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FAMILIES THRIVE WITH GOOD MENTAL HEALTH

Pharmacotherapy approaches for perinatal depression and anxiety

NEW YORK STATE | Office of Mental Health

Speaker:

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I will not discuss any investigational (non-FDA approved) products.

The silent storm

Peripartum depression is common, under-diagnosed and undertreated

- Peripartum mental health disorders (i.e., depression, anxiety disorders, obsessive-compulsive disorder, PTSD, bipolar disorder) affect more than **1 in 7 perinatal individuals** and are among the most common complications of pregnancy and the year after delivery (Wisner KL et al, 2013; Fawcett EJ et al, 2019; Masters GA et al, 2022).

- U.S. Preventative Services Task Force (USPSTF), American Academy of Pediatrics (AAP) and American Academy of Family Physicians (AAFP) and American Psychiatric Association (APA) recommend screening for depression in pregnant and postpartum individuals (JAMA 2016; APA position statement 2018)

- ACOG recommends screening individuals for depression and anxiety symptoms using a standardized, validated tool at the initial prenatal visit, later in pregnancy and at a postpartum visit (ACOG Clinical Practice Guideline June 2023, Obst Gynecol)

- National estimate: 30.8% of women with PPD are identified in clinical settings; 15.5% receive treatment; 6.3% receive adequate treatment; 3.2% achieve remission (Cox EQ et al, 2016)

- At NYP/Weill Cornell (2000-2023): among 27,393 perinatal women, 3.0% (prior to mandate) and 14.2% (after mandate) were screened for anxiety and depression and in clinics with mandatory screening, 23.2% of women reported clinical depression symptoms and 8.8% reported suicidality. 17.3% received MH services and showed more rapid depression reduction vs. untreated women. (Solomonov N et al, 2025)

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Peripartum mental health disorders are associated with severe maternal morbidity and are the leading cause of pregnancy-related death in the US

- Individuals with peripartum mental health disorders experience increased rates of severe maternal morbidity and mortality and increased hospital transfers, lengths of stay and delivery-related costs compared to other deliveries (McKee K et al, 2020).

- The top three causes of pregnancy-related deaths include (Maternal Morbidity Review Committees (MMRC) in 36 states, 2017-2019; Trost SL et al, CDC 2022)

  mental health conditions: 22.7%

  hemorrhage: 13.7%

  cardiac and coronary conditions: 12.8%

- Mental health conditions include deaths of suicide, overdose/poisoning related to substance use disorder, and other deaths determined by the MMRC to be related to a mental health condition, including substance use disorder.

- Among those pregnancy-related deaths with a determination, 82/971 (8.4%) were determined to be a suicide.

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Perinatal mental health disorders are associated with adverse maternal, obstetrical, infant and child developmental outcomes

- Decreased maternal functioning (Field, T, 2010)
- Psychosis, suicidal ideation, homicidal ideation and suicide attempt are psychiatric emergencies that lead to psychiatric hospitalization, maternal death (Rodriguez-Cabezas et al, 2019)
- Bidirectional relationship between depression and gestational diabetes mellitus (Fischer et al, 2023)
- Preterm labor (Bansil P et al, 2010) ,preterm birth (Grigoriadis S et al, 2013), stillbirth/neonatal death and hypertensive disorders of pregnancy (Staub et al, 2012, Thombre et al, 2015, Delanerolle et al, 2022)
- Increased requirement for cesarean delivery (Bansil P et al, 2010)
- Inadequate maternal-infant bonding prenatally and post-delivery (Rossen et al, 2016; Betcher et al, 2020, Dagher et al, 2021)
- Lactation failure or unplanned weaning (Dennis CL & McQueen K, 2009; Stuebe AM et al, 2014)
- Impaired child cognitive development (Tuovinen S et al, 2018)
- Impaired child behavioral and emotional development (Leis JA et al, 2014; Pearson RM et al, 2013)
- Impaired child brain development/antenatal stress from mental illness is associated with accelerated development of offspring neural networks via fetal (developmental) programming (Schinost D et al, 2016; Rotem-Kohavi, N et al, 2020)

Diagnosing unipolar peripartum depression

Major depressive disorder with peripartum onset

includes 5 of the following symptoms, one of which must be either depressed mood or decreased interest or pleasure, beginning in pregnancy or within 4 weeks of delivery and causing impairment of functioning

- Depressed mood, often overshadowed by severe anxiety, crying episodes
- Markedly diminished interest or pleasure in activities- do not enjoy family, baby
- Appetite disturbance- food has no taste, forces self to eat, poor gestational wt
- Sleep disturbance- cannot fall or stay asleep
- Physical agitation (on-edge) or feeling slowed down
- Fatigue, exhausted
- Feelings of worthlessness or excessive or inappropriate guilt
- Decreased concentration or ability to make decisions
- Recurrent thoughts of death or suicidal ideation –my family would be better off without me

†Symptoms must be present most of the day nearly every day for two weeks.

