	Exclude
628	Other Coverage Reject Code Required for OCC 3	Exclude
513	RECIPIENT NAME AND NUMBER DISAGREE	Exclude
503	DATE DISPENSED AFTER BILLING DATE	Exclude
270	HEADER TOTAL BILLED AMOUNT INVALID	Exclude
268	BILLED AMOUNT MISSING	Exclude
238	RECIPIENT NAME IS MISSING	Exclude
221	DAYS SUPPLY MISSING	Exclude
209	DISPENSE AS WRITTEN CODE 02 NOT ALLOWED.	Exclude
3002	NDC REQUIRES PA	**Include**
3000	UNITS EXCEED AUTHORIZED UNITS ON PA MASTER FILE	**Include**

Appendix 2: Prior Authorization Criteria

Zuranolone (Zurzuvae)

Goal(s):

- ~~To e~~Ensure appropriate duration~~s~~ of treatment ~~use of~~ for zuranolone in patients with post-partum depression.

Length of Authorization:

- One time use only.

Requires PA:

- Zuranolone for durations > 14 days per year. ~~requires a prior authorization approval due to safety concerns.~~

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		
1. What diagnosis is being treated?	Record ICD10 code.	
2. ~~Is this an FDA approved indication and age (e.g., ≥18 years)?~~	~~**Yes**: Go to #3~~	~~**No:** Pass to RPh. Deny; medical appropriateness~~
3. Does the patient have ~~moderate to severe~~ post-partum depression? Note: Zuranolone is not indicated for major depressive disorder but can be covered for depression meeting the clinical diagnosis of post-partum depression (e.g., moderate to severe depression with peripartum onset).	**Yes:** Go to #4	**No:** Pass to RPh. Deny; medical appropriateness
4. Has the patient been previously treated with zuranolone for ~~severe~~ post-partum depression related to their most recent pregnancy?	**Yes:** Pass to RPh. Deny; medical appropriateness. Multiple courses of zuranolone have not been studied.	**No:** Approve for a single 14-day treatment.