Gemeinsamer Bundesausschuss

Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie

und

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

und

Schriftliche Beteiligung der wissenschaftlich-medizinischen Fachgesellschaften und der Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ) zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: 2025-B-099 Zuranolon

Stand: Juni 2025

I. Zweckmäßige Vergleichstherapie: Kriterien gemäß 5. Kapitel § 6 VerfO G-BA	
Zuranolon **[Postpartale Depression]** **Kriterien gemäß 5. Kapitel § 6 VerfO**	
Sofern als Vergleichstherapie eine Arzneimittelanwendung in Betracht kommt, muss das Arzneimittel grundsätzlich eine Zulassung für das Anwendungsgebiet haben.	Siehe Übersicht „II. Zugelassene Arzneimittel im Anwendungsgebiet“.
Sofern als Vergleichstherapie eine nicht-medikamentöse Behandlung in Betracht kommt, muss diese im Rahmen der GKV erbringbar sein.	• Psychotherapeutische Verfahren gemäß Psychotherapie-Richtlinie • Elektrokonvulsionstherapie (EKT)
Beschlüsse/Bewertungen/Empfehlungen des Gemeinsamen Bundesausschusses zu im Anwendungsgebiet zugelassenen Arzneimitteln/nicht-medikamentösen Behandlungen	• Beschluss vom 16.09.2010 über eine Änderung der AM-RL: Anlage III – Übersicht der Verordnungseinschränkungen und -ausschlüsse – Reboxetin: Verordnungsausschluss • Beschluss vom 15.10.2015 über eine Änderung der AM-RL: Anlage XII - Nutzenbewertung von Arzneimitteln mit neuen Wirkstoffen nach § 35a SGB V – Vortioxetin • Beschlüsse vom 19.08.2021 und 21.09.2023 über eine Änderung der AM-RL: Anlage XII - Nutzenbewertung von Arzneimitteln mit neuen Wirkstoffen nach § 35a SGB V – Esketamin
Die Vergleichstherapie soll nach dem allgemein anerkannten Stand der medizinischen Erkenntnisse zur zweckmäßigen Therapie im Anwendungsgebiet gehören.	Siehe systematische Literaturrecherche.

II. Zugelassene Arzneimittel im Anwendungsgebiet

Wirkstoff **ATC-Code** **Handelsname**	**Anwendungsgebiet** (Text aus Fachinformation)
Zu bewertendes Arzneimittel:	
Zuranolon	Anwendungsgebiet laut Beratungsanforderung: „Zuranolon ist indiziert zur Behandlung von Erwachsenen nach der Geburt mit einer postpartalen Depression.“
Tri- und tetrazyklische Antidepressiva (TZA) – nichtselektive Monoamin-Rückaufnahme-Inhibitoren (NSMRI)	
Amitriptylin N06AA09 generisch	Behandlung von depressiven Erkrankungen (Episoden einer Major Depression) bei Erwachsenen.
Amitriptylinoxid N06AA09 generisch	Behandlung depressiver Erkrankungen.
Clomipramin N06AA04 generisch	Depressive Syndrome unabhängig von ihrer nosologischen Zuordnung.
Dosulepin N06AA16 Idom mite®	Depressive Erkrankungen. *[Hinweis: Der Wirkstoff wird in Deutschland derzeit nicht vertrieben.]*
Doxepin N06AA12 generisch	- Depressive Erkrankungen. - Unruhe, Angst oder Schlafstörungen im Zusammenhang mit depressiven Erkrankungen oder leichten Entzugssyndromen.
Imipramin N06AA02 generisch	Depressive Syndrome unabhängig von ihrer nosologischen Zuordnung.
Maprotilin	Depressive Erkrankungen.

II. Zugelassene Arzneimittel im Anwendungsgebiet	
N06AA21 generisch	
Nortriptylin N06AA10 generisch	Behandlung depressiver Erkrankungen (Episoden einer Major Depression) bei Erwachsenen.
Trimipramin N06AA06 generisch	Depressive Erkrankungen (Episoden einer Major Depression) mit den Leitsymptomen Schlafstörungen, Angst, innere Unruhe.
Selektive Serotonin-Rückaufnahme-Inhibitoren (SSRI)	
Citalopram N06AB04 generisch	Behandlung von Episoden einer Major Depression
Escitalopram N06AB10 generisch	Behandlung von Episoden einer Major Depression.
Fluoxetin N06AB03 generisch	Erwachsene: Episoden einer Major Depression.
Fluvoxamin N06AB08 generisch	Depressive Erkrankungen (Episoden einer Major Depression).
Paroxetin N06AB05 generisch	Behandlung von Episoden einer Major Depression.
Sertralin N06AB06 generisch	Episoden einer Major Depression. Rezidivprophylaxe von Episoden einer Major Depression.

II. Zugelassene Arzneimittel im Anwendungsgebiet	
Vortioxetin N06AX26 Brintellix®	Behandlung von Episoden einer Major Depression bei Erwachsenen. *[Hinweis: Der Wirkstoff wird in Deutschland derzeit nicht vertrieben.]*
Selektive Serotonin-/ Noradrenalin- Rückaufnahme-Inhibitoren (SSNRI)	
Venlafaxin N06AX16 generisch	- Behandlung von Episoden einer Major Depression - Rezidivprophylaxe von Episoden einer Major Depression
Desvenlafaxin N06AX23 Desveneurax®	Behandlung der Major Depression bei Erwachsenen.
Duloxetin N06AX21 generisch	Zur Behandlung von depressiven Erkrankungen (Major Depression).
Milnacipran N06AX17 generisch	Behandlung von Episoden einer Major Depression bei Erwachsenen.
Alpha2-Rezeptor-Antagonisten	
Mirtazapin N06AX11 generisch	Behandlung von Episoden einer Major Depression.
Mianserin N06AX03 generisch	Depressive Störungen.
Monoaminoxidase (MAO)-Inhibitoren	
Moclobemid N06AG02 generisch	Behandlung depressiver Erkrankungen (Episoden einer Major Depression).

II. Zugelassene Arzneimittel im Anwendungsgebiet	
Tranylcypromin N06AF04 generisch	Zur Behandlung von depressiven Episoden (Episoden einer Major Depression). Dieses Arzneimittel sollte als Reserveantidepressivum zum Einsatz kommen, d.h. - wenn eine adäquate Therapie mit 2 antidepressiven Standardwirkstoffen (einschließlich trizyklischer Antidepressiva) keinen ausreichenden Erfolg brachte oder - wenn solche Standardwirkstoffe kontraindiziert sind oder vom Patienten nicht vertragen werden.
Sonstige	
Agomelatin N06AX22 generisch	Behandlung von Episoden einer Major Depression bei Erwachsenen.
Bupropion N06AX12 generisch	Behandlung von Episoden einer depressiven Erkrankung (Episoden einer Major Depression).
Johanniskraut N06AX25 generisch	Behandlung von leichten bis mittelschweren depressiven Episoden.
Reboxetin N06AX18 Edronax®	Behandlung akuter depressiver Erkrankungen/Major Depression. Die Behandlung sollte bei Patienten, die initial auf dieses Arzneimittel angesprochen haben, zur Aufrechterhaltung der klinischen Besserung fortgeführt werden.
Sulpirid N05AL01 generisch	Depressive Erkrankungen, wenn die Behandlung mit einem anderen Antidepressivum erfolglos war.
Tianeptin N06AX14 generisch	Behandlung von Episoden einer Major Depression bei Erwachsenen.
Trazodon N06AX05 generisch	Depressive Erkrankungen.

II. Zugelassene Arzneimittel im Anwendungsgebiet

Als Zusatztherapie und/oder bei Therapieresistenz	
Esketamin N06AX27 Spravato®	- Spravato®, in Kombination mit einem SSRI oder SNRI, wird bei Erwachsenen mit therapieresistenter Major Depression angewendet, die in der aktuellen mittelgradigen bis schweren depressiven Episode auf mindestens zwei unterschiedliche Therapien mit Antidepressiva nicht angesprochen haben. - Spravato®, in Kombination mit einer oralen antidepressiven Therapie, wird angewendet bei erwachsenen Patienten mit einer mittelgradigen bis schweren Episode einer Major Depression als akute Kurzzeitbehandlung zur schnellen Reduktion depressiver Symptome, die nach ärztlichem Ermessen einem psychiatrischen Notfall entsprechen.
Lithiumcarbonat N05AN01 generisch	- Zur Prophylaxe der bipolaren affektiven Störung und Episoden einer Major Depression. - Bei bestimmten akuten Depressionen, z.B. bei Therapieresistenz oder Unverträglichkeit von Antidepressiva.
Quetiapin retard N05AH04 generisch	Behandlung depressiver Erkrankungen (Episoden einer Major Depression) als Zusatztherapie bei Patienten, die unzureichend auf die Monotherapie mit einem Antidepressivum angesprochen haben. Vor Beginn der Behandlung sollte der behandelnde Arzt das Sicherheitsprofil von Quetiapin beachten.