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Distinguishing Baby Blues From PPD

	Baby Blues	Peripartum Depression
Prevalence	40-75% of mothers	14% of mothers
Onset	First few days after delivery, typically peaking on fourth or fifth day	Typically emerges in pregnancy and within 6-8 weeks postpartum
Duration	A few hours or a few days, remitting spontaneously within 2 weeks of delivery	Longer than 2 weeks; can last up to 3 years
Severity	Mild symptoms (mood lability, tearfulness, anxiety, irritability)	Clinical diagnosis of major depressive episode
Impaired functioning	No	Yes
Symptom resolution	**Resolves spontaneously**	Requires treatment
Association with psychopathology	Unrelated to psychiatric history and not predictive of future problems	More common in women with history of major depression and bipolar disorder and predictive of future depressive episodes

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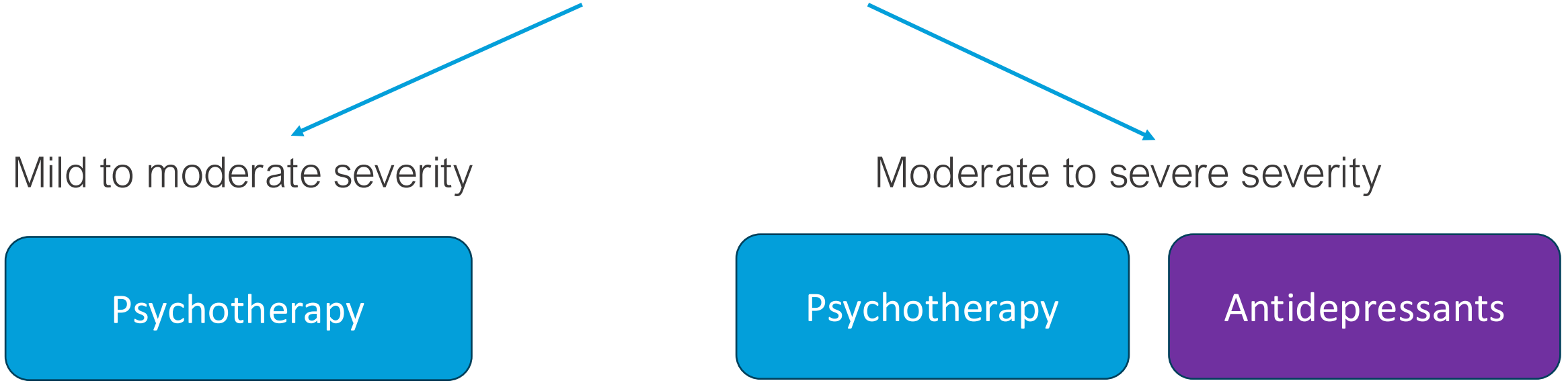
Peripartum anxiety disorders

- group of distinct but interrelated conditions characterized by excessive fear, elevated emotional response to perceived/real threat, and related behavioral disturbances
- overall prevalence of having at least 1 or more anxiety disorder is estimated to be 20.7% (1 in 5) (Fawcett EJ et al 2019)
- high co-morbidity of anxious symptoms with perinatal depression, up to 50%
- generalized anxiety disorder: excessive worry that is difficult to control, agitation, irritability, easy fatigue, sleep disturbance
- obsessive compulsive disorder: time-consuming and functionally impairing intrusive, unwanted, thoughts/images/urges (obsessions) and repetitive behaviors or mental acts performed to relieve the anxiety from obsessions (compulsions)

Treatment of peripartum depressive and anxiety disorders



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Poll

When your patient with recurring episodes of depression and chronic anxiety (well treated with fluoxetine 40mg and clonazepam 1mg) becomes pregnant, do you:

a) Panic!

b) Advise that both medications should be discontinued and not restarted until 2nd trimester.

c) Advise that both medications should be discontinued during pregnancy and not restarted until patient has finished breastfeeding.

d) Advise to stop fluoxetine and clonazepam and switch to sertraline.

e) Continue both medications at current doses and call Project TEACH for phone consultation.

