North West Coast Clinical Networks

Psychotropic Medications in the perinatal period

Version 2, May 2025

Contents

This document was developed by members of the North West Coast Clinical Network for Perinatal Mental Health. With special thanks to Laura Ambridge, Dr Snehita Joshi and the Lancashire and South Cumbria specialist perinatal mental health midwives and pharmacists

Introduction

Prescribing to women in the perinatal period can provoke anxiety in the prescriber, the woman and her family. Women often receive conflicting advice from professionals, friends, family and the internet.

This document is aimed at all healthcare professionals working with women of childbearing age including those working in maternity, neonatology and paediatrics across the NWC perinatal network footprint.

This guidance within this document aims to give a brief overview to facilitate conversations with women and their families who have been prescribed psychotropic medication whilst pregnant and when breast feeding.

The resources referenced provide additional help for women and professionals to help weigh up the benefits and risks of taking medication during pregnancy, balanced with the risk of illness. Please see summary of recommended guidance and resources (appendix 1).

Information contained within these tables were written based on best evidence available at the time. The most up to date medication information must always be sought from.

Please refer to the medication tables in this document for further information on psychotropic medications in relation to additional antenatal care, place of birth, neonatal risk, breastfeeding and resources.

NICE 115 (2016) quality statement 3 recommends that *'Pregnant women with a previous severe mental health problem or any current mental health problem are given information at their booking appointment about how their mental health problem and its treatment might affect them or their baby.'* The information within these medication tables should be used as part of a discussion with the woman to ensure she can make an informed decision to start, stop, continue or alter her medication. Most psychotropic medications do not appear to increase risks to the

pregnancy or the foetus above background rates, particularly when the background confounders of mental illness are accounted for, though evidence is from naturalistic studies and there will always remain unknown unknowns. It is important that the limitations of the evidence are acknowledged in conversations with women and their families.

Due to a lack of understanding of the symptoms of poor neonatal adaptation syndrome, there is no validated scoring system for assessing symptoms in the neonate following antenatal exposure to psychotropic medication (Kautzky et al 2021, Acta Psychiatr Scan, 2022). As such there is no national guidance (including NICE) to support a specific regimen of neonatal observations or prolonged hospital stay.

The withdrawal effects of psychotropic medication are accepted to be short lived and self-limiting. Babies exposed to psychotropic medication may be discharged home on an individual basis as long as they have passed pulse oximetry, have normal observations, and display no clinical concerns. Support with decisions on an individual basis can be accessed via liaison with Neonatologists/ paediatricians, for example in cases of polypharmacy involving concomitant use of benzodiazepine (particularly long-term use), 'z-drugs' and illicit substances.

Safety netting information must be provided to all parents when a baby is at risk of Poor Neonatal Adaptation Syndrome (PNAS) with information provided (appendix 2).

Breast Feeding

NICE guidance is that breast feeding should be supported unless the mother is taking clozapine, carbamazepine, lithium or valproate where specialist advice should be sought on an individual basis. Information provided within this document is for **healthy, full-term** infants as premature infants may not be able to metabolise medication. However, breastmilk can be especially beneficial for pre-term infant therefore specialist advice should be sought on an individual basis and mum should be supported to preserve lactation whilst this specialist advice is obtained. Mothers should not co-sleep when sedative medication has been taken.

Antipsychotic and Mood Stabilising Medication

In cases where women are taking antipsychotic and/or mood stabilising medication, changes to medication should only be made under direction of the named Psychiatrist or the prescriber if different. It is recommended that if the prescriber is not a Psychiatrist with experience of prescribing in the perinatal period, they liaise with a Perinatal Psychiatrist based within their local Specialist Perinatal Mental Health Team.

Terminology:

Throughout this document the terminology 'poor neonatal adaptation syndrome' (PNAS) and 'withdrawal symptoms' is used. This is in line with the UK Teratology Information Service from which the information is referenced.

Neonatal adaptation syndrome refers to a cluster of symptoms in the neonate including irritability, sleep disturbance, persistent crying, tachypnoea, hypoglycaemia, poor thermal regulation, and occasionally seizures which has been related to the use of psychotropic medication during pregnancy.

There is uncertainty whether it is, in all cases, caused by withdrawal, or whether it may be related to excess of the relevant drug in the neonate. The condition is varyingly referred to as poor neonatal adaptation, neonatal withdrawal or neonatal abstinence syndrome within various literature and individual NHS trusts policies.

Neonatal abstinence syndrome (NAS) where withdrawal symptoms may be observed following use of opioids or misuse of other substances for which the Finnegan score is used as an assessment tool. This is not the same as PNAS where no specific assessment tool exists.

Governance:

This document has been developed by the NWC clinical network which does not have its own Drugs and therapeutic committee. The intention is that this guideline is adopted by local acute trusts and approved through their own governance processes.

Further advice:

Further advice and support can be obtained from the local specialist perinatal mental health services as required.