Quellen: AMIce-Datenbank, Fachinformationen

Gemeinsamer Bundesausschuss

Abteilung Fachberatung Medizin

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie

Vorgang: 2025-B-099 (Beratung nach § 35a SGB V) Zuranolon

Auftrag von:	Abt. AM
Bearbeitet von:	Abt. FB Med
Datum:	29. April 2025

Inhaltsverzeichnis

Abkürzungsverzeichnis

ACOG	American College of Obstetricians and Gynecologists
AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
BA	behavioural activation
CANMAT	Canadian Network for Mood and Anxiety Treatments
CBT	Cognitive–behavioural therapy
CI	Konfidenzintervall
ECRI	Emergency Care Research Institute
G-BA	Gemeinsamer Bundesausschuss
GIN	Guidelines International Network
GoR	Grade of Recommendations
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HR	Hazard Ratio
IPT	interpersonal psychotherapy
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
LoE	Level of Evidence
MDD	major depressive disorder
MDE	major depressive episode
NICE	National Institute for Health and Care Excellence
OR	Odds Ratio
PPD	postpartum depression
PPHN	pulmonary hypertension of the newborn
RR	Relatives Risiko
SIGN	Scottish Intercollegiate Guidelines Network
SNRI	serotonin norepinephrine reuptake inhibitors
SSRI	serotonin reuptake inhibitors
TCA	tricyclic antidepressants
TRIP	Turn Research into Practice Database
WHO	World Health Organization

1 Indikation

Erwachsene nach der Geburt mit einer postpartalen Depression.

Hinweis zur Synopse: Informationen hinsichtlich nicht zugelassener Therapieoptionen sind über die vollumfängliche Darstellung der Leitlinienempfehlungen dargestellt.

2 Systematische Recherche

Es wurde eine systematische Literaturrecherche nach systematischen Reviews, Meta-Analysen und evidenzbasierten systematischen Leitlinien zur Indikation *postportale Depression* durchgeführt und nach PRISMA-S dokumentiert [A]. Die Recherchestrategie wurde vor der Ausführung anhand der PRESS-Checkliste begutachtet [B]. Es erfolgte eine Datenbankrecherche ohne Sprachrestriktion in: The Cochrane Library (Cochrane Database of Systematic Reviews), PubMed. Die Recherche nach grauer Literatur umfasste eine gezielte, iterative Handsuche auf den Internetseiten von Leitlinienorganisationen. Ergänzend wurde eine freie Internetsuche (https://www.google.com/) unter Verwendung des privaten Modus, nach aktuellen deutsch- und englischsprachigen Leitlinien durchgeführt.

Der Suchzeitraum der systematischen Literaturrecherche wurde auf die letzten fünf Jahre eingeschränkt und die Recherchen am 22.04.2025 abgeschlossen. Die detaillierte Darstellung der Recherchestrategie inkl. verwendeter Suchfilter sowie eine Auflistung durchsuchter Leitlinienorganisationen ist am Ende der Synopse aufgeführt. Mit Hilfe von EndNote wurden Dubletten identifiziert und entfernt. Die Recherchen ergaben insgesamt 1689 Referenzen.

In einem zweistufigen Screening wurden die Ergebnisse der Literaturrecherche bewertet. Im ersten Screening wurden auf Basis von Titel und Abstract nach Population, Intervention, Komparator und Publikationstyp nicht relevante Publikationen ausgeschlossen. Dabei wurde für systematische Reviews, inkl. Meta-Analysen, ein Publikationszeitraum von 2 Jahren und für Leitlinien von 5 Jahren betrachtet. Zudem wurde eine Sprachrestriktion auf deutsche und englische Referenzen vorgenommen. Im zweiten Screening wurden die im ersten Screening eingeschlossenen Publikationen als Volltexte gesichtet und auf ihre Relevanz und methodische Qualität geprüft. Dafür wurden dieselben Kriterien wie im ersten Screening sowie Kriterien zur methodischen Qualität der Evidenzquellen verwendet.

Basierend darauf, wurden insgesamt 3 Referenzen eingeschlossen. Es erfolgte eine synoptische Darstellung wesentlicher Inhalte der identifizierten Referenzen.

3 Ergebnisse

3.1 Cochrane Reviews

Es konnten keine Cochrane Reviews eingeschlossen werden.

3.2 Systematische Reviews

Es konnten keine systematischen Reviews eingeschlossen werden.

3.3 Leitlinien

Vigod SN et al., 2025 [3].

Canadian Network for Mood and Anxiety Treatments (CANMAT)

Canadian Network for Mood and Anxiety Treatments 2024 Clinical Practice Guideline for the Management of Perinatal Mood, Anxiety, and Related Disorders

Methodik

Grundlage der Leitlinie

- Repräsentatives Gremium; trifft zu
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt; trifft zu aber Umgang damit im Konsensusprozess nicht erläutert
- Systematische Suche, Auswahl und Bewertung der Evidenz; trifft zu
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt; trifft zu
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt; trifft zu
- Regelmäßige Überprüfung der Aktualität gesichert; trifft zu

Recherche/Suchzeitraum:

- PubMed, EMBASE, PsycINFO, MEDLINE, CINAHL, Cochrane and Web of Science databases were searched for English- and French-language systematic reviews and meta-analyses published from 1 January 2013 to 29 October 2023
- In the absence of systematic reviews of RCTs (e.g., for medication safety in pregnancy), systematic reviews of large observational studies were included. Targeted searches for single RCTs and other studies were conducted when systematic review data were limited or absent (Supplement 2. Search Strategy).

LoE und GoR

Table 2. CANMAT Criteria for Level of Evidence.

Level of evidence	Symbol: Efficacy Positive	Symbol: Efficacy Negative	Symbol: Perinatal safety	Criteria
1				High-quality meta-analyses with narrow confidence intervals or replicated RCTs with adequate sample size
2				Lower-quality meta-analyses with wide confidence intervals and/or one or more RCTs with adequate sample size
3				At least 1 small-sample RCT or high-quality, controlled observational studies
4				Pilot studies, uncontrolled trials, anecdotal reports or expert consensus opinion

Note. For Level 1 and Level 2, RCTs are required (adequate sample size is at least $n \geq 30$ per treatment arm). Recommendations from epidemiological data primarily arise from observational studies, where the highest level of evidence is usually Level 3. Higher order recommendations (e.g., principles of care) reflect higher level judgement of strength of evidence from various data sources and therefore are primarily Level 3 or 4 evidence. RCT = randomized controlled trial.

Table 3. CANMAT Criteria for Line of Treatment.

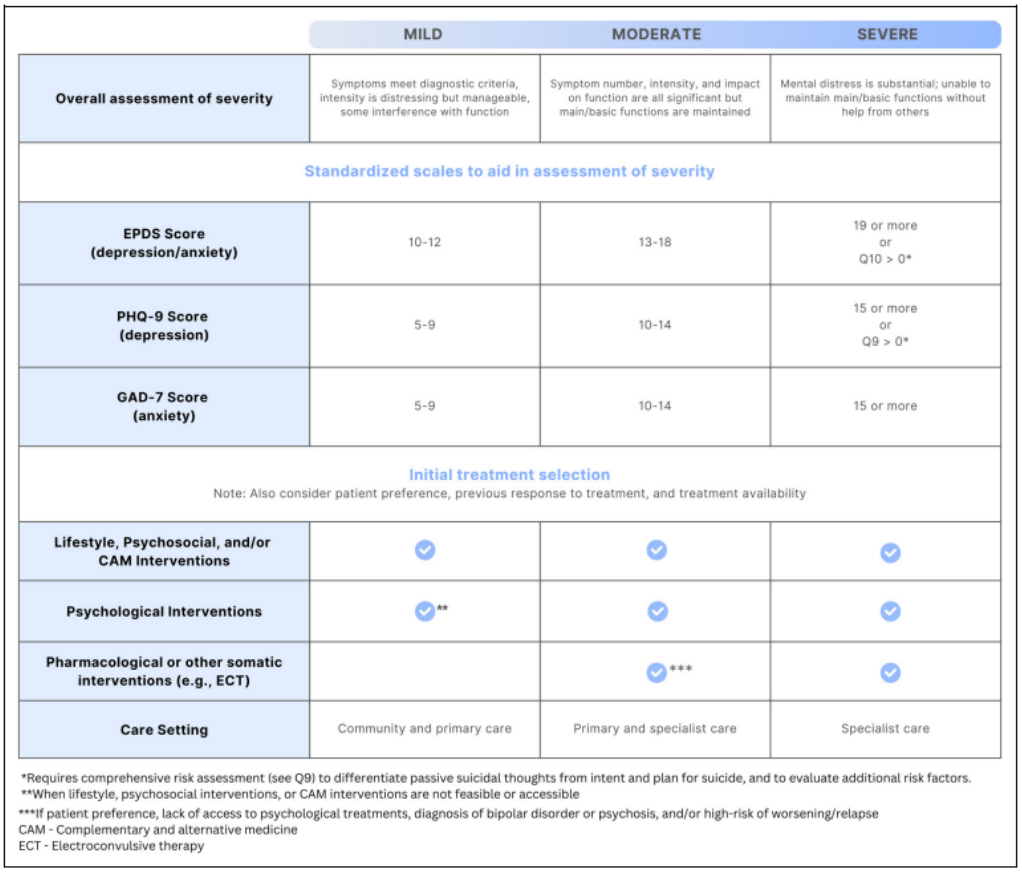
Line of treatment	Criteria[a]
First-line	Level 1 or Level 2 evidence plus clinical support
Second-line	Level 3 evidence or higher plus clinical support
Third-line	Level 4 evidence or higher plus clinical support
Not recommended	Level 1 or 2 evidence for lack of efficacy or safety concerns, plus clinical support