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Informed decision making, informed consent for peripartum psychopharmacological treatment

- Establish that the patient has capacity to make treatment decisions
- Propose suggested treatment while elaborating on alternative treatment options (including option/risk of no treatment)
- Involve baby's father if possible
- Perform risk vs. risk analysis of treatment
  - Risk of usual side effect profile for medication
  - Risk of teratogenicity (baseline vs. that with medication exposure)
  - Risk of obstetric complications
  - Risk to the newborn
  - Risk of negative long term neurodevelopmental or other health outcome
  - Risk of non-treatment

- Document all the above so that it can be understood years later.
- Obtain releases from patient to share this documentation with and to communicate with the treating obstetrician/midwife/family physician and infant's pediatrician so that treatment team is all on the same page

Antidepressants for peripartum depression and anxiety

Serotonergic antidepressants (SSRI, SNRI, etc.): **moderate/severe** unipolar perinatal depression

- *No* randomized, placebo-controlled trials (RCT) of antidepressants for antenatal depression
- Meta-analysis of 11 postpartum RCTs showed that there may be a benefit of SSRIs over placebo in response (55% versus 43%; pooled risk ratio (RR) 1.27, 95% CI 0.97 to 1.66) and remission (42% versus 27%; RR 1.54, 95% CI 0.99 to 2.41) at 5 to 12 weeks' follow-up. (Brown JVE et al, Cochrane Database Syst Rev, 2021)
- Antepartum vs postpartum use is associated with different risks
- Treatment approach: titrate until efficacy/tolerability then treat acute episode at that dose -> once reach euthymia, continue treatment (continuation phase) for several months (or longer) to prevent relapse.
- Often best to combine with psychotherapies

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Antidepressant dosing for peripartum depression and anxiety (see drug labels at: https://dailymed.nlm.nih.gov for full prescribing info)

Medication Generic	FDA Indication	Medication Trade	Initial dosage	FDA range
Sertraline	MDD, GAD, OCD	Zoloft	25mg	50-200mg
Fluoxetine	MDD, GAD, OCD	Prozac	10-20mg	20-80mg; increase by 20mg q3-4 weeks
Citalopram	MDD, GAD	Celexa	20mg	20-40mg
Escitalopram	MDD, GAD	Lexapro	5-10mg	10-20mg; increase by 5mg q3-4 weeks
Desvenlafaxine	MDD	Pristiq	25-50mg	50mg
Duloxetine	MDD, GAD	Cymbalta	30mg x 1 wk	60mg-120mg; increase by 30mg q3-4 weeks
Bupropion	MDD, nicotine dependence	Wellbutrin XL	150mg	300-450mg; may increase to 300mg qAM after 4 days
Mirtazapine	MDD	Remeron	7.5-15mg	15-45mg

1st trimester: 1 to 13
2nd trimester: 14 to 27
3rd trimesters: 28 to 40

Antepartum antidepressant use and birth outcomes

- CDC PTB national rate =10.4% Preterm Birth | Maternal Infant Health | CDC
- increased risk of moderate-to-late preterm birth (Rommel at al., 2022):
  - gestational age: 2.3 day decrease in gestational age
  - birthweight: 51 g decrease in birthweight
  - other outcomes: higher risk of moderately low birthweight, postnatal adaptation syndrome, and neonatal admission
  - no differences were found for persistent pulmonary hypertension or birth defects
- ACOG recommends all women of reproductive age take a prenatal vitamin with at least 400mcg of folic acid, starting at least one month before pregnancy and continuing through the first 12 weeks.

