Clinical Policy: Zuranolone (Zurzuvae)

Reference Number: PA.CP.PHAR.650
Effective Date: 12/2023
Last Review Date: 10/2023

Description
Zuranolone (Zurzuvae™) is a neuroactive steroid gamma-aminobutyric acid (GABA) A receptor positive modulator.

FDA Approved Indication(s)
Zurzuvae is indicated for the treatment of postpartum depression (PPD) in adults.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of PA Health & Wellness® that Zurzuvae is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Postpartum Depression (must meet all)**:**

1. Diagnosis of a major depressive episode that began no earlier than the third trimester and no later than the first 4 weeks following delivery, as diagnosed by Structured Clinical Interview for DSM-5;
2. Prescribed by or in consultation with psychiatrist;
3. Age ≥ 18 years;
4. Member meets one of the following (a, b, c, d, or e):
   a. HAMD score is ≥ 17 (moderate/severe depression) (*see Appendix D*);
   b. MADRS score is ≥ 20 (moderate/severe depression) (*see Appendix D*);
   c. PHQ-9 score is ≥ 15 (moderate/severe depression) (*see Appendix D*);
   d. If member does not have moderate/severe depression as demonstrated by at least one of the depression scores above (a, b, or c), documentation of severe depression as evidenced by a psychiarist clinical interview;
   e. Failure of a 4-week trial of one of the following oral antidepressants at up to maximally indicated dose but no less than the commonly recognized minimum therapeutic dose, unless clinically significant adverse effects are experienced or all are contraindicated: selective serotonin reuptake inhibitor (SSRI), serotonin-norepinephrine reuptake inhibitor (SNRI), tricyclic antidepressant (TCA), bupropion, mirtazapine (*see Appendix B*);
5. No more than 12 months have passed since member has given birth;
6. Member has not received prior treatment with Zulresso™ or Zurzuvae for the current pregnancy;
7. Dose does not exceed a 14 day treatment course and both of the following (a and b):
   a. 50 mg per day;
   b. 2 capsules per day.

Approval duration: 30 days (one 14 day treatment course per pregnancy)

B. Other diagnoses/indications
1. Refer to the off-label use policy if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

II. Continued Therapy

A. Postpartum Depression
1. Re-authorization is not permitted. Members must meet the initial approval criteria.

Approval duration: Not applicable

A. Other diagnoses/indications (must meet 1 or 2)**:**
1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 12 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – PA.CP.PMN.53

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
HAM-D: Hamilton Rating Scale for Depression
MADRS: Montgomery-Åsberg Depression Rating Scale
PHQ-9: Patient Health Questionnaire
PPD: postpartum depression
SNRI: serotonin-norepinephrine reuptake inhibitor
SSRI: selective serotonin reuptake inhibitor
TCA: tricyclic antidepressant