Note. CANMAT = Canadian Network for Mood and Anxiety Treatments.
[a]Clinical support reflects the authors' expert opinion/consensus on the relevance of the evidence on safety, efficacy and feasibility of the intervention. For pharmacological treatment recommendations, due to the paucity of perinatal-specific randomized controlled trials, Level 3 or 4 evidence on efficacy and safety in perinatal-specific populations might be considered sufficient for a first-line or second-line recommendation in the presence of Level 1 or 2 evidence for efficacy in non-perinatal populations.

Ergebnisse

General Treatment Considerations

As shown in Figure 1, depression, anxiety and related disorders of mild or moderate severity can often be successfully managed with non-pharmacological options alone, including with lifestyle, psychosocial, psychological and complementary and alternative medicine (CAM) interventions. Medications and other somatic treatments may then be used in addition when symptoms do not respond to non-pharmacological treatment alone. As also shown in Figure 1, medications are typically needed to successfully manage depression, anxiety and related disorders when symptoms are of moderate-severity or severe, and in the treatment of BD. They are also used to prevent relapse or recurrence of symptoms when an individual was taking medication for maintenance treatment prior to pregnancy. In these cases, non-pharmacological interventions may also be implemented to complement the pharmacological treatment (e.g., peer support programs or psychological therapy may still be beneficial alongside a medication treatment). Other somatic treatments, such as non-invasive neuromodulation or electroconvulsive therapy (ECT) may be needed when medication options have not led to adequate remission, or for ECT when there is very severe illness and a rapid response to treatment is required (e.g., acute psychosis or catatonia.



	MILD	MODERATE	SEVERE
Overall assessment of severity	Symptoms meet diagnostic criteria, intensity is distressing but manageable, some interference with function	Symptom number, intensity, and impact on function are all significant but main/basic functions are maintained	Mental distress is substantial; unable to maintain main/basic functions without help from others
Standardized scales to aid in assessment of severity			
EPDS Score (depression/anxiety)	10-12	13-18	19 or more or Q10 > 0*
PHQ-9 Score (depression)	5-9	10-14	15 or more or Q9 > 0*
GAD-7 Score (anxiety)	5-9	10-14	15 or more
Initial treatment selection Note: Also consider patient preference, previous response to treatment, and treatment availability			
Lifestyle, Psychosocial, and/or CAM Interventions	✓	✓	✓
Psychological Interventions	✓**	✓	✓
Pharmacological or other somatic interventions (e.g., ECT)		✓***	✓
Care Setting	Community and primary care	Primary and specialist care	Specialist care

*Requires comprehensive risk assessment (see Q9) to differentiate passive suicidal thoughts from intent and plan for suicide, and to evaluate additional risk factors.
**When lifestyle, psychosocial interventions, or CAM interventions are not feasible or accessible
***If patient preference, lack of access to psychological treatments, diagnosis of bipolar disorder or psychosis, and/or high-risk of worsening/relapse
CAM - Complementary and alternative medicine
ECT - Electroconvulsive therapy

Figure 1. How PMAD illness severity can guide initial treatment selection. For a given illness severity, the lowest checkmarked intervention type is typically needed, but interventions in higher rows may also be implemented to complement the effect of the main intervention.
PMAD = perinatal mood, anxiety and related disorder.
Source: Adapted from the Care Pathway for the Management of Perinatal Mental Health (Ontario Provincial Council for Maternal and Child Health).

Question 5. What Are the Recommendations for the Use of Psychological Interventions?

Psychological treatment is recommended as a first-line option for treating moderate-severity presentations of depression, anxiety, OCD and PTSD or in mild-severity illness when lifestyle and psychosocial interventions alone are not fully effective, or are not accessible. Severe forms of these illnesses will not generally respond adequately to psychological treatments alone, and pharmacotherapy or other somatic interventions (e.g., neuromodulation) may be required to attain remission. While medications are foundational for the successful treatment of BD, adjunctive psychological interventions (i.e., in addition to medication) can be helpful in the treatment of depressive episodes, in relapse prevention and to improve quality of life.

Depression and Anxiety

Psychological treatments are also effective in treating MDEs in pregnancy and postpartum, with and without comorbid anxiety symptoms (Level 1 ●).200,205,216–222 The modalities for which there is the most evidence for efficacy are the manualized therapies, such as CBT,200,205,216,217,220–222 IPT,200,205,217,218 mindfulness-based therapies (e.g., mindfulness- based stress reduction and mindfulness-based cognitive therapy),216,219,222 and behavioural activation (BA)223 (Level 1 ●).

Psychological treatments for depression and anxiety are typically delivered weekly, frequently ranging from 4–16 sessions, although there is also evidence for 1-day CBT workshops in the reduction of postpartum depressive and anxiety symptoms (Level 1 ●). 224–226. They are effective when delivered individually or in group format, in-person or in

virtual care (i.e., by telephone or video-conference) (Level 1 ●). 153,155,158,160,200,205,216–222,227–236

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Table 9. Psychological Interventions for the Treatment of PMADs.

PMAD	Line of treatment	Intervention	Level of evidence
Depression	First-line	CBT[a]	
		IPT[a]	
		Mindfulness-based therapies[a]	
		BA[a]	
		Guided internet-based self-help including iCBT and iBA in pregnancy	
	Second-line	Guided internet-based self-help interventions including iCBT and iBA postpartum	
Anxiety	First-line	CBT for anxiety symptoms	
		Mindfulness-based therapies for anxiety symptoms	
		Psychological therapies with CBT elements for symptoms of fear of childbirth	
	Second-line	Guided internet-based self-help for anxiety symptoms	
	Third-line	Guided iCBT for fear of childbirth	
OCD	Second-line	CBT with exposure and response prevention elements	
PTSD	Third-line	Trauma-focused psychological treatments with evidence in non-perinatal populations	
	Not recommended	Psychological debriefing after traumatic childbirth	
Bipolar disorder	Third-line	Adjunctive CBT for MDE and quality of life	
		Adjunctive family-focused therapy for MDE and quality of life	
		Adjunctive interpersonal and social rhythms therapy for MDE and quality of life	

Note. BA = behavioural activation; CBT = cognitive–behaviour therapy; IPT = interpersonal therapy; MDE = major depressive episode; OCD = obsessive–compulsive disorders; PMAD = perinatal mood, anxiety and related disorders; PTSD = post-traumatic stress disorder.
[a]For MDE and for those with elevated depressive symptoms (with or without MDE diagnosis).

Question 6. What Are the Recommendations for the Use of Pharmacological Interventions?

Medications are most often used in depressive disorders, anxiety disorders, OCD and PTSD when non-pharmacological therapies are ineffective, and as first-line treatment when the initial symptoms are moderate-to-severe or severe. They may also be used as initial treatments in patients with milder symptoms who are unable to access psychological interventions, or who prefer medication over psychotherapy.

Postpartum.

Antidepressants are also the mainstay of pharmacotherapy postpartum. It is expected that the efficacy of antidepressants would be similar in the postpartum as in nonperinatal periods, but there is also some RCT evidence for the efficacy of SSRIs over placebo in treating PPD specifically (Level 2 ◔).352 For those who are breastfeeding, there is reassuring data for several antidepressants in terms of their safety in lactation to guide recommendations about lines of treatment (Table 11). The only antidepressant not recommended in lactation is the TCA doxepin given its potential to cause excessive somnolence in exposed infants.281

Insufficient safety data exist for most newer agents. However, if a patient and clinician feel that the benefit of continuing that medication outweighs its drawbacks, they may select it, and close infant monitoring is recommended.

For those who are not breastfeeding, concerns about exposure to the infant do not apply, so general guidelines for treatment of MDD can be followed, also incorporating the possibility of postpartum-depression specific pharmacotherapies. Brexanolone (IV) and zuranolone (PO) (not yet available in Canada) are synthetic analogs of allopregnanolone that have been shown in RCTs to be effective for treating PPD in those who developed depression in the 3rd trimester of pregnancy or in the first 4 weeks postpartum specifically (Level 1 ●).252,253 The onset of symptom reduction appears to be within hours for brexanolone and within days for zuranolone. However, common side effects of these medications include headache, dizziness and drowsiness or sedation, and brexanolone requires about 72 h of continuous monitoring in an inpatient setting for the intravenous infusion due to the potential for excessive sedation and sudden loss of consciousness. There is as yet an insufficient amount of safety data on these agents in lactation, so until data in lactation are available, they can be considered outside of lactation where available, feasible to administer and not cost-prohibitive.