References:

- Scottish Intercollegiate Guidelines Network (SIGN). Perinatal mental health disorders. Edinburgh: SIGN; 2023. (SIGN publication no. 169). Available from URL: http://www.sign.ac.uk [Accessed May 2024]
- NICE (2016) Antenatal and postnatal mental health. Quality standard (QS115). National Institute for Health and Care Excellence.[online] Available from: https://www.nice.org.uk/guidance/qs115 [Accessed May 2024]
- National Institute for Health and Care Excellence. (2014). Antenatal and postnatal mental health: clinical management and service guidance. Clinical *guideline (CG192).* [online] Available from: https://www.nice.org.uk/guidance/cg192 . [Accessed May 2024]

Anxiolytics/Anti-Anxiety

Licensed indications*: short term relief of severe anxiety; panic disorder resistant to antidepressant therapy; insomnia (short term use); acute behavioural disturbance. (For illicit benzodiazepine use refer to local policies) substance misuse policies.
*NB: medications may also be used off-label for other indications e.g. promethazine for anxiety and insomnia.

Anxiolytics/Anti-Anxiety	Additional Antenatal Care	Neonatal Risk	Breastfeeding
Benzodiazepines: **Longer acting -** • Diazepam, Nitrazepam, Flurazepam, Alprazolam, Chlordiazepoxide, Clobazam, Clonazepam **Shorter acting -** • Lorazepam, Loprazolam, Lormetazepam, Temazepam, Oxazepam No evidence to support NAS observations	Consultant Obstetrician led care. Provide link to BUMPS/Breast Feeding Network (BNF) website. Add neonatal alert on maternity records.	Observe for neonatal withdrawal symptoms and/or 'floppy infant' syndrome. Symptoms reported following use include hypotonia, CNS depression, apnoea, hyporeflexia, low Apgar scores, hypothermia and hyperbilirubinaemia. Observe for neonatal respiratory depression.	Breastfeed with caution. Avoid longer acting drugs if possible, short acting medication such as lorazepam is preferable. Infants receiving breastmilk should be observed for sedation, slowed breathing rate, poor feeding and adequate weight gain.
'Z' drugs: • Zopiclone, Zolpidem No evidence to support NAS observations	Consultant Obstetrician led care. Provide link to BUMPS/BFN website. Add neonatal alert on maternity records.	Apgar score may be lowered. Observe for signs of hypoglycaemia, neonatal respiratory complications and CNS complications.	Breastfeed with caution. Small amounts present in breast milk. Infants receiving breastmilk should be observed for drowsiness, slowed breathing rate and dry mouth.
Sedating Antihistamines Promethazine No evidence to support NAS observations	Consultant Obstetrician led care. Provide link to BUMPS/BFN website. Add neonatal alert on maternity records.	Risk of neonatal irritability and excitement if promethazine used during the last two weeks of pregnancy.	Extensive experience of safe use in breastfeeding. May interfere with lactation.

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			Infants receiving breastmilk should be observed for drowsiness, irritability, dry mouth and any changes in feeding.
Beta Blockers: Propranolol No evidence to support NAS observations	Consultant Obstetrician led care. Provide link to BUMPS/BFN website. Add neonatal alert on maternity records. Consider growth scans	Potential for neonatal adrenoceptor blockade. Monitor for bradycardia, hypotension and hypoglycaemia in accordance with Trust guidelines. Observe for respiratory distress.	Small amounts in breastmilk. Not expected to cause any adverse effects.
Anti-epileptic Pregabalin (licensed for generalized anxiety disorder) No evidence to support NAS observations	Consultant Obstetrician led care. Provide link to BUMPS/BFN website. Add neonatal alert on maternity records. Refer to MHRA drug safety alert. https://bnf.nice.org.uk/drugs/pregabalin/ Follow the MHRA drug safety advice on use of antiepileptic drugs in pregnancy. Folic acid 5mg recommended 3 months preconception and during the first trimester.	Observe for symptoms suggestive of withdrawal symptoms and/or poor neonatal adaptation syndrome	Limited data suggests low levels in breastmilk, side effects not expected in breast fed infants.

References:

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- McAllister-Williams, R.H., Baldwin, D.S., Cantwell, R., Easter, A., Gilvarry, E., Glover, V., Green, L., Gregoire, A., Howard, L.M., Jones, I., Khalifeh, H., Lingford-Hughes, A., McDonald, E., Micali, N., Pariante, C.M., Peters, L., Roberts, A., Smith, N.C., Taylor, D., Wieck, A., Yates, L.M. and Young, A.H. (2017) British Association for Psychopharmacology consensus guidance on the use of psychotropic medication preconception, in pregnancy and postpartum 2017. *Journal of psychopharmacology (Oxford),* 31 (5), pp. 519-552 [online] Available from: https://spiral.imperial.ac.uk/handle/10044/1/48784 [Accessed March 2024].

Anxiolytics/Anti-Anxiety

Licensed indications*: short term relief of severe anxiety; panic disorder resistant to antidepressant therapy; insomnia (short term use); acute behavioural disturbance. (For illicit benzodiazepine use refer to local policies) substance misuse policies.
*NB: medications may also be used off-label for other indications e.g. promethazine for anxiety and insomnia.