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
SSRIs		
citalopram (Celexa®)	20 mg PO QD; may increase to 40 mg PO QD after one week	40 mg/day (≤ 60 years) 20 mg/day (> 60 years)
escitalopram (Lexapro®)	10 mg PO QD; may increase to 20 mg PO QD after 1 week	20 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
fluoxetine (Prozac®, Prozac Weekly®)	Prozac: 20 mg PO QD; may increase by 10-20 mg after several weeks Prozac Weekly: 90 mg PO q week beginning 7 days after the last daily dose	Prozac: 80 mg/day Prozac Weekly: 90 mg/week
paroxetine (Paxil®, Paxil CR®, Pexeva®)	Paxil, Pexeva: 20 mg PO QD; may increase by 10 mg every week as needed Paxil CR: 25 mg PO QD; may increase by 12.5 mg every week as needed	Paxil, Pexeva: 50 mg/day Paxil CR: 62.5 mg/day
sertraline (Zoloft®)	50 mg PO QD; may increase every week as needed	200 mg/day
SNRIs		
duloxetine (Cymbalta®)	20 mg PO BID or 30 mg PO BID or 60 mg PO QD	120 mg/day
venlafaxine (Effexor®, Effexor XR®)	Effexor: 75 mg/day PO in 2-3 divided doses; may increase by 75 mg every 4 days as needed Effexor XR: 75 mg PO QD; may increase by 75 mg every 4 days as needed	Effexor: 225 mg/day (outpatient) or 375 mg/day (inpatient) Effexor XR: 225 mg/day
desvenlafaxine (Pristiq®, Khedezla®)	50 mg PO QD	400 mg/day
Fetzima® (levomilnacipran)	20 mg PO QD for 2 days, then 40 mg PO QD; may increase by 40 mg every 2 days	120 mg/day
TCAs		
amitriptyline (Elavil®)	25 to 50 mg/day PO QD or divided doses	150 mg/day
amoxapine	25 to 300 mg/day PO in divided doses	400 mg/day (300 mg/day if geriatric)
clomipramine* (Anafranil®)	12.5 to 150 mg/day PO QD	250 mg/day (200 mg/day if pediatric)
desipramine (Norpramin®)	25 to 300 mg/day PO QD	300 mg/day (100 mg/day if pediatric)
doxepin (Sinequan®)	25 to 300 mg/day PO QD	300 mg/day
imipramine HCl (Tofranil®)	25 to 200 mg/day PO QD or divided doses	200 mg/day (150 mg/day if geriatric or pediatric)
imipramine pamoate (Tofranil PM®)	25 to 200 mg/day PO QD or divided doses	200 mg/day (100 mg/day if geriatric or pediatric)
nortriptyline (Pamelor®)	25 to 150 mg/day PO QD	150 mg/day

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
protriptyline (Vivactil®)	10 to 60 mg/day PO in divided doses	60 mg/day (30 mg/day if geriatric or pediatric)
trimipramine (Surmontil®)	25 to 200 mg/day PO QD	200 mg/day (100 mg/day if geriatric or pediatric)
Other Antidepressants		
bupropion (Aplenzin®, Budeprion SR®, Budeprion XL®, Forfivo XL®, Wellbutrin®, Wellbutrin SR®, Wellbutrin XL®)	Varies	Immediate-release: 450 mg/day (300 mg/day if pediatric) Sustained-release: 400 mg/day Extended-release (HCl): 450 mg/day Extended-release (HBr): 522 mg/day
mirtazapine (Remeron®)	15 to 15 mg PO QD	45 mg/day

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Boxed warning(s): impaired ability to drive or engage in other potentially hazardous activities
- Contraindication(s): none reported

Appendix D: General Information

- HAM-D scale is a 17-item depression assessment scale to assess severity of, and change in, depressive symptoms.

HAM-D Score	Depression Rating
0 – 7	Normal, absence or remission of depression
8 – 16	Mild depression
17 – 23	Moderate depression
> 23	Severe depression

- MADRS is a 10-item diagnostic questionnaire used to measure the severity of depressive episodes in patients with mood disorders.

MADRS Score	Depression Rating
0 – 6	Normal/symptom absent
7 – 19	Mild depression
20 – 34	Moderate depression
> 34	Severe depression

- PHQ-9 is a 9-item multiple choice questionnaire used for diagnosis, screening, monitoring and measuring the severity of depression.

PHQ-9 Score	Depression Severity
5 – 9	Minimal symptoms
10 – 14	Minor depression

PHQ-9 Score	Depression Severity
	Major depression, mild
15 – 19	Major depression, moderately severe
> 19	Major depression, severe

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
PPD	50 mg PO QD in the evening for 14 days Dosage may be reduced to 40 mg once daily if CNS depressant effects occur	50 mg/day

VI. Product Availability

Capsules: 20 mg, 25 mg, 30 mg

VII. References

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Reviews, Revisions, and Approvals	Date	P&T Approval Date
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