Antepartum antidepressant use and neonatal complications

Postnatal adaptation syndrome (PNAS):

infant irritability, abnormal crying, tremor, lethargy, hypoactivity, decreased feeding, tachypnea, respiratory distress, irritability, hypothermia, and hypoglycemia

- severity and length are impacted by multiple factors including dose, timing and duration of exposure and SSRI pharmacology including half-life, presence of active metabolites and maternal and infant metabolism, etc.
- delayed neonatal adaptation occurred in 11.2% of exposed vs 4.4% of unexposed infants RR 2.52 (CI 2.36 to 2.70) (Cornet et al, 2024)
- most often been reported after exposure to escitalopram and venlafaxine
- symptoms can last through 1st month postnatal life; discontinuing 3rd trimester antidepressant use does not reduce PNAS risk (Salisbury AL 2016)

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Antepartum antidepressant use and neonatal complications

Persistent pulmonary hypertension of the newborn (PPHN): can result whenever cardiopulmonary transition does not occur

- Reduced length of gestation and premature birth has been associated with increased risk of PPHN
- 1.9/1000 gen pop vs. 2.9-3.5/1000 w late gestation SSRI use (Becker M et al, 2016; Huybrecht et al., 2015) but no association found by Rommel AS et al, 2022
- NNH=285 for 1 infant to develop PPHN with late gestation SSRI exposure (Norby U, 2016)
- Infants with PPHN present within twelve hours of birth with cyanosis and mild respiratory distress and can develop severe respiratory failure requiring intubation and mechanical ventilation
- PPHN can be fatal in approximately 10-20% of cases

Antepartum antidepressant use and child development

Antidepressant exposure compared with no exposure was not associated with an increased risk of autism spectrum disorder or ADHD (Brown et al., 2017; Malm H et al, 2016; Rommel AS et al, 2020; Vega ML et al, 2020)

Women with depression during pregnancy have an increased risk of having a child with autism spectrum disorder, regardless of antidepressant use (Wilcox Hagberg et al, 2018).

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FDA-approved neuroactive steroid antidepressant for unipolar peripartum depression (postpartum use only)

- **Zuranolone** is a synthetic analog of allopregnanolone and is a positive allosteric modulator of GABA-A receptors
- First oral FDA-approved PPD (ICD-10 = F53.0) treatment in 2023
- Allopregnanolone (natural neurosteroid, metabolite of progesterone) plus addition of a cyanopyrazole ring
- Can be taken as monotherapy or as an adjunct to another antidepressant medication
- Administer with a fat-containing food or meal
- Per drug label: at 30mg dosing, lactation relative infant dose (RID) of 0.357% compared to maternal dose, not detectable in breastmilk by 4-6 days after last dose
- Schedule IV, see package insert: https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f18e53b0-d0bb-422d-8de7-ab64b7292b29
- RX must be sent to 1 of 4 national **specialty pharmacies** (Accredo Specialty, CVS Specialty, Alto Specialty, Walmart Specialty)

Dosing for postpartum depression

(see https://dailymed.nlm.nih.gov for full prescribing info)

Medication Generic	Medication Trade	Recommended dosage
Zuranolone	Zurzuvae	50mg PO qPM x 14 days, if excessive sedation reduce dose to 40mg PO qPM; total course not to exceed 14 days treatment

There is no up or down-titration for the medication
It is a single acute treatment course (14 days only)
Postpartum use only (not in pregnancy) with onset of PPD during pregnancy or after delivery up to 1 year
Not for use in bipolar disorder (has not been well studied and is not FDA approved for that use)