- Medicines Health and Safety Agency. (2022). Pregabalin (Lyrica): findings of safety study on risks during pregnancy. [online] Available from: https://www.gov.uk/drug-safety-update/pregabalin-lyrica-findings-of-safety-study-on-risks-during-pregnancy [Accessed December 2023].
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Antidepressants

Licensed indications*: depressive illness; panic disorder; generalized anxiety disorder; obsessive compulsive disorder; bulimia nervosa; social anxiety disorder; post-traumatic stress disorder; pain.
*NB medication may also be used off-label for other indications

NICE guideline [NG235]: Intrapartum care (point 1.11.15) advises on monitoring babies whose mothers have taken SSRI or SNRI antidepressants during pregnancy due to the small but increased risk of persistent pulmonary hypertension of the newborn, post-partum haemorrhage and neonatal withdrawal symptoms. The reader is referred to the NICE guideline on antenatal and postnatal mental health and the MHRA advice on the use of SSRI and SNRI antidepressants in pregnancy.

Antidepressant	Additional Antenatal Care	Neonatal Risk	Breastfeeding
Selective Serotonin Re-uptake Inhibitors (SSRIs) • Citalopram, Escitalopram, Fluoxetine, Paroxetine, Sertraline, Fluvoxamine No evidence to support NAS observations	Provide link to BUMPS/BFN website. Obstetric review. Document on maternity records.	Observe for PNAS. See additional information below Be aware of possible Persistent Pulmonary Hypertension of the Newborn (PPHN). See additional information below	Breastfeeding should be supported if this is the woman's choice. Be aware of possibility of colic, drowsiness, poor feeding/ adequate weight gain and irritability/restlessness.
Serotonin and Noradrenaline Re-uptake Inhibitors (SNRIs) • Venlafaxine, Duloxetine No evidence to support NAS observations	Provide link to BUMPS/BFN website. Obstetric review. Document on maternity records.	Be aware of possible poor neonatal adaptation syndrome. See additional information below Be aware of Persistent Pulmonary Hypertension of the Newborn (PPHN) (theoretical concern) Observe for respiratory problems.	Infants receiving breast milk should be observed for irritability, restlessness, drowsiness, colic, gastrointestinal symptoms, poor feeding or not waking to feed and appropriate weight gain. May theoretically mitigate against infant venlafaxine withdrawal symptoms.
Other antidepressants • Mirtazapine	Provide link to BUMPS/BFN website. Obstetric review.	Be aware of possible neonatal withdrawal symptoms including central nervous system, motor, respiratory and gastrointestinal symptoms.	Low levels in milk and would not be expected to cause any adverse effects in breastfed infant.

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No evidence to support NAS observations	Document on maternity records.	Be aware of Persistent Pulmonary Hypertension of the Newborn (PPHN). **(theoretical concern)** **NB:** Mirtazapine has a long elimination half-life. Due to immature metabolic capabilities, neonatal clearance of mirtazapine following in utero exposure may also be prolonged, and as such neonatal effects may be delayed.	Monitor breastmilk fed baby for irritability, drowsiness, gastrointestinal symptoms, changes in feeding or not waking to feed, and appropriate weight gain.
Tricyclic Antidepressants (TCAs) and related • Amitriptyline, Clomipramine, Dosulepin (black listed in LSCMMG), Doxepin, Imipramine, Lofepramine, Nortriptyline, Trimipramine, Trazodone (tricyclic like antidepressant) No evidence to support NAS observations	Provide link to BUMPS website. Consultant obstetrician review. Add alert on maternity records.	Be aware of possible neonatal withdrawal symptoms including central nervous system, motor, respiratory and gastrointestinal symptoms.	Infants receiving breast milk should be monitored for drowsiness, poor feeding, constipation, reduced wet nappies and irritability/behavioural effects. Avoid **doxepin** due to significant amounts in the breast milk
Other antidepressants: Vortioxetine No evidence to support NAS observations **NB:** As a newer medication, we have less experience in pregnancy. Due to vortioxetine mechanism of action,	Provide link to BUMPS website. Consultant obstetrician review. Add alert on maternity records.	Be aware of possible poor neonatal adaptation syndrome including central nervous system, motor, respiratory and gastrointestinal symptoms (as vortioxetine is a centrally acting drug). Be aware of Persistent Pulmonary Hypertension of the Newborn (PPHN). **(theoretical concern)**	Breastfeed with caution. Lack of published data on breastfeeding as this is a newer agent. However, amounts of vortioxetine in milk appear to be low.

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Licensed indications*: depressive illness; panic disorder; generalized anxiety disorder; obsessive compulsive disorder; bulimia nervosa; social anxiety disorder; post-traumatic stress disorder; pain.
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theoretical risks are largely drawn from experience with SSRIs.		Apgar score may be low **(theoretical concern)**. Monitor for respiratory problems **(theoretical concern)**.	
Monoamine Oxidase Inhibitors (MAOIs) rarely prescribed • Phenelzine, Isocarboxazide, Tranylcypromine • Moclobemide (reversible-MAOI) No evidence to support NAS observations	Consultant obstetrician review Add alert on maternity records. Further advice and support can be obtained from the specialist perinatal mental health services, if required. **NB:** No BUMPS website leaflets or Toxbase monograph available. Consider direct discussion with UKTIS if these medications are encountered during pregnancy to establish monitoring plan.		**Reversible MAOI:** Infants receiving breast milk should be monitored for drowsiness, poor feeding and restlessness. **Avoid first generation MAOIs** in breast feeding (limited data and significant food/drug interactions). May theoretically mitigate against infant withdrawal symptoms.