There have been 2 small RCTs that studied psychotropic medications vs. placebo (sertraline n=22, nortriptyline, n=51) for preventing PPD in euthymic individuals with a history of PPD not taking medication. Sertraline was protective against PPD (Level 3 ◐) but nortriptyline was not (Level 2 ◔).354 Given the uncertainty of the available evidence, clinicians are advised to consider risk for patient relapse on an individualized basis when making recommendations about whether to start (or restart) antidepressants in euthymic patients with a history of PPD in the postpartum period.

Table 11. Medications for Major Depressive Disorder in Lactation.

Line of treatment	Medications	Level of evidence (efficacy vs. placebo)		Justification for placement
		Non-perinatal	Postpartum	
First-line	Citalopram			
	Escitalopram			Most reassuring safety data of antidepressants
	Sertraline			
Second-line	Bupropion			Rare case reports of infant seizure
	Desvenlafaxine			Less safety data than first-line agents
	Duloxetine			Less safety data than first-line agents
	Fluoxetine			Longer half-life and higher RID than first- and second-line agents, more side effects reported, no severe concerns
	Fluvoxamine			Less tolerability at higher doses
	Mirtazapine			Less safety data than first-line agents and potential for maternal sedation
	Venlafaxine			Less tolerability than first-line agents
Third-line	Paroxetine			Downgraded due to possible higher risk for CV malformations in a future pregnancy
	Quetiapine			Maternal metabolic impacts, sedation
	Trazodone			Maternal tolerability concerns at high doses
	Tricyclics (except doxepin)		[a]	Maternal tolerability concerns
Not recommended	Doxepin	n/a	n/a	Concern about excessive infant sedation
Insufficient data	Agomelatine, brexanolone, dextromethorphan/bupropion, ketamine, levominacipran, mianserin, milnacipran, moclobemide, phenelzine, reboxetine, tranylcypromine, vilazodone, vortioxetine, zuranolone			

Note. Insufficient data = insufficient data on safety in pregnancy/lactation; not recommended = not recommended due to concerns about safety in lactation; n/a = not applicable as safety concerns outweigh the value of efficacy evidence.

[a]One trial identified in the systematic review of antidepressant efficacy for PPD ($n = 58$) found problem-solving therapy was superior to amitriptyline in the treatment of postpartum depression in Africa (Level 2).[353]

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Question 7. What Are the Recommendations for the Use of Neuromodulation?

No recommendations can be made at this time for the use of rTMS or tDCS perinatally for anxiety, OCD, PTSD or BD. ECT, which is typically delivered 2–3 times a week, requires a general anaesthetic and is associated with more adverse effects than less invasive treatments, is also included in this category. In non-perinatal populations, ECT is generally used in severe depression, mania, psychosis and/or acute suicidality.7,11 Maintenance ECT is vital in some cases of refractory depression, and ECT may work particularly quickly in treating acute psychotic depression and in treating mania, so its use is clinically important in the perinatal period as well. Studies on ECT safety in the perinatal period are limited to

case studies or series, often with no comparison groups, and there are no RCTs.372,373 Reports of ECT use in pregnancy are limited to severe depression, psychosis and mania (with and without medications). ECT appears relatively safe even when administered during the first trimester of pregnancy. Adverse effects reported in pregnancy include fetal arrhythmia, fetal bradycardia, premature birth, abdominal pain, uterine contractions, vaginal bleeding, placental abruption, threatened abortion and fetal death, but it is difficult to quantify risk attributable to ECT in these high-risk cases (Level 3 ◐).

Based on these considerations, ECT is an appropriate firstline intervention for acute depression with severe psychotic or catatonic features, acute suicidality or deteriorating physical condition in pregnancy. ECT is also recommended for severe presentations of depression, mania, mixed states or psychosis, when pharmacological treatments are not successful. ECT in pregnancy should occur in close collaboration with anaesthesia and obstetrical services. While most general anaesthetics and muscle relaxants used in ECT administration are considered compatible with pregnancy, several strategies to optimize safety of the patient and foetus have been recommended.374 These include administering antinausea agents prior to the procedure, adding sodium citrate (oral) to prevent aspiration, avoiding hyperventilation prior to induction (as pregnancy is already a state of mild hyperventilation), elevation of the right hip (especially after 20 weeks gestation) to avoid aortal-caval compression of placental blood flow and fetal monitoring before, during and after procedure (including continuous fetal monitoring throughout the procedure and for some time afterward once it is possible to do so based on the number of weeks gestation). Intubation may be required depending on the stage of pregnancy to avoid the risk of aspiration.

Safety concerns with ECT are less in the postpartum relative to pregnancy. It can be used for severe cases as in non-perinatal populations with consideration given to the perinatal context (e.g., needs for assistance with childcare). It is generally recommended that patients can resume breastfeeding immediately after anaesthesia as the passage of anaesthetic medications into the breastmilk is minimal.375

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American College of Obstetricians and Gynecologists (ACOG), 2023 [1].

Treatment and Management of Mental Health Conditions During Pregnancy and Postpartum: ACOG Clinical Practice Guideline No. 5

Methodik

<u>Grundlage der Leitlinie</u>

- Repräsentatives Gremium; unklar
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt; trifft zu aber Umgang damit im Konsensusprozess nicht erläutert
- Systematische Suche, Auswahl und Bewertung der Evidenz; trifft zu

- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt; Konsensusprozess nicht beschrieben
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt; trifft zu
- Regelmäßige Überprüfung der Aktualität gesichert; trifft zu.

Recherche/Suchzeitraum:

- ACOG medical librarians completed a comprehensive literature search for primary literature within Cochrane Library, Cochrane Collaboration Registry of Controlled Trials, EMBASE, PubMed, and MEDLINE.
- the literature search was limited to the end date of the AHRQ search until 2021.
- An updated literature search was completed in December 2022 and reviewed by two members of the writing team using the same systematic process as the original literature search. A final supplemental literature search was performed in February 2023 to ensure that any newly published high-level sources were addressed in the Clinical Practice Guideline

LoE und GoR

- A modified GRADE (Grading of Recommendations Assessment, Development and Evaluation) evidence-todecision framework was applied to interpret and translate the evidence into draft recommendation statements, which were classified by strength and evidence quality (54, 55). Ungraded Good Practice Points were incorporated to provide clinical guidance in the case of extremely limited or nonexistent evidence. They are based on expert opinion as well as review of the available evidence (56).

Empfehlungen

ACOG recommends that psychotherapy be considered a first-line treatment for mild-to moderate perinatal depression. (STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)

Psychotherapy, including CBT or interpersonal therapy, is an effective treatment for perinatal depression (98). The use of psychotherapy as an initial treatment approach aligns with the recommendations of multiple professional societies, including the American Psychiatric Association (99) and the National Institute for Health and Care Excellence (76). Although psychotherapy is appropriate as a first-line treatment for some pregnant and postpartum people, shared decision making and individualized patient-centered care are prudent. For example, for individuals who previously did not respond to psychological interventions, those for whom culturally responsive psychotherapy is not accessible, or those for whom the resource commitment for psychotherapy precludes engagement, pharmacotherapy should be considered as a first-line treatment option. Access to psychotherapy remains limited for many pregnant and postpartum individuals, including but not limited to those who are non–English-speaking, uninsured, or geographically isolated. Future research on the role of psychotherapy embedded within digital mental health tools may show promise in improving access to evidence-based psychotherapy.

ACOG recommends that selective serotonin reuptake inhibitors be used as first-line pharmacotherapy for perinatal depression. Serotonin-norepinephrine reuptake inhibitors are reasonable alternatives. Pharmacotherapy should be individualized based on prior response to therapy (if applicable). If there is no pharmacotherapy history, sertraline or escitalopram are reasonable first-line medications. (STRONG RECOMMENDATION, LOW-QUALITY EVIDENCE)

Hintergrund

No randomized trials have evaluated the efficacy or safety of pharmacotherapy for antenatal depression. The paucity of high-quality evidence is of particular importance considering the number

of pregnant women exposed to antidepressants (100). Clinical decision making regarding pharmacology relies on extrapolation of efficacy data from the general population. Meta-analytic data demonstrate antidepressant medications to be more effective than placebo (101). This conclusion holds true for the use of antidepressants in primary care settings, where SSRIs have a median number needed to treat of 7 and a number needed to harm of 20–90 (102). Although the efficacy of adequately dosed SSRIs or SNRIs is unlikely to differ due to pregnancy or lactation, the potential pregnancy associated pharmacokinetic changes raise concerns about how to best achieve a therapeutic response (103).