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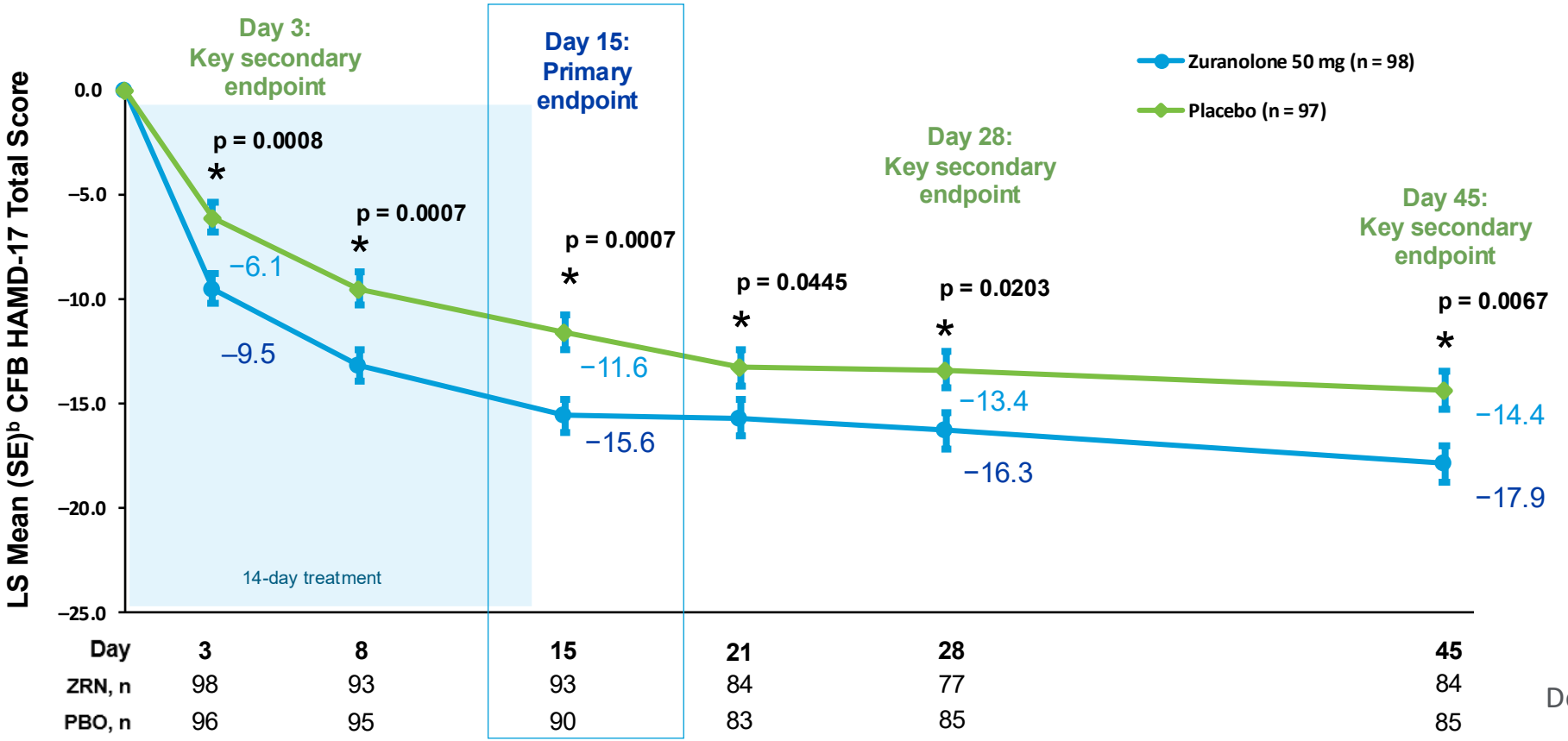
Zuranolone SKYLARK RCT results

Primary Endpoint and Key Secondary Endpoints



HAMD-17 at Baseline, Mean (SD)	
Zuranolone 50 mg	28.6 (2.49)
Placebo	28.8 (2.34)

D15 response rate:
57% ZRN vs. 38.9%*

Deligiannidis KM et al, *Am J Psychiatry*, 2023.

FAS = full analysis set; HAMD-17 = 17-Item Hamilton Rating Scale for Depression; LS = least squares; MMRM = mixed model of repeated measures; PBO = placebo.

*** Statistically significant (per fixed hierarchal testing for key secondary endpoints). Data at Days 8 and 21 were not adjusted for multiplicity, and p-values were considered nominal.**

[a] FAS was defined as all randomised participants who were administered zuranolone 50 mg or placebo with valid baseline and ≥ 1 postbaseline efficacy endpoint assessment. [b] LS mean and treatment difference along with CI and p-values were calculated using MMRM. The key secondary endpoints were tested in the following fixed sequence to control for multiplicity: CFB in HAMD-17 at Days 3, 28, and 45. If an endpoint was not significant at the 5% level, the following endpoints in the sequence were interpreted only with nominal p-value.