References:

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Antidepressants

Licensed indications*: depressive illness; panic disorder; generalized anxiety disorder; obsessive compulsive disorder; bulimia nervosa; social anxiety disorder; post-traumatic stress disorder; pain.
*NB medication may also be used off-label for other indications

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Antipsychotic medication

Licensed indication*: Schizophrenia; Psychosis; Mania, Hypomania and Rapid tranquilization. NB: medications may also be used off-label for other indications e.g EUPD

Antipsychotic	Additional Antenatal Care	Neonatal Risk	Breastfeeding
First generation 'typicals' Haloperidol, Chlorpromazine, Flupenthixol, Sulpiride, Zuclopentixol No evidence to support NAS observations	Provide link to BUMPS website. Consultant Obstetrician review. Birth in consultant lead unit should be planned. Offer referral to Specialist perinatal mental health service. Add alert on maternity records. **NB:** Monitor for gestational diabetes. FGA such as phenothiazine's have been associated with impaired glucose tolerance and diabetes in non-pregnant patients.	Monitor for withdrawal symptoms and/or signs of Poor Neonatal Adaptation Syndrome (PNAS). Monitor for signs of extra pyramidal symptoms (abnormal muscle movements). **For haloperidol:** Monitor infant for adverse neonatal effects including agitation, hypertonia, hypotonia, tremor, somnolence, respiratory distress and feeding disorders.	Infants receiving breast milk should be monitored for sedation, poor feeding, extrapyramidal symptoms (abnormal muscle movement), behavioural effects (irritability) and developmental milestones.
Second generation 'atypicals' Amisulpride, Aripiprazole, Clozapine, Quetiapine, Olanzapine, Risperidone, Paliperidone, Lurasidone, Asenapine. No evidence to support NAS observations	Provide link to BUMPS website. Consultant Obstetrician review. Birth in consultant lead unit should be planned. Offer referral to Specialist perinatal mental health service. Monitor for gestational diabetes. Refer women taking a second-generation antipsychotic for a Glucose Tolerance Test. Add alert on maternity record.	Monitor for withdrawal symptoms and/or signs of Poor Neonatal Adaptation Syndrome (PNAS). Monitor for extra pyramidal symptoms (abnormal muscle movements).	Infants receiving breast milk should be monitored for sedation, poor feeding, extrapyramidal symptoms (abnormal muscle movement), behavioural effects (irritability) and developmental milestones. **Aripiprazole** may lower prolactin levels, affecting milk supply. Breastfeeding is **not recommended** if a woman is taking **Clozapine** (theoretical risk of agranulocytosis and seizures)

Antipsychotic medication

Licensed indication*: Schizophrenia; Psychosis; Mania, Hypomania and Rapid tranquilization. NB: medications may also be used off-label for other indications e.g EUPD

References:

- McAllister-Williams, R.H., Baldwin, D.S., Cantwell, R., Easter, A., Gilvarry, E., Glover, V., Green, L., Gregoire, A., Howard, L.M., Jones, I., Khalifeh, H., Lingford-Hughes, A., McDonald, E., Micali, N., Pariante, C.M., Peters, L., Roberts, A., Smith, N.C., Taylor, D., Wieck, A., Yates, L.M. and Young, A.H. (2017) British Association for Psychopharmacology consensus guidance on the use of psychotropic medication preconception, in pregnancy and postpartum 2017. *Journal of psychopharmacology (Oxford),* [Online] 31 (5), pp. 519-552 Available from: https://journals.sagepub.com/doi/full/10.1177/0269881117699361. [Accessed March 2024].
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Mood Stabilisers

Licensed indications*: treatment and prophylaxis mania; bipolar disorder and re-current depression; aggressive or self-harming behaviour; prevention of depressive episodes associated with bipolar disorder.
*NB: medications may also be used off-label for other indications e.g. EUPD

MOOD STABILISER	Additional Antenatal Care	Neonatal Risk	Breastfeeding
Lamotrigine (anti-epileptic mood stabiliser) No evidence to support NAS observations	Provide link to BUMPS website. Consultant led care. Birth in consultant lead unit should be planned. Offer referral to Specialist perinatal service. Recommend Folic Acid 5mg preconception and during first trimester Add alert on maternity records. Follow the MHRA safety advice on use of antiepileptic drugs in pregnancy. Physiological changes during pregnancy may affect lamotrigine levels and/or therapeutic effect. There have been reports of decreased lamotrigine plasma levels during pregnancy due to increased clearance. This reduces after birth and levels may increase rapidly with a risk of dose-related adverse events. Some guidelines including NICE recommend monitoring of lamotrigine serum concentrations in the woman frequently during the perinatal period. It is suggested as a pragmatic approach that doses be adapted according to clinical response or dose-related undesirable effects.	Monitor for Rash. Monitor for symptoms suggestive of poor neonatal adaptation syndrome (PNAS). [Recommended for all CNS acting medications].	Significant amounts can be present in breast milk although use is not directly contra-indicated. Infants receiving breast milk should be monitored for apnoea, drowsiness or poor suckling. Consider monitoring platelet count and liver function if symptomatic or other side-effects experienced. Also monitor for signs or symptoms suggestive of toxicity. Plasma levels may be measured if there are concerns. **Rash:** If a breastmilk fed infant develops a rash, breastmilk should be withheld until the cause can be established