For individuals with a prior history of pharmacologic treatment of depression, any previously effective medication should be considered first-line treatment for reinitiation during pregnancy and postpartum. For those without a history of effective treatment or with incident depression, SSRIs are preferred as first-line treatment. Although SSRIs and SNRIs are both effective treatments for major depressive disorder in adults, SSRIs are generally preferred because of their safety and tolerability. Specifically, when compared with unexposed women with depression, SNRIs were associated with an increased risk of preeclampsia in two studies (8.8% vs 5.4%, adjusted relative risk 1.52, 95% CI 1.25–1.83; 4.5% vs 2.4%, adjusted relative risk 1.95, 95% CI 1.25–3.03) (52). Similarly, one cohort study (N59,014) identified an increased risk of spontaneous abortion in individuals exposed to SNRIs in the first trimester compared with those with a history of depression (15.0% vs 8.1%) and found a 1.7-fold increased risk (95% CI 1.2–2.6) of spontaneous abortion after adjusting for confounders and correcting for induced abortions (104). However, the quality of evidence for the risks of preeclampsia and spontaneous abortion is low; thus, if an individual is stable on an SNRI or has had therapeutic benefit in the past, the risk– benefit balance likely favors use of the previously effective medication. Although some data suggest a class effect for SSRIs (105), other data suggest that sertraline and escitalopram are favored first-line SSRIs because of their efficacy and tolerability profiles (86). However, other factors, such as comorbid illnesses, potential drug–drug interactions, cost, and side-effect profile, should be considered for each individual patient.

Although most SSRIs are generally well-tolerated, side effects can occur. These include nausea, dry mouth, insomnia, diarrhea, headache, dizziness, agitation or anxiety, drowsiness, and sexual dysfunction. Most of these side effects dissipate with time, with the notable exception of sexual dysfunction. Specifically, some patients, particularly those with comorbid anxiety symptoms, report an initial exacerbation of agitation or anxiety symptoms. This particular side effect is often mitigated by starting with half of the lowest dose and gradually up-titrating over 4–10 days. Insofar as most individuals with perinatal depression have concomitant anxiety symptoms (4), many experts consider dose titration to be a best practice for initiating treatment for perinatal depression. In addition, activating antidepressants such as fluoxetine, duloxetine, venlafaxine, and bupropion may exacerbate anxiety symptoms. Thus, in someone with moderate-to-severe comorbid anxiety, alternatives to these medications should be considered when appropriate.

Selective serotonin reuptake inhibitors are perhaps one of the best studied class of medications in pregnancy. Although randomized trials to assess safety have not been conducted, multiple observational studies support a favorable safety profile. Some of the safety risks that have been evaluated in the literature, referencing some of the highest quality data available, are described in Table 2. Importantly, much of the published literature uses a comparison framework of exposure to antidepressant medications for the treatment of depression compared with no exposures (ie, no history of depression and no use of antidepressant medications). These types of comparisons can lead to false or misleading conclusions because they do not account for the underlying medical illness.

The two neonatal risks consistently identified in the literature when the proper comparison groups were used include persistent pulmonary hypertension of the newborn (PPHN) and neonatal adaptation syndrome (with resultant neonatal intensive care unit [NICU] admission). Persistent pulmonary hypertension of the newborn is a rare but potentially fatal condition, characterized clinically by respiratory distress within the first hours of life and carrying a 10– 20% risk of mortality. Biological plausibility for an association between SSRI exposure in utero and PPHN exists because serotonin exposure can cause vasoconstriction and smooth muscle cell proliferation in the fetal lung. In 2006, the U.S. Food and Drug Administration (FDA) issued a public health advisory regarding

SSRIs based on a case–control study that identified increased odds of PPHN with exposure to SSRIs after 20 weeks of gestation (adjusted odds ratio [aOR] 6.1, 95% CI 2.2–16.8) (106). Multiple observational studies and meta-analyses have corroborated the association between antenatal exposure to SSRIs or SNRIs and PPHN (107–109). When ranked by individual drug-related risk, sertraline ranked as the least likely to be associated with PPHN, followed by escitalopram (108).

Notably, each of the aforementioned studies is limited by confounding by indication. Attempting to account for this residual bias, a cohort study nested within an administrative database of individuals with Medicaid insurance defined a relevant exposure to antidepressants as 90 days before delivery through delivery (110). Women were considered exposed if they filled at least one prescription for an antidepressant and International Classification of Diseases, Ninth Revision diagnostic codes defined the outcome of PPHN. Analyses were restricted to women with a diagnosis of depression and used propensity score stratification to address additional confounding by disease severity. The primary analysis demonstrated no increased odds of PPHN for those exposed to SSRIs (aOR 1.12, 95% CI 0.95–1.31) or non- SSRI antidepressants (aOR 1.01, 95% CI 0.76–1.35). Secondary analyses, focused on primary PPHN, restricted the sample by excluding preterm infants and infants with congenital cardiac malformations or lung abnormalities. These analyses identified increased odds of PPHN for SSRIs (aOR 1.28, 95% CI 1.01–1.64) but not for non-SSRI antidepressants (aOR 1.14, 95% CI 0.74–1.74). This body of literature, in its totality, suggests that there may be an increased risk of PPHN associated with SSRI exposure. Importantly, the absolute risk of PPHN is low (approximately 1–2/1,000 additional cases of PPHN) and should be balanced against the significant risks associated with untreated depression. Accordingly, the FDA updated their guidance and advised clinicians to not alter their clinical practice of treating depression during pregnancy due to concerns for PPHN (106).

Neonatal adaptation syndrome includes a constellation of neonatal symptoms that have been associated with SSRI and SNRI exposure in utero, including irritability, restlessness, tremors, hyperreflexia, hypoglycemia, hypothermia, disruptions in sleep, poor feeding, and, rarely, seizures. Neonatal adaptation symptoms typically emerge within the first few days of life and resolve within 2 weeks (111). The estimated prevalence of neonatal adaptation syndrome varies widely due to heterogeneity in the case definition and ranges in the published literature from 5% to 85% (112), although most studies estimate the incidence to be 10% to 30%. Fluoxetine and paroxetine have been implicated more commonly in neonatal adaptation syndrome (113).

The phenomenology of neonatal adaptation syndrome is poorly understood. Some hypothesize that the symptoms are related to serotonergic withdrawal, whereas others suggest that they are related to serotonergic toxicity. As with much of the literature on antenatal SSRI exposure, many of the data compare newborns exposed to antidepressant medications with newborns not exposed to either perinatal depression (or with an unknown depression status) or antidepressant medications (112, 114). Importantly, although neonatal adaptation syndrome is self-limited without evidence of long-term risks, pregnant individuals taking an SSRI or SNRI should deliver in a hospital to facilitate pediatric assessment and monitoring if needed. Supportive measures, such as skin-to-skin contact and frequent feedings, can be used for neonatal symptom management.

To mitigate against the risk of neonatal adaptation syndrome, some have suggested discontinuing or decreasing the dose of the SSRI or SNRI in the third trimester, before delivery. Observational data suggest that these changes are not associated with neonatal adaptation syndrome risk mitigation (58, 59). Moreover, tapering antidepressant medication increases the risk of symptom relapse. Thus, discontinuing or decreasing the dose of the antidepressant before delivery to reduce the risk of neonatal adaptation syndrome is not recommended clinical practice.

Two randomized trials (N5162, N538) have evaluated the efficacy of SSRIs (specifically sertraline) for the treatment of postpartum depression (115, 116). In these studies, sertraline improved response and remission rates relative to placebo, although the small sample size and loss to follow-up limit the quality of this evidence (52).

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ACOG recommends consideration of brexanolone administration in the postpartum period for moderate to-severe perinatal depression with onset in the third trimester or within 4 weeks postpartum. The decision to use brexanolone should balance the benefits (eg, rapid onset of action) with the risks and challenges (eg, limited access, high cost, lack of data supporting safety with breastfeeding, requirement for inpatient monitoring during the infusion, lack of efficacy data beyond 30 days). (STRONG RECOMMENDATION, MODERATE-QUALITY EVIDENCE)

Research Innovation and Sustainable Pan-European Network in Peripartum Depression Disorder (Riseup-PPD), 2023 [2]

Evidence-based clinical practice guidelines for prevention, screening and treatment of peripartum depression

Methodik

Grundlage der Leitlinie

- Repräsentatives Gremium; trifft zu
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt; trifft zu aber Umgang damit im Konsensusprozess nicht erläutert
- Systematische Suche, Auswahl und Bewertung der Evidenz; trifft zu
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt; trifft teilweise zu

- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt; trifft teilweise zu
- Regelmäßige Überprüfung der Aktualität gesichert; unklar

Recherche/Suchzeitraum:

- The search strategy included systematic reviews and meta-analysis only
- Treatment of PPD: Psychological interventions: CINAHL (Ebsco), the Cochrane Database of Systematic Reviews, Medline (Ebsco), PsycInfo (Ebsco) and Web of Science (Clarivate) were all searched from 2020 until 16 January 2023
- Treatment of PPD: Pharmacological interventions: CINAHL (Ebsco), the Cochrane Database of Systematic Reviews, Medline (Ebsco), PsycInfo (Ebsco) and Web of Science (Clarivate) were all searched from 2010 until 3 January 2023.

LOE:

To assess the quality of the evidence, the GRADE system's four levels (high, moderate, low and very low) were used.

GoR:

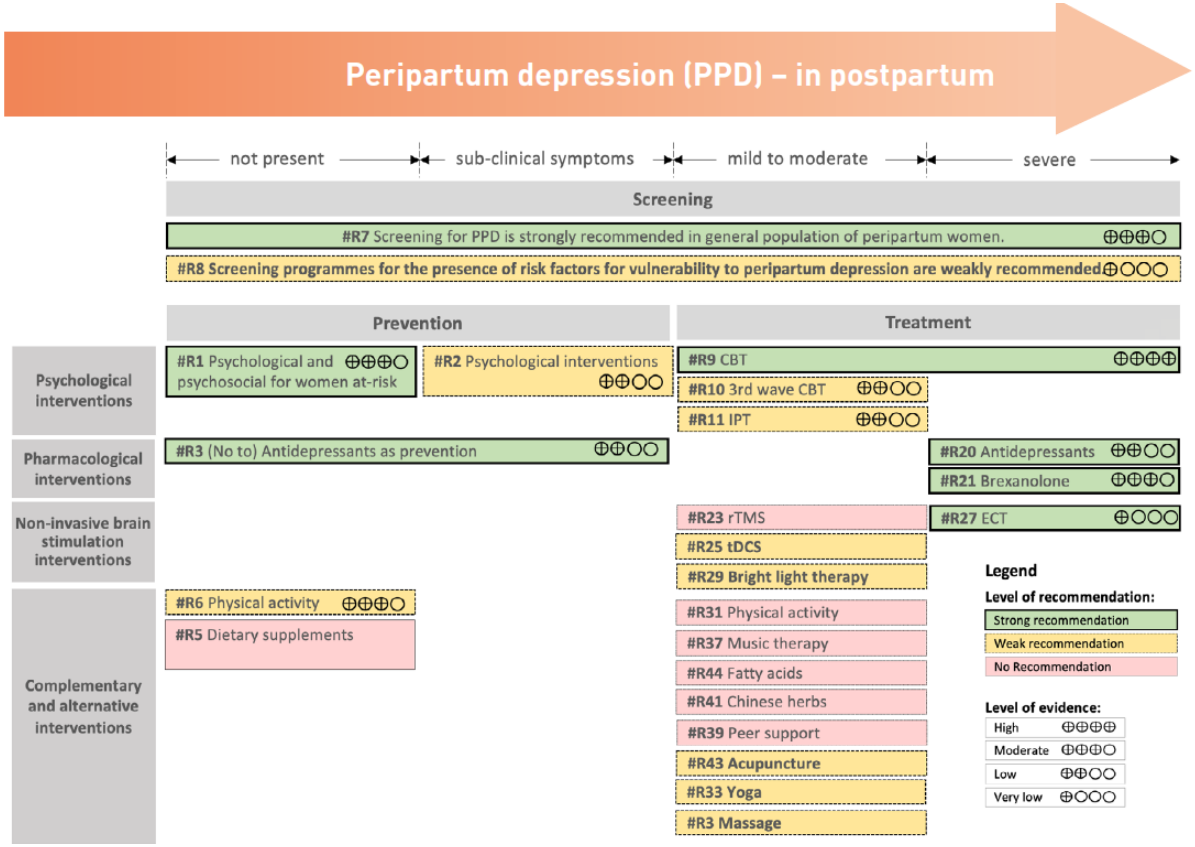
Following the GRADE framework, two types of recommendations were used: strong recommendations and weak recommendations. A strong recommendation is suggested when the RU-GDG finds strong evidence that desirable effects greatly overweight the undesirable ones. A weak recommendation is suggested when the RU-GDG is not absolutely certain of the balance between desirable and undesirable effects and the factors that support it, and therefore, increased caution is warranted.

Additionally, a Good Practice Point (GPP) may be added when there is a recommendation for best practice based on the experience of the RU-GDG.

Methodische Hinweise:

Es wurden nur systematische Reviews und Meta-Analysen berücksichtigt. Fragestellungen, zu denen Evidenz aus diesen Quellen nicht vorliegt, wurden entsprechend in der Leitlinie vermutlich nicht umfänglich berücksichtigt zumal die Fragen nicht auf bestimmte Arzneimittel oder Methoden fokussierten (z.B. Are pharmacological interventions effective in treating PPD?"). Die vorliegenden Informationen können daher nicht als umfassende Einordnung aller zur Verfügung stehenden Therapieoptionen herangezogen warden.

Ergebnisse


Peripartum depression (PPD) – in postpartum
not present
sub-clinical symptoms
mild to moderate
severe
Screening
#R7 Screening for PPD is strongly recommended in general population of peripartum women. ⊕⊕⊕◯
#R8 Screening programmes for the presence of risk factors for vulnerability to peripartum depression are weakly recommended ⊕◯◯◯
Prevention
Treatment
Psychological interventions
#R1 Psychological and psychosocial for women at-risk ⊕⊕⊕◯
#R2 Psychological interventions ⊕⊕◯◯
#R9 CBT ⊕⊕⊕⊕
#R10 3rd wave CBT ⊕⊕◯◯
#R11 IPT ⊕⊕◯◯
Pharmacological interventions
#R3 (No to) Antidepressants as prevention ⊕⊕◯◯
#R20 Antidepressants ⊕⊕◯◯
#R21 Brexanolone ⊕⊕⊕◯
Non-invasive brain stimulation interventions
#R23 rTMS
#R25 tDCS
#R29 Bright light therapy
#R27 ECT ⊕◯◯◯
Complementary and alternative interventions
#R6 Physical activity ⊕⊕⊕◯
#R5 Dietary supplements
#R31 Physical activity
#R37 Music therapy
#R44 Fatty acids
#R41 Chinese herbs
#R39 Peer support
#R43 Acupuncture
#R33 Yoga
#R3 Massage
Legend
Level of recommendation:
Strong recommendation
Weak recommendation
No Recommendation
Level of evidence:
High ⊕⊕⊕⊕
Moderate ⊕⊕⊕◯
Low ⊕⊕◯◯
Very low ⊕◯◯◯

Interventions for treating PPD				
Psychological treatment				
9	Cognitive-behavioural therapy (CBT) is strongly recommended for the treatment of depressive symptoms during pregnancy and postpartum.	Strong	High ⊕⊕⊕⊕	Most women find psychological treatment acceptable and were satisfied. The major advantage is that for most women, any undesirable effects will probably be trivial, and no adverse effects for pregnant women, mothers and foetus/infants are expected.
10	Third wave CBT therapies, including behavioural activation and mindfulness techniques, are weakly recommended for the treatment of depressive symptoms during pregnancy and postpartum.	Weak	Low ⊕⊕◯◯	There is a lack of information about acceptability and satisfaction with third-wave CBT therapies. However, undesirable and adverse effects for pregnant women, mothers and foetus/infants are not expected.
11	Interpersonal therapy (IPT) is weakly recommended for the treatment of depressive symptoms during pregnancy and postpartum.	Weak	Low ⊕⊕◯◯	There is a lack of information about acceptability and satisfaction with IPT However, undesirable and adverse effects for pregnant women, mothers and foetus/infants are not expected.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Pharmacological treatment				
Postpartum				
20	It is strongly recommended to treat depression during the postpartum period with antidepressant medication, after careful consideration of individual risk-benefit ratio for each woman and her child if breastfed. The decision-making about antidepressant intervention should consider the history of depression recurrence and severity in the woman, previous response to the intervention, and individual preference as well as the health condition of the breastfed child.	Strong	Low ⊕⊕◯◯	Few data are available about the efficacy of antidepressant intervention in postpartum. However, as opposed to reproductive safety data about antidepressants in pregnancy, there is substantially less data about the short- and long-term safety of children exposed to antidepressant while breastfed. However, the risk of untreated depression and the benefits of breastfeeding on those negative outcomes needs to be weighed in each woman and child individually. In case a woman does not breastfeed, there is weak evidence of the effectiveness of antidepressant treatment for postpartum depression, however, there is also no risk to the child to be considered.

21	It is strongly recommended to use brexanolone for moderate to severe postpartum depression treatment if available and if accepted as a treatment option by the woman.	Strong	Moderate ⊕⊕⊕◯	The strong recommendation is based on the clinical effectiveness of this intervention. However, it must be considered that few aspects may affect its use : (i) need of inpatient care, which may be less acceptable for women, due to the possibility of separation of the newborn; (ii) breastfeeding cessation for 3 days, which also may affect women's acceptability of the intervention; (iii) the very high cost, making the intervention less accessible than others; (iv) there is scarcity of evidence on the safety of brexanolone exposure via breast milk on the infant. Brexanolone is currently not licensed In Europe. Therefore, although brexanolone is strongly recommended for moderate to severe cases of depression, its use requires careful discussion between the woman and her HCP.

#	Recommendation	Strength of the recommendation	Quality of the evidence	Comments
Electroconvulsive therapy (ECT)				
Postpartum				
27	ECT is strongly recommended for the treatment of therapy resistant or life-threatening severe depression in the postpartum period.	Strong	Very Low ⊕◯◯◯	ECT is a relatively fast-acting treatment that seems to be beneficial in severe cases of postpartum depression. Risks of adverse effects (prolonged seizures due to co-administered medication and transient memory loss particularly after the first ECT sessions) are small. ECT should be offered within specialised hospitals to women presenting severe depression (with or without psychotic features) which did not respond to previous regular treatment or in need of urgent treatment due to life-threatening situations.

4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library - Cochrane Database of Systematic Reviews (Issue 4 of 12, April 2025) am 10.04.2025

#	Suchschritt
1	MeSH descriptor: [Depression, Postpartum] explode all trees
2	(perinatal OR (peri NEXT natal) OR postnatal OR (post NEXT natal) OR postpart* OR (post NEXT part*) OR peripart* OR (peri NEXT part*) OR prenatal OR (pre NEXT natal) OR antenatal OR (ante NEXT natal) OR antepartum OR (ante NEXT partum) OR postpregnan* OR (post NEXT pregnan*) OR postbirth OR birth OR childbirth OR puerperium OR puerperal OR maternal):ti,ab,kw
3	MeSH descriptor: [Depression] explode all trees
4	MeSH descriptor: [Depressive Disorder] explode all trees
5	(depress*):ti,ab,kw
6	(#2) AND (#3 OR #4 OR #5)
7	#1 OR #6
8	#7 with Cochrane Library publication date from Apr 2020 to present
9	#7 with Cochrane Library publication date from Apr 2023 to present
10	#8 NOT #9

Leitlinien und systematische Reviews in PubMed am 10.04.2025

verwendete Suchfilter für Leitlinien:
Konsentierter Standardfilter für Leitlinien (LL), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 21.06.2017.

verwendete Suchfilter für systematische Reviews:
Konsentierter Standardfilter für Systematische Reviews (SR), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 15.01.2025.

#	Suchschritt
	Leitlinien
1	depression, postpartum[mh]
2	postpartum period[mh] OR peripartum period[mh] OR maternal health[mh] OR puerperal disorders[mh] OR postnatal care[mh]
3	perinatal[tiab] OR peri natal[tiab] OR postnatal[tiab] OR post natal[tiab] OR postpart*[tiab] OR post part*[tiab] OR peripart*[tiab] OR peri part*[tiab] OR prenatal[tiab] OR pre natal[tiab] OR antenatal[tiab] OR ante natal[tiab] OR antepartum[tiab] OR ante partum[tiab] OR postpregnan*[tiab] OR post pregnan*[tiab] OR postbirth[tiab] OR birth[tiab] OR childbirth[tiab] OR puerperium[tiab] OR puerperal[tiab] OR maternal[tiab]
4	depression[mh] OR depressive disorder[mh]
5	depress*[tiab]
6	dysthymi*[tiab] OR dysphori*[tiab] OR melanchol*[tiab] OR mood[tiab]

#	Suchschritt
7	(#2 OR #3) AND (#4 OR #5 OR #6)
8	depress*[ti]
9	#1 OR #7 OR #8
10	(#9) AND (Guideline[ptyp] OR Practice Guideline[ptyp] OR guideline*[ti] OR Consensus Development Conference[ptyp] OR Consensus Development Conference, NIH[ptyp] OR recommendation*[ti])
11	(#10) AND ("2020/04/01"[PDAT] : "3000"[PDAT])
12	(#11) NOT ("retracted publication"[pt] OR "retraction notice"[pt] OR "retraction of publication"[pt] OR "preprint"[pt])
	systematische Reviews
13	#3 AND (#4 OR #5)
14	#1 OR #13
15	(#14) AND ("systematic review"[pt] OR "meta-analysis"[pt] OR "network meta-analysis"[mh] OR "network meta-analysis"[pt] OR (systematic*[tiab] AND (review*[tiab] OR overview*[tiab])) OR metareview*[tiab] OR umbrella review*[tiab] OR "overview of reviews"[tiab] OR meta-analy*[tiab] OR metaanaly*[tiab] OR metanaly*[tiab] OR meta-synthes*[tiab] OR metasynthes*[tiab] OR meta-study[tiab] OR metastudy[tiab] OR integrative review[tiab] OR integrative literature review[tiab] OR evidence review[tiab] OR (("evidence-based medicine"[mh] OR evidence synthes*[tiab]) AND "review"[pt]) OR ((("evidence based"[tiab:~3]) OR evidence base[tiab]) AND (review*[tiab] OR overview*[tiab])) OR (review[ti] AND (comprehensive[ti] OR studies[ti] OR trials[ti])) OR ((critical appraisal*[tiab] OR critically appraise*[tiab] OR study selection[tiab] OR ((predetermined[tiab] OR inclusion[tiab] OR selection[tiab] OR eligibility[tiab]) AND criteri*[tiab]) OR exclusion criteri*[tiab] OR screening criteri*[tiab] OR systematic*[tiab] OR data extraction*[tiab] OR data synthes*[tiab] OR prisma*[tiab] OR moose[tiab] OR entreq[tiab] OR mecir[tiab] OR stard[tiab] OR strobe[tiab] OR "risk of bias"[tiab]) AND (survey*[tiab] OR overview*[tiab] OR review*[tiab] OR search*[tiab] OR analysis[ti] OR apprais*[tiab] OR research*[tiab] OR synthes*[tiab]) AND (literature[tiab] OR articles[tiab] OR publications[tiab] OR bibliographies[tiab] OR published[tiab] OR citations[tiab] OR database*[tiab] OR references[tiab] OR reference-list*[tiab] OR papers[tiab] OR trials[tiab] OR studies[tiab] OR medline[tiab] OR embase[tiab] OR cochrane[tiab] OR pubmed[tiab] OR "web of science" [tiab] OR cinahl[tiab] OR cinhal[tiab] OR scisearch[tiab] OR ovid[tiab] OR ebsco[tiab] OR scopus[tiab] OR epistemonikos[tiab] OR prospero[tiab] OR proquest[tiab] OR lilacs[tiab] OR biosis[tiab])) OR "technical report"[pt] OR HTA[tiab] OR technology assessment*[tiab] OR technology report*[tiab])
16	(#15) AND ("2020/04/01"[PDAT] : "3000"[PDAT])
17	(#16) NOT "The Cochrane database of systematic reviews"[Journal]
18	(#17) NOT ("retracted publication"[pt] OR "retraction notice"[pt] OR "retraction of publication"[pt] OR "preprint"[pt])
	systematische Reviews ohne Leitlinien
19	(#18) NOT (#12)
20	(#19) AND ("2023/04/01"[PDAT] : "3000"[PDAT])

#	Suchschritt
21	#19 NOT #20

Iterative Handsuche nach grauer Literatur, abgeschlossen am 22.04.2025

- Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)
- National Institute for Health and Care Excellence (NICE)
- Scottish Intercollegiate Guideline Network (SIGN)
- World Health Organization (WHO)
- Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF)
- Alberta Health Service (AHS)
- European Society for Medical Oncology (ESMO)
- National Comprehensive Cancer Network (NCCN)
- ECRI Guidelines Trust (ECRI)
- Dynamed / EBSCO
- Guidelines International Network (GIN)
- Trip Medical Database

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3. **Vigod SN, Frey BN, Clark CT, Grigoriadis S, Barker LC, Brown HK, et al.** Canadian Network for Mood and Anxiety Treatments 2024 Clinical practice guideline for the management of perinatal mood, anxiety, and related disorders. Can J Psychiatry 2025:7067437241303031.

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[B] **McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C.** PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. J Clin Epidemiol 2016;75:40-46. https://doi.org/10.1016/j.jclinepi.2016.01.021

Beteiligung von Fachgesellschaften und der AkdÄ zu Fragen der Vergleichstherapie nach §35a Abs. 7 SGB V i.V.m. VerfO 5. Kapitel § 7 Abs. 6

Verfahrens-Nr.: 2025-B-099

Verfasser	
Name der Institution	- Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde e. V. (DGPPN) - Deutsche Gesellschaft für Psychoanalyse, Psychotherapie, Psychosomatik und Tiefenpsychologie (DGPT) - Deutsche Gesellschaft für Gynäkologie und Geburtshilfe (DGGG) - Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin (DEGAM)
Datum der Erstellung	23. Mai 2025

(Bei mehreren beteiligten Fachgesellschaften bitte mit entsprechenden Angaben.)