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Postpartum use of zuranolone

- Can be taken as monotherapy or as an adjunct to another antidepressant medication
- Administer with a fat-containing food (e.g., 400 to 1,000 calories, 25% to 50% fat)
- Recommended dosage is 50mg PO in the evening x 14 days; may reduce to 40mg dosing if CNS depressant effects; 30mg dosing for severe hepatic impairment or moderate or severe renal impairment
- Strong CYP3A4 inhibitors: concomitant use may increase zuranolone-associated AEs; reduce zuranolone dosage to 30mg when used concomitantly with a strong CYP3A4 inhibitor
- Concomitant use with CYP3A4 inducers may decrease the efficacy of zuranolone
- Can cause CNS depressant effects such as somnolence and confusion. Across both studies, 1% of patients reported a transient confusional state.
- There is a **boxed warning** for impaired ability to drive or engage in other potentially hazardous activities due to CNS depressant effects. Patients should not drive or operate heavy machinery for at least 12 hours after taking each dose.

https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f18e53b0-d0bb-422d-8de7-ab64b7292b29#t2

Postpartum use of zuranolone

- Avoid EtOH use, concomitant benzodiazepine, opioids or other medication use that can increase impairment of psychomotor performance or CNS depressant effects
- Schedule IV with the potential for misuse, abuse and dependence; risk is lowered in that it is prescribed as a single 14-day acute treatment, with no further dosing ->abuse potential is similar to alprazolam in patients who have a history of recreational CNS depressant use
- Advise patients of reproductive potential to use effective contraception during treatment and for one week after the final dose.
- Healthcare providers are encouraged to register patients by calling the National Pregnancy Registry for Antidepressants at 1-844-405-6185 or visiting online at https://womensmentalhealth.org/research/pregnancyregistry/antidepressants/
- Per NIH LactMed: “Because of the low amounts of zuranolone in milk, it would not be expected to cause any adverse effects in breastfed infants. **If zuranolone is required by the mother, it is not a reason to discontinue breastfeeding**. Until more data are available, zuranolone should be used with careful infant monitoring for excessive sedation during breastfeeding, especially with higher dosages and in newborn and preterm infants.” (https://www.ncbi.nlm.nih.gov/books/NBK594292/)

https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=f18e53b0-d0bb-422d-8de7-ab64b7292b29#t2

Class comparison: antidepressant side effects

Sertraline (SSRI)

- Nausea (26%)
- Diarrhea/loose stools (18%)
- Insomnia (16%)
- Somnolence (13%)
- Dry mouth (16%)
- Tremor (11%)

Zuranolone (neurosteroid)

- Somnolence (36%)
- Dizziness (13%)
- Diarrhea (6%)
- Fatigue (5%)
- Urinary track infection (5%)

all data from
https://dailymed.nlm.nih.gov/dailymed/index.cfm

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Use of antidepressants during lactation

World Health Organization and The American Academy of Pediatrics recommends that children are breastfed for their first 2 years of life.

The American Academy of Family Physicians and the American Dietetic Association recommend exclusive breastfeeding for the first 6 months of life and breastfeeding with complementary food from 6 months until at least 12 months of age and as long thereafter as desired.

Antidepressant use should not discourage women from breastfeeding; overwhelming benefits of breastfeeding usually outweigh risks of medication use in women with unipolar depression +/- anxiety

- PND is associated with ↓ breastfeeding duration and ↑ breastfeeding difficulties (Dennis CL 2009)
- Relative infant doses (RID) less than 10% of maternal dosage are generally acceptable per FDA
- Side effects to watch for with serotonergic antidepressants: sedation, irritability, poor feeding, GI upset
- Side effects to watch for with zuranolone: sedation (potential, limited infant data currently)
- The National Library of Medicine at the NIH maintains the Drugs and Lactation Database (LactMed) found at: https://www.ncbi.nlm.nih.gov/books/NBK501922/
  - This useful database is maintained by a peer review panel who reviews scientific data to assure validity and currency. It includes information on levels of drugs in breastmilk and infant blood and the possible adverse effects in the nursing infant.

Infant exposure to maternal antidepressant use via breastmilk

The National Library of Medicine at the NIH maintains the Drugs and Lactation Database (LactMed) found at: https://www.ncbi.nlm.nih.gov/books/NBK501922/

Medication name	RID (%)
Bupropion	0.2-5.1
Citalopram	3-10
Desvenlafaxine	5.5-8.1
Dextromethorphan/ bupropion	Avoid during treatment and for 5 days after d/c; inadequate human data available (per manufacturer): dex (<1%);
Doxepin	AVOID: reports of hypotonia, sedation, vomiting, suppressed respiratory rate, weight loss
Duloxetine	<1
Escitalopram	5.2-7.9
Fluoxetine	0.6-20 (norfluoxetine detectable in infant serum)
Fluvoxamine	<2
Levomilnacipran	No data, monitor for agitation, irritability, poor feeding and poor weight gain
Mirtazapine	0.5-3
Nortriptyline	0.87-3.71 (watch for dry mouth, constipation, urinary retention)- favored TCA in lactation
Paroxetine	1.2-2.8
Sertraline	0.4-3
Venlafaxine	6-9
Vilazodone	No data, seek alternative
Vortioxetine	1.1-1.7
Zuranolone	<1