Mood Stabilisers

Licensed indications*: treatment and prophylaxis mania; bipolar disorder and re-current depression; aggressive or self-harming behaviour; prevention of depressive episodes associated with bipolar disorder.
*NB: medications may also be used off-label for other indications e.g. EUPD

Carbamazepine (anti-epileptic mood stabiliser) There is no evidence to support NAS observations	Ensure benefit/risk discussion has occurred considering the possibility of stopping (because of the risk of adverse drug interactions and foetal malformations). Follow the MHRA safety advice on use of antiepileptic drugs in pregnancy. Provide link to BUMPS website. Consultant led care. Birth in consultant lead unit should be planned. Offer referral to Specialist perinatal service. Recommend Folic Acid 5mg preconception and during first trimester. Add alert on maternity records.	Monitor for potential neonatal withdrawal syndrome symptoms (including neonatal vomiting, diarrhoea, respiratory depression and seizures) There is a possible increased risk of haemorrhagic disease of the New-born. Consider vitamin K as clinically indicated.	Relatively high, but sub therapeutic, amounts in breast milk. Infants receiving breast milk should be monitored for sedation, poor suckling, adequate weight gain, developmental milestones withdrawal reactions and symptoms of liver dysfunction.
Lithium No evidence to support NAS observations	Provide link to BUMPS website. Consultant led care. Birth in consultant lead unit should be planned. Offer referral to Specialist perinatal service. Add alert on maternity records. See additional lithium guidance within this document.	Monitor for potential neonatal complications which may include hypotonia, polyhydramnios, cyanosis, apnea, respiratory distress, goitre, hypoglycaemia, sedation, tachycardia, tremor and jaundice. Infants who are preterm, dehydrated, or have an infection, should receive hydration and be assessed for lithium toxicity.	Highly variable levels in breastmilk. Previous recommendations advised against breast feeding. However other sources suggest it may be used in mothers of full-term infants who are willing and able to monitor their infants following risk/ benefit discussion. Avoid use in dehydrated infants. [NB: contraindication by manufacture of priadel (leading lithium brand)]. Monitor infant for tremor, involuntary movements, cyanosis and effects on muscle tone.

Mood Stabilisers

Licensed indications*: treatment and prophylaxis mania; bipolar disorder and re-current depression; aggressive or self-harming behaviour; prevention of depressive episodes associated with bipolar disorder.
*NB: medications may also be used off-label for other indications e.g. EUPD

			Some sources suggest monitoring of infant serum lithium, creatinine and TSH levels. NB: there are practical difficulties in obtaining, assaying and interpreting lithium levels from infants- expert advice should be sought.
Sodium Valproate There is no evidence to support NAS observations	**Valproate is a SIGNIFICANT TERATOGEN. Use in pregnancy is CONTRAINDICATED. Please see the MHRA safety advice on valproate use by women and girls and additional alert for men for further information (September 2024).** NICE recommends valproate not be prescribed for women who are breastfeeding however levels in breastmilk are low and no definite adverse reactions in breastfed babies have been reported. As a cautious approach (due to theoretical concerns) monitor the baby for any signs of jaundice, unusual bruising or bleeding.		

Lithium Guidance.

***This section is included for Trusts who do not have access specific guidance. Please refer to your local Trusts guidance, policies and procedures where available*.**

Introduction: Lithium is licensed for the management of acute (hypo)mania, treatment-resistant depression, prophylaxis of bipolar affective disorder (BAD) and control of aggressive behaviour or intentional self-harm. Lithium has a narrow therapeutic index and therefore requires close monitoring of serum-lithium concentration to prevent sub therapeutic levels or toxicity in the non-pregnant patient. This is required more frequently throughout pregnancy and the postnatal period due to known fluctuating pharmacokinetics**.**

During pregnancy:

Lithium levels fluctuate during pregnancy which can present a risk of suboptimal maternal treatment or maternal/neonatal lithium toxicity.

Mood Stabilisers

Licensed indications*: treatment and prophylaxis mania; bipolar disorder and re-current depression; aggressive or self-harming behaviour; prevention of depressive episodes associated with bipolar disorder.
*NB: medications may also be used off-label for other indications e.g. EUPD

Dose requirements may increase during the second trimester, reduce slightly in the third trimester before abruptly returning to normal following delivery. Lithium levels should therefore be monitored with the dose adjusted as needed to maintain serum levels within the woman's therapeutic range (aiming for the lowest effective level). To accurately establish the serum lithium concentration, samples should be drawn into non-lithium heparin tubes, ideally 12 hours after the most recent dose.

Pregnancy complications, such as pre-eclampsia affecting renal function, may significantly alter lithium metabolism and increase the risk of toxicity. Maternal dehydration (such as a result of pregnancy sickness) may also rapidly increase serum lithium levels. Remind patients of and monitor closely for any signs or symptoms suggestive of toxicity and repeat lithium levels as clinically appropriate.

Lithium levels and eGFR should be checked every four weeks in the first two trimesters and weekly from 36 weeks until labour. Increase frequency if signs of preterm birth, pre-eclampsia, dehydration or other illnesses that can affect renal function.