Indikation
Behandlung von Erwachsenen nach der Geburt mit einer postpartalen Depression (ppD).
Fragen zur Vergleichstherapie
Was ist der Behandlungsstandard in o.g. Indikation unter Berücksichtigung der vorliegenden Evidenz? Wie sieht die Versorgungspraxis in Deutschland aus? *(Bitte begründen Sie Ihre Ausführungen; geben Sie ggf. zitierte Quellen in einer Referenzliste an.)*
Für die Behandlung peripartaler psychischer Störungen wird aktuell eine deutsche S3-Leitlinie erstellt (PERIPSYCH). Die Fertigstellung ist für 2026 geplant. Für die Behandlung der prä- und postpartalen Depression wurde im Rahmen einer European Cooperation in Science and Technology (EU COST) Action unter der Bezeichnung „Sustainable Pan-European Network in Peripartum Depression Disorder“ (Riseup-PPD, CA18138) eine europäische Praxis-Leitlinie im Oktober 2023 fertig gestellt (1,2). Eine deutsche Übersetzung ist in Arbeit (3). Daher wird im Folgenden auf diese relativ aktuelle Evidenz verwiesen (Fullversion S. 60ff, Tabellen ab S. 83, Short Version S.40-41). Eine zusätzliche Veröffentlichung im British Journal of Psychiatry ist bald verfügbar (4). Es kann eine Prävalenz postpartaler Depressionen (ppD) von 10-15% bei Müttern und 5-10 % bei Vätern angenommen werden (5,6,28). Diese werden noch viel zu selten erkannt und behandelt (7-10). Bei Nichtbehandlung neigen die postpartalen Depressionen zur Chronifizierung mit oft

langfristigen Folgen für die Betroffenen und insbesondere auch für die Kinder (11,12). Eine frühe Behandlung ist essenziell, um diese Risiken zu reduzieren (13).
Bei der Behandlung der ppD muss immer der mögliche Einfluss auf die Versorgung und das Wohlergehen der Kinder mitberücksichtigt werden (15). In Bezug auf pharmakologische Behandlung bedeutet dies:

- Stillt eine Mutter, sind Medikamente auszuwählen, die mit dem Stillen kompatibel sind (5).
- Muss eine Mutter/ein Vater ein Kind nachts alleine versorgen müssen sedierende Medikamente oder die Versorgung entsprechend an diese Situation angepasst werden.

Psychotherapie:
Eine hohe Evidenz besteht für die kognitive Verhaltenstherapie bei allen Schweregraden. Eine schwache Evidenz besteht für die dritte Welle der VT sowie für die Interpersonelle Psychotherapie und die psychodynamische Therapie (29).

Im Rahmen der psychotherapeutischen Behandlung ist in der Postpartalzeit besonderen Wert auf die elterliche Selbstwirksamkeit sowie die Qualität der Eltern-Kind-Interaktion zu legen (16). Aufgrund der bisher unzureichenden Studienlage besteht hier lediglich eine schwache Evidenz. Klinische Untersuchungen konnten jedoch zeigen, dass Einschränkungen in der mütterlichen Interaktionsfähigkeit durch spezielle bindungs- und affektfokussierte Therapieverfahren behandelt werden und bei frühzeitiger Erkennung die schwerwiegenden Folgen für das Kind schon in dieser frühen Lebensphase positiv beeinflussen (21, 22).

Die verbesserte Interaktion der Eltern kann auch für die betroffene Mutter therapeutisch wirksam sein. Klinische Untersuchungen haben gezeigt, dass eine Behandlung, die interaktionale Interventionen umfasst, neben einer gesünderen Mutter-Kind-Bindung auch zu einem stärkeren Rückgang der mütterlichen Depression führt (23).

Medikamentöse Therapie:
Laut der europäischen Leitlinie wird stark empfohlen, mittelgradige und schwere Depressionen in der Zeit nach der Geburt mit antidepressiven Medikamenten zu behandeln (schwache Evidenz), analog der Behandlung allgemeiner Depressionen gemäß NVL. Dabei soll eine sorgfältige Abwägung des individuellen Nutzen-Risiko-Verhältnisses für jede Frau und ihr Kind erfolgen, wenn es gestillt wird.

Bei einer postpartalen medikamentösen Neueinstellung sollten Antidepressiva eingesetzt werden, die eine geringe relative Dosis aufweisen, also nur in geringem Umfang über die Muttermilch zum Kind gelangen und die im kindlichen Organismus nicht akkumulieren.

Nach diesen Kriterien gehören Sertralin und Paroxetin in der Stillzeit zu den SSRI der Wahl (21,24). An sedierenden Antidepressiva gelten Mirtazapin und Amitriptylin als Mittel der Wahl. Laut www.embryotox.de sind folgende Antidepressiva mit dem Stillen kompatibel:

Sertralin relative Dosis: 2%, Mittel der Wahl
Paroxetin relative Dosis: 0,5 – 2%, Mittel der Wahl

Spiegelbestimmungen bei der Mutter und ggf. auch beim Kind (bei Sorgen der Eltern, ihrem Kind zu schaden oder Hinweisen auf Nebenwirkungen) sind zu empfehlen.

Da es keine Hinweise auf eine unterschiedliche Effektivität, unterschiedliches Nebenwirkungsprofil oder Prädiktoren für differentielles Ansprechen gibt, kann **entweder Paroxetin oder Sertralin als ZVT** verwendet werden. Eine zweiarmige Studie mit einem

dieser Präparate einerseits und der Prüfmedikation andererseits ist daher ausreichend.
Gibt es Kriterien für unterschiedliche Behandlungsentscheidungen in der o.g. Indikation, die regelhaft berücksichtigt werden? Wenn ja, welche sind dies und was sind in dem Fall die Therapieoptionen? *(Bitte begründen Sie Ihre Ausführungen; geben Sie ggf. zitierte Quellen in einer Referenzliste an.)*
Die Behandlungsempfehlungen richten sich zum einen nach Schweregraden wie auch bei Depressionen in anderen Lebensphasen (siehe auch die deutsche S3- Bzw. NV-Leitlinie Unipolare Depression, https://www.awmf.org/leitli-nien/detail/ll/nvl-005.html). Bei leicht- bis mittelgradiger Depression ist eine Psychotherapie einer medikamentösen Therapie als ebenbürtig anzusehen. Bei schwergradigen Depressionen sollte kombiniert medikamentös und psycho-therapeutisch behandelt werden. Bei leichten Depressionen könnten auch Bewegungstherapien hilfreich sein, hier muss allerdings bedacht werden, dass stärkere sportliche Tätigkeit erst wieder nach dem Rückbildungskurs nach ca. 10-12 Wochen postpartum aufgenommen werden sollte (25). Wenn die betroffene Frau stillt und eine medikamentöse Therapie indiziert ist, dann sollte primär eine Monotherapie initiiert werden, damit weiter gestillt werden kann, wenn dies gewünscht ist. Auf Benzodiazepine sollte bei stillenden Frauen möglichst verzichtet werden. Im Rahmen der Therapie sollte stets die Mutter-Kind-Bindung und Mutter-Kind-Interaktion, wie oben erwähnt, beachtet werden. Diese ist auch nach Besserung der depressiven Symptomatik häufig beeinträchtigt und erfordert dann eine spezielle dyadische Behandlung wie z.B. auch entwicklungspsychologische Beratung (26). Bei therapieresistenten Depressionen, die bei 5 % aller Frauen mit einer postpartalen Depression auftreten (27), werden ebenfalls die leitliniengerechten Optionen nach der deutschen S3-NV-Leitlinie angewendet. Unter Augmentation einer antidepressiven Therapie mit Quetiapin ist es dann vertretbar, auch noch weiter zu stillen aufgrund des sehr geringen Übergangs in die Muttermilch. Bei Lithiumaugmentation muss das weitere Stillen sehr kritisch abgewogen werden, da hier auch die Lithiumkonzentration beim Kind sowie Nieren- und Schilddrüsenwerte regelmäßig überprüft werden müssen. Bei einer Kombination von verschiedenen antidepressiven Substanzen wird aktuell aufgrund der spärlichen Datenlage auch noch eher vom Stillen abgeraten. Zukünftige Alternativoptionen bei Müttern mit postpartaler Depression könnten auch nicht-invasive Hirnstimulationsverfahren wie rTMS und tDCS sein. Diese zeigen einen moderaten Effekt auf die depressiven Symptome und relevantes Risiko für den gestillten Säugling (28). Elektrokrampftherapie und Esketaminbehandlung sind wie in anderen Lebensphasen auch Behandlungsoptionen bei der therapieresistenten PPD. Zusammenfassend ist die Datenlage zur PPD-Behandlung aber zum Teil noch recht spärlich, Studien mit sehr guten Studiendesigns und ausreichend großen Probandinnenzahlen fehlen häufig noch.

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