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Unipolar depression with peripartum onset treatment considerations

Psychotherapies: mild, moderate, severe depressive symptoms

Consider SSRI/SNRI

- Current moderate/severe symptoms, patient preference
- Patient presents to treatment in pregnancy
- Previous response/remission with acceptable tolerability
- Mild/moderate functional impairment
- Engaged in psychotherapy; past response/remission with psychotherapy
- Low risk for suicide/infanticide/homicide
- Active alcohol, opioid, sedative, hypnotic or anxiolytic use disorder
- Patient prefers not to use effective contraception required of zuranolone treatment (for 21d)

Consider Zuranolone

- Current moderate/severe symptoms
- Failed AD during gestation or prior MDEs
- Patient is postpartum and not trying to conceive
- Partial response to maximally dosed AD→ use as adjunct
- Moderate/severe functional impairment
- Challenges to engage in psychotherapy or failed psychotherapy
- Intolerability to other ADs
- Elevated risk for suicide/infanticide/homicide

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Peripartum benzodiazepine use for anxiety disorders

- Benzodiazepines with shorter half-lives and no/few active metabolites preferred over mid to long-acting (e.g. lorazepam, not clonazepam, not diazepam).

- Little evidence of birth defects with alprazolam, lorazepam or clonazepam use in first trimester (Grigoriadis et al 2019), but single study noted potential increased OR for Dandy-walker malformation (any benzo), anophthalmia or microphthalmia and esophageal stenosis (alprazolam) and pulmonary valve stenosis (lorazepam) (Tinker SC et al 2019).

- Increased risk of preterm birth (OR 1.28), small for gestational age (OR 1.24) and low birth weight (OR 1.51) (Wang X et al, 2024)

- In term neonates (>37 weeks GA), elimination is extended due to poor hepatic function (they do not have full Phase II metabolism yet). Neonates born prematurely can have prolonged plasma elimination (and thus increased side effects).

Peripartum benzodiazepine use for anxiety disorders

- **neonatal withdrawal syndrome: floppy baby syndrome:** poor tone, lethargy, hypothermia, low APGAR (Yonkers KA et al 2017); also hypertonia, hyperreflexia and tremors (Iqbal MM et al, 2002); worse neurobehavioral outcomes in SSRI + benzo than SSRI alone or depressed alone (Salisbury AL, 2016)

Alprazolam: 13hr half-life; RID=3%- we avoid due to increased risk of dependency

Lorazepam: 14hr half-life (is 85% bound to plasma proteins ; RID=2.5%, so low levels in breastmilk, preferred benzo if needed)

Clonazepam: 20-50hr half-life; RID=2.8, LactMed recommends use of shorter-half-life benzo over clonazepam

Diazepam: 30-60hr half-life for parent drug plus 30-100 hours major active metabolite dimethyldiazepam; RID = 7.1%, AVOID use in perinatal period

Other anxiolytics (on and off-label)

Buspirone:

- Not anticipated to increase the risk of congenital anomalies based on register study (Freeman MP et al, 2022)
- Excreted in breastmilk in low levels (RID range 0.21 to 2.17%), limited data in infants (LactMed)

Gabapentin:

Recent population-based cohort study of Medicaid patients with antenatal gabapentin use vs. unexposed (Patorno, et al 2020)

- Slight increase in risk for cardiac malformations (RR: 1.40 [1.03-1.90]) with 1st trimester use, and preterm birth (RR: 1.28 [1.08-1.52]), small for gestational age (RR1.39: [1.01-1.91]), NICU stay (RR: 1.35 [1.20-1.52]) with later trimester use
- later risks- also seen in depression/anxiety– difficult to tease out what is med and what is due to depr/anx
- limited information indicates that maternal doses of gabapentin up to 2.1 grams daily produce relatively low levels in infant serum (RID <3%). Monitor the infant for drowsiness, adequate weight gain, and developmental milestones, especially in younger, exclusively breastfed infants and when using combinations of anticonvulsant or psychotropic drugs