Use of lithium during the first trimester is associated with an increased risk of congenital cardiac malformation, although these risks have been found to be lower than originally estimate and the absolute risk remains low (2.25%). If the foetus has been exposed to lithium in the first trimester, the obstetrician should screen for cardiovascular anomalies and consider arranging a foetal cardiac echo.

Intra-partum Advice:

Women taking lithium should birth in hospital and be monitored by the obstetric team during labour and birth.

Fluid balance must be monitored throughout labour, birth and the initial post-partum period as dehydration increases the risk of lithium toxicity.

Owing to the risk of maternal/neonatal toxicity as a result of decreased renal clearance during delivery, a number of authors have suggested that lithium therapy should be slowly discontinued or reduced in late pregnancy. However, there are currently no published guidelines from the Royal College of Obstetricians (RCOG), Royal College of Psychiatrists (RCPsych) or NICE relating to the peripartum discontinuation/dose reduction of lithium. Furthermore, there is a lack of information on the effects of maternal lithium concentrations on the neonate.

Mood Stabilisers

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Current expert opinion guidelines have suggested that for cases where delivery by caesarean section or induction is planned, consideration could be given towards discontinuation of lithium 24-48 hours prior. For cases of spontaneous delivery, NICE guidelines suggest withholding lithium from presentation and for the duration of labour

The decision to reduce/withdraw lithium in late pregnancy therefore remains a clinical decision which should only be made following an assessment of the risk of relapse for each individual patient.

It is important that all patients exposed to lithium in late pregnancy have their maternal serum lithium levels monitored during labour (12 hours after the last dose, or as soon as possible if more than 12 hours have passed).

Hydration should be increased if clinically indicated to lower the systemic concentration and therefore reduce the risk of maternal and transient neonatal toxicity.

Potential interacting medication such as NSAIDS that are known to increase blood levels (potentially increasing the risk of toxicity) should be avoided.

Post-partum advice:

Monitor both mother and newborn for lithium toxicity as clinically indicated. Lithium levels should be checked urgently if there are any concerns regarding lithium toxicity. UKTIS recommends that all neonates exposed to lithium *in utero* should have their serum lithium level measured shortly after birth.

Signs and symptoms of lithium toxicity in adults may include increasing gastro-intestinal disturbances (vomiting, diarrhoea), visual disturbances (blurred), fine tremor increasing to coarse tremor, confusion, drowsiness, muscle weakness, lack of coordination, hypernatreamia, renal impairment / failure, electrocardiogram abnormalities, convulsions, coma.

To reduce the risk of maternal mental health relapse, consider (re-) initiating lithium as soon as possible after birth if this has been discontinued during pregnancy or at first signs of labour. If levels are within therapeutic range, restart lithium and check the level again after 5-7 days.

If lithium level is <1.0mmol/L. Then Lithium dose should be restarted the following evening. A subsequent Lithium level should then be repeated 12 hours post dose.

Mood Stabilisers

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If the Lithium Level is >1.0mmol/L please seek advice from Perinatal Consultant Psychiatrist (01254612731) within working hours, or OOH contact the Oncall Psychiatry Middle Grade/Consultant through switch board. If level is significantly raised/concerns about symptoms of toxicity, please gain urgent medical opinion. Please omit Lithium if serum concentration is >1.0mmol/L.

Measurement of serum lithium levels in the neonate shortly after delivery is also recommended. While UKTIS notes that these recommendations may be difficult to implement in obstetric practice, the potential for maternal and neonatal lithium toxicity should be borne in mind in all cases with peripartum exposure.

Normalisation of renal function can take up to a few weeks after delivery, consider monitoring lithium blood levels twice weekly for the first 2 weeks postpartum.

Lithium excretion into breastmilk and concentrations in infant serum are highly variable. Relative infant doses (RID) of up to 42% have been documented. Many sources (including the manufactures of lithium, NICE and BAPs) specifically contraindicate or do not recommend breastfeeding. Other sources however do not consider it an absolute contraindication, especially in healthy full-term infants over 2 months of age and during lithium monotherapy. Ensure a comprehensive discussion occurs considering benefits versus risks with the woman. Lactmed states that lithium may be used in mothers of full-term infants who are willing and able to monitor their infants.

If the mother chooses to breast feed, the infant should be monitored for tremor, involuntary movements, cyanosis and any effects on muscle tone. Some sources suggest monitoring of lithium levels, thyroid and renal function, whilst others only suggest this if clinically indicated e.g. if infant shows signs of unusual behaviour, restlessness, feeding difficulties, sedation or abnormal growth.

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Mood Stabilisers

Licensed indications*: treatment and prophylaxis mania; bipolar disorder and re-current depression; aggressive or self-harming behaviour; prevention of depressive episodes associated with bipolar disorder.
*NB: medications may also be used off-label for other indications e.g. EUPD

- UK Drugs in Lactation Service. [online] Monographs for lithium, carbamazepine and lamotrigine. Available from: UK Drugs in Lactation Advisory Service (UKDILAS) – SPS - Specialist Pharmacy Service – The first stop for professional medicines advice [Accessed March 2024]
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Additional Information and Comments

Women with a current or past severe mental health problem who are planning a pregnancy should be referred to a secondary mental health service (preferably a specialist perinatal mental health service) for preconception counselling.

Prescribers should ensure that the history includes medicines reconciliation and prescribed medication is reviewed for any potential drug interactions. This includes any drugs which may be administered during the perinatal period or obtained via alternate routes (e.g. 'over the counter' medication, from specialist hospital services or from the internet). Please note that the incidence and severity of poor neonatal adaptation syndrome (PNAS) may be increased when there is concomitant use of centrally acting drugs/polypharmacy (including benzodiazepines or anti-epileptics).

Information contained within these tables was written based on best evidence available at the time. The most up to date medication information must always be sought.

The National **NEWTT2** framework advises on the management of the deteriorating newborn. Psychotropic medication may impact on a newborn behaviour e.g. PNAS. Assessment in the first few hours after birth ensures effective transition and absence of clinically significant persistent pulmonary hypertension of the newborn, and ongoing assessment of infant behaviour including feeding is advised. Table 1 and 2 within the NEWTT2 document provides recommendations for assessment and monitoring for all newborn infants (including at risk groups). It is not possible to be prescriptive for each infant's unique situation, however observation frequency may need to be individualised (e.g. more or less frequent) in order to ensure safe care and provide an appropriate balance between observations of, and interruptions to, the parent and baby.

Normal monitoring and newborn checks should occur as they would in babies not exposed to maternal psychotropic medication unless there is clinical concern. Any additional monitoring requirements are contained within the medication tables throughout this document.

Babies presenting with symptoms such as lethargy, irritability and poor feeding should have physical causes investigated and excluded. It must not be assumed that the baby's symptoms are solely related to maternal psychiatric medication exposure.

NICE guidance is that breast feeding should be supported unless the mother is taking clozapine, carbamazepine, lithium (valproate is not recommended to treat mental health problems in women or girls of child bearing potential). This is for a **healthy term** infant. Premature infants may not be able to metabolise medication, and advice should therefore be sought on an individual basis. Caution should be exercised in decisions around maternal psychotropic prescribing for breastfed premature or sick infants, and/or if the mother is prescribed polypharmacy. Specialist advice may also be sought for mothers wishing to breastfeed who are taking clozapine, carbamazepine, lithium or valproate.

Monitoring will be undertaken by staff whilst a hospital inpatient then the community midwife following discharge. The mother/ parents/ carers should be provided with information regarding any monitoring required of the baby when home including any warning signs and actions to be taken if needed.

Information leaflets for mothers and their families containing up to date, reliable and evidence based information can be accessed via the 'Best Use of Medicines in Pregnancy (BUMPS) website (www.medicinesinpregnancy.org). Additional resources include the websites mothertobaby.org and e-lactancia.org which provide further information for breast feeding. Mental Health trusts also have access to choiceandmedication.org containing patient information leaflets for pregnant and breast-feeding women, please contact your local mental health trust for log in details.

Poor neonatal adaptation syndrome (PNAS)

- Use of any centrally acting drug throughout pregnancy or near delivery may potentially be associated with withdrawal symptoms in the neonate and/or poor neonatal adaptation syndrome (PNAS).
- PNAS may occur in approximately one-third of newborns who are exposed to SSRIs or SNRIs in utero, particularly during the third trimester.
- PNAS differs from neonatal abstinence syndrome (NAS) for which a validated screening tool (finergan score) can be used. There is no screening tool as yet for PNAS.
- There is no evidence (with the exception of lithium) to support a specific regimen of neonatal observations or prolonged hospital stay postnatally. Advice can often be conflicting recommending prolonged hospital stays.
- The symptoms of PNAS are generally mild and self-limiting. They usually begin shortly after birth and generally resolve within days to 2 weeks. Symptoms may include poor muscle tone, tremors, jitteriness, irritability, feeding difficulties, sleep disturbances, hypoglycaemia, and respiratory distress.
- PNAS does not usually require pharmacological treatment and responsive parenting should be supported.
- Cornet et a. (2023) population-based cohort study noted use of SSRI later in pregnancy was associated with increased incidence of delayed PNAS which was dose and SSRI type dependant. Citalopram, fluoxetine, and escitalopram were associated with a higher risk than sertraline. When exposure was discontinued before 30 weeks there was no increased risk of delayed neonatal adaptation suggesting a time-dependant mechanism.
- Risk of neonatal withdrawal syndrome is likely to be increased with concomitant use of other centrally-acting medications in pregnancy, such as benzodiazepines or antiepileptic agents.
- For mothers taking antidepressants, anti-psychotics and mood stabilisers (lamotrigine, carbamazepine, lithium) , breastfeeding may theoretically mitigate against infant withdrawal symptoms.

Persistent pulmonary hypertension of the newborn (PPHN)

- SSRIs taken after 20 weeks gestation have been associated with an increased risk for PPHN, although the absolute risk is low. Due to their mechanism of action, there are theoretical concerns that exposure to other antidepressants such as SNRIs and mirtazapine could also result in PPHN. Although there are no published data which identify an association, data are insufficient to disprove this theory and an increased risk cannot be excluded.
- Infants with PPHN may present with a wide range of breathing difficulties from mild respiratory distress to respiratory failure.
- All newborns should receive routine pulse oximetry testing and any concerns acted upon.