Other anxiolytics (on and off-label)

- **Hydroxyzine**: may increase miscarriage (high doses in animals); data do not suggest risk of major malformations but too few exposures to conclude lack of risk, usually recommend **doxylamine** instead; hydroxyzine may cause PNAS; small occasional doses not expected to cause adverse effects in breastfed infants; larger doses or prolonged use may cause drowsiness or decrease milk supply, other agents preferred, no RID available

- **Pregabalin:** limited data indicate that amounts in breastmilk are low, but use caution in newborn or preterm infant; manufacturer recommends avoid use due to potential of tumorigenicity based on high-dosed animal studies; no RID available

- **Propranolol:** not anticipated to be teratogenic, may be associated with intrauterine growth restriction; use in late pregnancy can be associated with neonatal apnea, respiratory distress, bradycardia and hypoglycemia; RID estimated <1%, adverse reactions are not expected, and special precautions are not required

Clinical considerations

First and foremost, consider how you would treat the patient's unipolar depression/anxiety if the patient was not pregnant/lactating.

Consider…

- the risk to the patient and the fetus/infant of stopping or reducing current pharmacotherapies
  - Risk of untreated illness to patient and fetus/infant
- the risk to the patient and the fetus/infant of continuing those pharmacotherapies
  - Consider antenatal vs. postnatal (lactational) risks
- the risk of switching to an alternative pharmacotherapy
  - Is the alternative really safer? Will the alternative control depressive/anxiety symptoms as well as the current regimen?

Clinical considerations

- When possible, any changes to a medication regimen should be made prior to conception to ensure symptom stability and to minimize exposure to the fetus. Abrupt discontinuation of antidepressants in pregnant women with a history of depression is associated with high risk of relapse without known benefit (L.S. Cohen et al., 2006).
  - Preconception planning!

- Women with history of recurrent unipolar MDD or history of symptom recurrence associated with past reduction or discontinuation of antidepressants **should not discontinue their antidepressant during pregnancy.**

- If SSRI/SNRI dose increased in pregnancy, monitor for side effects after delivery, can decide when to reduce SSRI/SNRI dose (if at all) once reassured of continued euthymia; don't immediately resume pre-pregnancy dose as could precipitate MDD relapse.

Which antidepressant for which pregnant patient?

SSRIs and SNRIs are the main antidepressant categories used in the treatment of depression and anxiety in pregnancy

If the patient has never taken an antidepressant in the past, an antidepressant with a short half-life and low concentration in the breastmilk such as sertraline can be recommended

If the patient has a history of previous antidepressant trials, it is recommended to use medications that were helpful in the past and resulted in remission of symptoms (with good tolerability)

How to start and monitor treatment with SSRI/SNRI

Start low and discuss with the patient the most common side effects such as gastrointestinal distress, headache, and possible activation such as temporary increase in anxiety

Discuss with a patient that it usually takes 4-6 weeks for the patient to notice benefits

At each visit, check for possible side effects and use screening tools (e.g., PHQ, EPDS) at each visit to help monitor the treatment response

Increase the dose based on clinical presentation, the goal of the treatment is complete remission of symptoms

Monitor for expected peripartum changes in serotonergic antidepressant metabolism

Pregnancy hormones can increase P450 metabolism of antidepressants after 20 weeks gestation:

- citalopram, escitalopram, sertraline, fluoxetine, fluvoxamine, paroxetine, clomipramine and imipramine
- If SSRI/SNRI dose increased in pregnancy, monitor for side effects after delivery, can decide when to reduce SSRI/SNRI dose (if at all) once reassured of continued euthymia; don't immediately resume pre-pregnancy dose as could precipitate MDD relapse.
- Doses of tricyclic antidepressants may need to be increased as much as 1.6 times the pre-pregnancy dose to maintain therapeutic levels. Check levels monthly in pregnancy, decrease towards preconception dose during 2-6 weeks after delivery to avoid TCA postpartum toxicity, check levels frequently

Finally,

When possible, monotherapy in adequate dose is preferred over polypharmacy

The goal of treatment is full symptom remission, and medications should be adjusted to the lowest efficacious and fully therapeutic dose

Project TEACH is here to help.

Call us: 1-855-227-7272

M-F 9a-5p

ProjectTEACH
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