Postpartum haemorrhage (PPH)

- The use of SSRI, SNRIS and vortioxetine during the month before delivery may result in a small increased risk of postpartum haemorrhage (1.3-fold, absolute risk of 13 to 20% -background 10 to 15%).
- Risk may be significant in individual patients when combined with other risk factors for post-partum haemorrhage.
- Do not stop anticoagulant medication in women at high risk of thrombotic events in reaction to these data but be aware of the risk identified.
- Refer to information and guidance contained within the MHRA alert.

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Appendix 1: Recommended clinical guidance, reference and information sources for health care professionals

NICE CG192 Antenatal and postnatal mental health: Clinical management and service guidance

Published: 17 December 2014, Last updated: 11 February 2020
https://www.nice.org.uk/guidance/cg192

- This guideline covers recognising, assessing and treating mental health problems in women who are planning to have a baby, are pregnant, or have had a baby or been pregnant in the past year. It covers depression, anxiety disorders, eating disorders, drug- and alcohol-use disorders and severe mental illness (such as psychosis, bipolar disorder and schizophrenia). It promotes early detection and good management of mental health problems to improve women's quality of life during pregnancy and in the year after giving birth.

British Association of Psychopharmacologists consensus guidance on the use of psychotropic medication, preconception, in pregnancy and postpartum

https://www.bap.org.uk/pdfs/BAP_Guidelines-Perinatal.pdf

- These consensus guidelines aim to provide pragmatic advice regarding decisions about the use of psychotropic medication in pregnancy owing to the uncertainties around risks of the illness itself to mother and fetus/infant, effectiveness of medications in pregnancy and risks to the fetus/infant from in utero exposure or via breast milk. They are divided into sections on risks of untreated illness in pregnancy; general principles of using drugs in the perinatal period; benefits and harms associated with individual drugs; and recommendations for the management of specific disorders.

The UK Teratology Information Service (UKTIS) individual drug monograph summaries

http://www.uktis.org/index.html

- UKTIS produce evidence-based information on fetal risk for medicines and chemical exposures during pregnancy. There is open access to UKTIS pregnancy summaries for healthcare professionals.

The 'Best Use of Medicines in Pregnancy'- BUMPS website

https://www.medicinesinpregnancy.org/

- Patient-facing information factsheets available. May be useful in discussions between pregnant women and their partners and their healthcare provider.

Specialist Pharmacy Services (SPS) website (resources on prescribing during pregnancy and breastfeeding)

https://www.sps.nhs.uk/home/guidance/safety-in-pregnancy/

- SPS produces some medicines and condition-specific advice during pregnancy

UK Drugs in Lactation Advisory Service (breastfeeding resource accessed via SPS website)
https://www.sps.nhs.uk/?s=&cat%5B%5D=3008

- Produces medicines specific advice during breastfeeding, which provides directive answers and should be your initial source of reference. It includes advice on individual medicines therapeutic groups, as well as more detailed information on our most frequently asked questions.

e-lactancia

https://www.e-lactancia.org/

- A Spanish website with an English version provided. Wide coverage of products with succinct entries including a lactation risk category. Some monographs have short additional notes. Suitable alternatives are given where available. Relevant pharmacokinetic data is also available.

LactMed
https://www.ncbi.nlm.nih.gov/books/NBK501922/

- American database which is part of the US National Library of Medicine website. It is considered a reputable and up to date resource although not all medicines are included. Provides a thorough review of the evidence that is available. Also provides information on whether the medicine affects the lactation process itself.

Breastfeeding Network (BFN)
https://www.breastfeedingnetwork.org.uk/

- The BFN is a UK charity which provides support for breastfeeding in general, including a helpline accessed via Facebook. The website includes patient leaflets on some medicines, however there are some concerns that the advice does not appear to be sufficiently evidence-based.

Mother-to-Baby website
https://mothertobaby.org/

- An americian website similar to BUMPS. Provides up to date evidence-based patient information about medications and other exposures during pregnancy and breastfeeding.

Additional guidance:

Electronic Medicines Compendium
http://www.medicines.org.uk/emc

- The eMC has Summaries of Product Characteristics (SmPCs) and Patient Information Leaflets (PILs).
- Please note that this information clarifies the licensed status of a medicine's use in pregnancy and breastfeeding. It is not clinical advice. Manufacturers generally take a very cautious approach because of a lack of data. Confirmation that a product is licensed in pregnancy or lactation can be very useful in making treatment recommendations.
- This should not be used as a sole information source for medicines in pregnancy or lactation questions.

BNF

- As above, BNF statements on use of medicines during pregnancy and lactation are brief and may be based largely on SmPC statements. As such, the information is generally over cautious and gives little additional guidance over and above the SmPC.

Appendix 2: Suggested letter for sharing information:

Baby's details
Name:
NHS number:
Hosp Number:
DOB:
Discharge address and phone number:
Looked after child: yes/no

Mother's details
Name:
NHS number:
Hosp Number:
DOB:
Discharge address and phone number:

Main carer (if not mother):
Name:
DOB:
Discharge address and phone number:

Baby……..has been exposed during the pregnancy to the following psychotropic Medication:

1.
2.
3.

Breastfeeding is/ not contraindicated

The following signs may be observed and the baby will need to be supported with skin to skin care, gentle swaddling etc.

1.
2.
3.

If at any time the baby appears unwell, drowsy or has feeding difficulties they should be referred to the local paediatric team for rapid assessment.

Professionals involved:

Follow up plans: