Psychotropic Medications for Mothers and Babies Guidelines

South Island Perinatal Mental Health Service guidelines for health professionals caring for pregnant women taking psychotropic medicines and infants exposed to psychotropic medicines in utero and while breastfeeding.

Contents

Introduction

This document is intended to provide guidance for practitioners caring for women taking, or considering taking, psychotropic medicines in pregnancy and breastfeeding, and their babies. It has been prepared through multidisciplinary consultation based on current evidence and practice guidelines. The document includes a table: Perinatal Effects of Individual Classes of Psychotropic Medicines. It aims to provide general advice to standardise and optimise outcomes of new born term infants, born to mothers taking psychotropic medicine during pregnancy and/or breastfeeding. It should be used in conjunction with other supporting resources such as below, and discussion with a perinatal psychiatrist or your local Medication Information Service:

- Bumps (http://www.medicinesinpregnancy.org)
- Mother to Baby (www.mothertobaby.org)
- Lactmed (https://toxnet.nlm.nih.gov/newtoxnet/lactmed.htm)

Background

- Psychotropic medicines are some of the most commonly prescribed medicines for pregnant and breastfeeding women. Psychotropic medicines include antidepressants, mood stabilisers, antipsychotics, anxiolytics, and sleeping tablets.
- The decision regarding the use of psychotropic medicine in pregnancy and breastfeeding should be made weighing up the risks versus the benefits in each individual case. It should involve an informed choice between the woman and clinician.
- Ideally, discussions about psychotropic medicines in pregnancy and breastfeeding should occur pre-conceptually or in the antenatal period when parents have more time to consider the information.
- Historically concerns have been raised regarding the risk of fetal malformations secondary to in utero exposure to psychotropic medicines. Much of the evidence for fetal malformations is conflicting (see Table). Interpreting the data in relation to risks to the new born baby following exposure to maternal psychotropic medicine can be difficult and confusing, particularly if women are on more than one medicine.
- When considering potential risks to the infant it is important to remember that unstable maternal mental illness is the greatest risk to infant outcomes and supporting good maternal mental health, which may include the use of medicine, should be at the cornerstone of our care.
- Mental illness in pregnancy is associated with increased rates of pregnancy complications such as pre-term birth, growth restriction, and postnatal depression.
- The perinatal period is a high-risk time for mental illness to develop or deteriorate.
- Postnatal depression is associated with poor maternal-infant attachment and poorer long-term developmental outcomes for the child.
- Most currently used psychotropic medicines are considered relatively safe in pregnancy and breastfeeding, however there are a few exceptions (see Table). Adverse effects may occur, and babies exposed in utero or while breastfeeding may require closer monitoring.
- Women taking psychotropic medicines for their mental health during pregnancy and/or breastfeeding may experience anxiety and discomfort about this and be sensitive to perceived criticism. It is important that any discussions about medicine use are therefore approached in a non-judgemental way, with careful choice of words e.g. use of the ‘chance’ instead of ‘risk’. Discontinuation of medicine should be discouraged without full consultation with the prescriber.

Definitions

CWH: Christchurch Women's Hospital

LMC: Lead Maternity Carer

NA: Neonatal Abstinence

NTD: Neural Tube Defect

PNA: Poor Neonatal Adaptation

PPHN: Persistent Pulmonary Hypertension of the new born

RID: Relative Infant Dose = infant dose (mg/kg/dose)/ maternal dose (mg/kg/dose)

SNRI: Serotonin and Noradrenaline Reuptake Inhibitor

SSRI: Selective Serotonin Reuptake Inhibitor

Principles regarding prescription of psychotropic medicine in pregnancy

- Choice of treatment is best guided by what is most effective for the individual woman. This is likely to be the treatment the woman is currently receiving or has responded well to in the past.
- Switching to an ineffective psychotropic medicine may risk more harm to the
- mother and infant than a small chance of an adverse effect from a beneficial psychotropic medicine.
- Advising a mother to stop her psychotropic medicine may have significant adverse effects for her and her child. A decision as to whether a pregnant woman continues psychotropic medicines is a balance between the health of the mother and the potential effects on the baby.
- Changes to the mother's psychotropic medicine should only be made in discussion with the clinician managing her mental health. If you have concerns about the possible effects of this medicine on her infant please refer to the accompanying table "Perinatal Effects of Individual Classes of Psychotropic Medicines", or discuss with the prescriber, a perinatal psychiatrist, or hospital medicine information service.
- Women may require higher doses of medication in the third trimester due to hypovolaemic and metabolic changes
- Higher doses increase the risk of maternal and infant adverse effects. The lowest effective dose should be used.
- Babies of women who are on multiple psychotropic medicines are at greatest risk of adverse effects therefore avoid polypharmacy if possible.
- Tapering or stopping antidepressants before birth because of concerns around neonatal adverse effects is generally not recommended. This may leave the mother with no antidepressant cover at a vulnerable time and has not been shown to reduce the risk of Poor Neonatal Adaptation (see below).
- Tapering or stopping benzodiazepines (particularly long-acting or when taken regularly) close to term may be appropriate for some women to reduce the risk of Neonatal Abstinence (see below).
- First trimester of pregnancy is the highest risk time for fetal malformations. Pregnancy is often identified after fetal exposure has already occurred.
- Relapse of mental illness often requires the use of higher doses and multiple psychotropic medicines. The increased exposure to psychotropic medicines from relapse of mental illness often outweighs the risks associated with continuing maintenance psychotropic therapy during pregnancy and/or breastfeeding.

General support for pregnant or postpartum women living with mental illness

- Mental illness, particularly in the context of the stress of the postpartum period, may impair a mother's ability to comprehend or retain information and make decisions.
  - Communication should be honest, clear, well documented and consideration should be given to providing written information and having a support person present when conveying complex or distressing information about their baby.
  - BUMPS (http://www.medicinesinpregnancy.org) and Mother to Baby (www.mothertobaby.org) publish good information sheets.
- The consultation with the mother should be undertaken in an open and compassionate manner holding in mind that stigma in relation to mental health problems may be a barrier to provision of good care, communication, and help-seeking.
- While privacy considerations are very important, it is also important that there is good communication between health professionals caring for a mother with mental illness.
- It is also important to involve the father in discussions about the care of his infant. However, be mindful that there can be complex relationship and communication issues between the parents of the baby, as well as legal and confidentiality issues.
- Women with mental health conditions are more likely to have exposure to other factors that affect the fetal and infant well-being, including smoking, alcohol and substance misuse, poverty, social adversity, family violence, and trauma. These need to be assessed with respect to safeguarding infant and family well-being.
- Mothers with mental illness may struggle to bond with their infant and care should be sensitive and support the mother-infant relationship and minimise periods of separation. The mother may need to be encouraged and supported to hold the infant close, maintain eye contact, and respond to her baby's cues.
- Pre-pregnancy consultation with a perinatal psychiatrist is recommended for women with Bipolar Disorder, psychosis, or severe depression (e.g. requiring hospitalisation or requiring mood stabilisers such as Lithium). In Christchurch this can be accessed via GP referral to the South Island Perinatal Mental Health Service.

Antenatal Considerations

- It is particularly important that women who are taking psychotropic medicines during pregnancy have a routine fetal morphology scan and are supported to complete routine antenatal care.
- The lead maternity carer (LMC) should be aware of any medicines a woman is taking and specifically ask about any medicines she takes to support mental health.
- Women with mental health issues may use alcohol or drugs of abuse to help alleviate symptoms. The LMC should routinely enquire about alcohol use and illicit drug use, including cannabis, opiates, methamphetamine, and prescription medicines. This should be done at booking and close to birth to ascertain risk to the baby.
- If maternal medicines carry a risk of Poor Neonatal Adaptation or Abstinence after birth or other risks to the neonate, this should be discussed with the mother prior to birth so a birth and postnatal care plan can be developed.
- LMC should ensure a full medicine history is available to midwifery, obstetric, anaesthetic, and neonatal staff involved in her care and that this is recorded on birth summary.

Antenatal Care Plans

- It is strongly recommended that women with complex mental illness have a birth plan prepared by the team supporting her with her mental health. This should be distributed to professionals involved in the woman's care by 32 weeks of pregnancy and a copy placed in her clinical notes to be available for birth.
- If new health professionals become involved in the care of a woman (or her infant) with complex mental illness, they should review the care plan prior to assessment.
- Most women on psychotropic medicines will be cared for by their LMC midwife and GP and will not have such a plan in place.

Birthing Considerations

- The decision for place of birth in women with a history of mental illness will take into account factors such as the medicines a woman is on, her current mental state, any co-existing medical or obstetric conditions, the risk of a postnatal deterioration, and the support that is available at home.
- Women with mild mental illness, on single medicines, and with an uncomplicated pregnancy can birth at a primary birthing unit or at home providing there is someone present who is trained in new born life support and that oxygen and an ambu bag is available.
- Persistent Pulmonary Hypertension of the New born (PPHN) is a rare complication where the fetal circulation persists at birth and will present with cyanosis. The risk is slightly increased with maternal antidepressants. If the infant is delivered and given immediate skin to skin contact, it is important that the infant's colour and breathing is closely checked. If any concern oxygen should be administered, pulse oximetry checked, and the neonatal team called.
- The Neonatal Team do not need to routinely attend the birth of infants exposed to psychotropic medicines unless there is concern about potential need for resuscitation, e.g. Lithium exposed infants, compromised pregnancy, high dose medicines that can cause respiratory depression close to the time of birth, complex polypharmacy, or coexisting substance abuse. LMCs who are unsure whether neonatal attendance is advised can discuss this with the Neonatal Team.

Postnatal Considerations

1. Feeding

- Maternal mental illness may affect infant feeding, therefore there should be close observation and support of feeding.
- Exposure to some maternal mental health medicines can interfere with establishing feeding in some infants, necessitating monitoring infant feeding and weight gain.
- Mothers may find it difficult to recognise infant hunger cues, may need to prioritise sleep, and may struggle with the chaotic pattern of new born feeding. In addition, some women may have sensitivities around breastfeeding relating to past trauma.
- Breastfeeding should be encouraged if mother wishes to and there are no contraindications. Formula feeding should be supported if it is the mother's informed decision. Almost all infants should be able to have colostrum if the mother agrees to this.
- Mixed feeding with breastmilk and formula should be supported if it the best way to protect maternal wellbeing, as lack of sleep is a common precipitating factor for a relapse of severe psychiatric illness.

- A method for estimating risk to the baby from exposure to maternal psychotropic medicine via breastmilk is to consider the Relative Infant Dose (RID). The RID is the dose (as a percentage) the baby receives via milk (mg/kg/dose), compared with the mother's weight-adjusted dose (mg/kg/dose). A RID <10% is generally considered compatible with breastfeeding. The RID for most psychotropic medicines is <10% (see Table).

2. Poor Neonatal Adaptation (PNA) and Neonatal Abstinence (NA)

- PNA is a collection of symptoms seen in some neonates exposed to psychotropic medicines in utero, particularly with antidepressants and antipsychotics. Whether the symptoms relate to adverse effects of the medicine or a withdrawal phenomenon is often not clear.
- Symptoms of PNA may include:
  - poor feeding, vomiting or diarrhoea
  - tremors, irritability or lethargy
  - hyper/hypotonia
  - body temperature instability
  - nasal congestion, tachypnoea
  - hypoglycaemia.
- Studies suggest up to a third of infants exposed to antidepressants may develop PNA, but in most infants, symptoms are mild and self-resolve, usually within 72 hours.
- Regular maternal use of benzodiazepines or opiates during the third trimester can cause:
  - hypotonia
  - hypothermia
  - respiratory depression, and/or

    Neonatal abstinence (withdrawal):
    - tremors
    - irritability
    - hypertonicity
    - vomiting and diarrhoea
    - vigorous sucking
    - feeding difficulty
- There is an increased risk and severity of symptoms with higher maternal doses and polypharmacy (particularly when benzodiazepines are combined with antidepressants).
- Benzodiazepines and opiate withdrawal can begin within 24 hours of birth or be delayed to 2-3 days after the birth and last for 2-3 weeks. A longer observation time is necessary. Finnegan scoring can be used for evaluating for opiate withdrawal in term infants who are usually admitted to the neonatal unit for observation and management. More recently the “Eat, Sleep, Console” care programme has been adopted by many centres. Some infants may require medication to manage withdrawal effects.
- Never assume infant irritability/lethargy/poor feeding/jitteriness is solely due to maternal medicines. They could be signs that an infant is seriously medically unwell. If signs or symptoms are present, they must be assessed and investigated appropriately. The effect of maternal medicines is a diagnosis of exclusion.
- Supportive care should include an explanation of the infant’s symptoms to the mother, consider swaddling/skin to skin cuddles/pacifier use for settling and support for feeding.
- Babies should not be separated from their mothers in anticipation of symptoms occurring. Admission to the Neonatal Unit should be based on clinical need rather than maternal mental health history

3. Babies Exposed to Lithium

- Lithium has a narrow therapeutic index and requires close monitoring to avoid toxicity.
- Lithium levels can fluctuate during pregnancy and at the time of birth.
- Lithium crosses the placenta freely. Babies exposed to Lithium in utero may be at mildly increased risk (data is conflicting) of Epstein's anomaly or other cardiac defects (first trimester exposure) and should have had a fetal anatomy scan.
- Infant lithium levels are likely to be highest at birth and in the first 2 days. Some exposed infants may be hypotonic and require initial breathing support after birth and the Neonatal Team should be present at the birth.
- Infant's may be at risk of Lithium toxicity in the immediate postpartum if they become dehydrated. Extra monitoring and support with feeding may be needed.
- Some infants exposed to high levels of Lithium may experience side effects immediately after birth such as hypotonia, lethargy, poor sucking, tachypnoea, tachycardia, respiratory distress syndrome, cyanosis, and rarely arrhythmias. For this reason, it is recommended the Neonatal Team should do the 24hr check.
- Infant Lithium levels should be measured after birth and close attention paid to preventing dehydration. The initial lithium level can be done on cord blood and then if 'high', or there is clinical concern, rechecked 24-48 hours later with a neonatal blood test. There is no consensus on what level should be considered 'high' for an infant. Any level associated with symptoms of lithium toxicity should be considered 'high'. The authors of this guide recommend rechecking a neonatal level on any infant with a cord blood level >0.5.
- As lithium freely crosses the placenta, levels completely equilibrate between mother and foetus. Therefore, the cord blood level is likely to be the highest serum level in the infant with lithium levels declining after birth even if there is exposure through breast milk.
- If at any time there is concern an infant may be showing signs of Lithium toxicity (lethargy, hypotonia, poor feeding) a Lithium level, electrolytes, and renal function should be checked. Neonatal renal function should ideally be checked after 24 hours of age as an earlier creatinine tends to reflect maternal creatinine.
- As Lithium can also affect thyroid function, it is important to ensure exposed infants have their new born screening test.

Breastfeeding on Lithium has potential risks for the infant as Lithium is excreted into breast milk in variable amounts (up to 30%), and there is a risk of neonatal toxicity, particularly if the baby is unwell or premature or maternal levels are high. There is a paucity of data on long term outcomes however there is little evidence of harm. It is likely that the risk of high lithium levels and symptoms of toxicity occur predominantly within the first few days of life or in the context of ongoing exposure to high levels in breastmilk in an infant who is dehydrated. Breastfeeding on Lithium needs to be considered carefully on case by case basis. If a mother decides to breastfeed on Lithium, the risks and uncertainties need to be carefully explained to the mother, and there needs to be careful clinical oversight by a Perinatal Mental Health Team with infant blood monitoring. In Christchurch we recommend blood tests on cord blood, day two, and day seven and then three monthlies while breastfeeding for Lithium level, urea, creatinine, electrolytes. Thyroid function should be checked on new-born screening test and at 3 and 6 months. Additional lithium testing should be done if baby becomes unwell or if maternal levels are high and should be considered if maternal dose is increased (allow 5 days before testing for steady state drug level to be reached). If baby stops breastfeeding or is predominantly formula milk fed, then this monitoring is not needed. If the baby is mixed feeding (formula/solids) and levels have been low, discontinuation of monitoring can be considered. It is important to emphasise that this monitoring does not guarantee the infant will not suffer adverse effects.

An initial feed with colostrum can be offered if the mother wishes.

4. Newborn Examination

- LMCs are responsible for ensuring that the initial post-birth and 24-hour check are completed (except for Lithium exposed babies who should be seen by the Neonatal Team). Attention should be paid to the palate and cardiovascular system and a review of feeding.
- An LMC or core midwife can request a review by the Neonatal Team at any time if they have any concerns.

5. Discharge Planning

- Babies born in hospital may be safely discharged home after 24 hours if there are no concerns. A further assessment should be carried out at 48 hours by the LMC.
- Safe sleep practices should be promoted. Many psychotropic medicines can be sedating which, in combination with co-sleeping, can increase the risk of sudden unexpected death in infancy.
- Health professionals should offer practical advice about feeding, settling the baby, and where to seek help, and encourage the mother to seek support from family and friends.
- Maternal mental illness may impair the development of a positive mother-infant social-emotional connection. Health professionals need to provide care and advice that supports the mother-infant relationship.
- Any care and protection concerns should be discussed with the mother and a safety plan put in place prior to discharge. Concerns and safety plan should be communicated to all professionals involved in supporting this family.

Antidepressants

Indications: Depression, Panic Disorder, Generalised Anxiety Disorder, Obsessive Compulsive Disorder, Bulimia Nervosa, Social Anxiety Disorder, Post-Traumatic Stress Disorder, pain.

Class and individual dose ranges	Antenatal and obstetric care	Newborn risks	Breastfeeding
SSRIs Citalopram 20-40 mg/day Escitalopram 10-20 mg/day Fluoxetine 20-60 mg/day Paroxetine 20-60 mg/day Sertraline 50-200 mg/day **Of the antidepressants, SSRIs and Venlafaxine have the most safety data in pregnancy and breastfeeding.**	Usual care including routine fetal morphology scan. Possible small ↑ risk of congenital cardiac malformations. Possible ↑ risk of post-partum haemorrhage, suggest active 3rd stage.	Some studies have suggested a small ↑ risk of cardiac malformations. Cardiac anatomy checked during routine fetal morphology scan. PPHN (see notes above) - Presents as cyanosis. - Rare complication, maternal SSRI use slightly ↑ risk (from 2 up to 3 in 1000 births). - Closely monitor infant colour and breathing. If concerned: give oxygen, check pulse oximetry, and call Neonatal Team. PNA (see notes above) - Usually mild, developing within 8 – 48 hours postpartum and resolving within 72 hours. - ↑risk and severity with higher maternal doses and polypharmacy. - Exclude medical causes of symptoms and give supportive	**RID:** Citalopram = up to 10.9% Escitalopram = up to 8.3% Fluoxetine = up to 14.6% - slow clearance in breastfed infant, consider alternative SSRI, unless used in pregnancy. Paroxetine = up to 3% Sertraline = up to 3% Generally, the benefits of these drugs for maternal mental illness outweigh the potential risks of infant exposure to small amounts via breastmilk. Serious adverse effects in infants have not been observed. However, there is still a lack of information regarding long term risks. Monitor infant for sedation, irritability, not waking to feed/poor feeding and adequate weight gain. Higher maternal doses and polypharmacy increases the risk of infant adverse effects.

		care, e.g. swaddling, skin to skin cuddles, or pacifier use for settling, and support for feeding	
SNRIs Venlafaxine 75-375 mg/day	As for SSRIs Doses above 225 mg/day after 20 weeks gestation may ↑ risk of maternal hypertension, pre-eclampsia, and eclampsia. Ensure routine maternal blood pressure monitoring. Possible ↑ risk of post-partum haemorrhage, suggest active 3rd stage.	As for SSRIs, except - Neonatal seizures reported rarely, but causality not established.	**RID:** Venlafaxine = 4-15 % but usually <10%. As for SSRIs, except neonatal seizures have been reported but causality not established.
Bupropion 150-300mg/day Noradrenaline and dopamine reuptake inhibitor Few data supporting safety in pregnancy and breastfeeding Also used for smoking cessation.	As for SSRIs, except No association with increased risk of fetal malformations to date, but data limited.	As for SSRIs, except - No association with increased risk of fetal malformations to date, but data limited. - Neonatal seizures reported rarely, but causality not established.	**RID:** Bupropion = up to 5.7% As for SSRIs, except: - safety data are very limited. - neonatal seizures have been reported but causality not established. Theoretically dopaminergic effects of bupropion may suppress milk production
Mirtazapine 15-45 mg/day Noradrenaline and selective serotonin reuptake inhibitor. Few data supporting safety in pregnancy and breastfeeding	As for SSRIs, except No association with increased risk of fetal malformations to date, but data limited.	As for SSRIs, except - data limited. tracheomalacia, vesicoureteral reflux reported but causality not established	**RID:** Mirtazapine = 1.6 to 6.3% As for SSRIs, except safety data are very limited.

Also has sedative, antiemetic, and antihistamine effects			
Tricyclic Antidepressants Amitriptyline 25-150 mg/day Clomipramine 25-250 mg/day Dosulepin (Dothiepin) 50-225 mg/day Doxepin 75-300 mg/day Imipramine 75-200 mg/day Nortriptyline 10-100 mg/day - metabolite of amitriptyline Although used since the 1960's, safety in pregnancy and breastfeeding is not as well studied as for the SSRIs and venlafaxine. Less commonly prescribed for depression/ anxiety. Also used for migraine prophylaxis and pain.	As for SSRIs, except Some uncertainty over risk of fetal malformations, but wide use of these drugs over several decades suggests any risk is very small.	As for SSRIs, except - Some uncertainty over risk of fetal malformations, but wide use of these drugs over several decades suggests any risk is very small. - Maternal use of Dosulepin (Dothiepin) during the 3rd trimester reported to cause fetal tachyarrhythmia.	**RID:** Amitriptyline = 1 to 3% Clomipramine = 1 to 3% Dosulepin = 1-2% (Dothiepin) Doxepin = 0.3 to 3% - slow clearance in the breastfed infant, may cause sedation and respiratory depression. Imipramine = 0.1 to 4.4% Nortriptyline = 1.7 to 3. 4% As for SSRIs, except - Anticholinergic effects of tricyclic antidepressants may reduce milk supply.
Moclobemide 300-600 mg/day Reversible monoamine oxidase inhibitor (Reversible MAOI)	As for SSRIs, except No association with increased risk of fetal malformations to date, but data limited Doses > 600 mg daily can cause hypertension from interaction with dietary tyramine. Ensure routine	As for SSRIs, except No association with increased risk of fetal malformations to date, but data limited.	**RID:** Moclobemide = up to 3.4% As for SSRIs, except safety data are very limited.

	maternal blood pressure monitoring. Antenatal anaesthetic consult. ↑ risk of hypertension due to interaction with some anaesthetic drugs.		
Monoamine Oxidase Inhibitors (irreversible MAOIs) Phenelzine 15-90 mg/day Tranylcypromine 10-30 mg/day **Usually avoid use in pregnancy because of suspected ↑ risk of fetal malformations and risk of hypertensive crisis.**	As for SSRIs, except Atrioventricular septal defect and ↓ uterine and placental blood flow resulting in dysmorphia reported. Risk of hypertensive crisis from interaction with dietary tyramine. Ensure routine maternal blood pressure monitoring. Antenatal anaesthetic consult. ↑ risk of hypertension due to interaction with some anaesthetic drugs	As for SSRIs, except Atrioventricular septal defect and ↓ uterine and placental blood flow resulting in dysmorphia reported.	**RID:** Phenelzine = not studied Tranylcypromine = not studied **Avoid breastfeeding** - no data. - cardiovascular adverse effects are of concern.

Antipsychotics

Indications: Schizophrenia, psychoses, mania and hypomania, mood stabilisers.

Class and individual dose ranges	Antenatal and obstetric care	New born risks	Breastfeeding
First Generation Antipsychotics (FGAs) Chlorpromazine oral 75-1000 mg Flupentixol depot injection 25-300 mg every 2-4 weeks Haloperidol oral 2-20 mg/day Zuclopenthixol oral 20-40 mg/day Zuclopenthixol depot injection 200-400 mg every 2-4 weeks **Most safety in pregnancy and breastfeeding information is with oral chlorpromazine and haloperidol.**	Usual care including routine fetal morphology scan. Some uncertainty over risk of fetal malformations, but wide use of these drugs over several decades suggests any risk is very small.	Some uncertainty over risk of fetal malformations, but wide use of these drugs over several decades suggests any risk is very small. Extrapyramidal adverse effects (abnormal muscle movements, hypertonia, tremor, dystonia, motor restlessness), jaundice, and sedation. PNA (see notes above) - ↑risk and severity with higher maternal doses and polypharmacy. - Exclude medical causes of symptoms and give supportive care e.g. swaddling, skin to skin cuddles, or pacifier use for settling, and support for feeding.	**RID:** Chlorpromazine = up to 0.3% - Infant sedation reported Flupentixol = up to 1.75% - slow clearance in breastfed infant Haloperidol = up to 12% Zuclopenthixol = up to 1.5% - limited data Generally, the benefits of these drugs for maternal mental illness outweigh the potential risks of infant exposure to small amounts via breastmilk. Serious adverse effects in infants have not been observed. However, there is a lack of information regarding long term risks. Monitor infant for sedation or irritability, apnoea, not waking to feed/poor feeding, dry mouth, constipation, weight gain and extrapyramidal symptoms. Higher maternal doses and polypharmacy increases the risk of infant adverse effects.

Second Generation Antipsychotics (SGAs) Amisulpride 50-1200 mg/day Olanzapine 5-30 mg/day Paliperidone depot injection 25-150 mg /month — metabolite of Risperidone Quetiapine 25-800 mg/day Risperidone 0.5-16 mg/day **Weight gain and obesity are particularly associated with Olanzapine, Quetiapine, Risperidone, and Paliperidone, however all SGAs may ↑risk of gestational diabetes.**	As for FGAs, except: - Less well studied. - Most data with Olanzapine. - Risk of gestational diabetes may be increased. Maternal full glucose tolerance test at 24 to 28 weeks gestation (earlier if high risk)	As for FGAs, except: - Less well studied - Malformations reported; macrocephaly, macrosomia, hip dysplasia, and NTDs are probably related to maternal obesity or gestational diabetes.	**RID:** Amisulpride = up to 10.7% Olanzapine = up to 2. 3% Paliperidone approx. < 4.3% - from Risperidone data Quetiapine = up to 0.4% Risperidone = up to 9.0% As for FGAs, except: - Most safety data with Olanzapine. - Limited information on Amisulpride, Paliperidone, Quetiapine, Risperidone.
Aripiprazole 10-30 mg/day	As for FGAs, except: - very limited data. - theoretical increased risk of small for gestational age and intrauterine growth restriction. Suggest growth scan at 34 weeks gestation and at term	As for FGAs except very limited data (see Antenatal and obstetric care).	**RID:** Aripiprazole = up to 8.3%. - slow clearance in breastfed infant, consider alternative, unless used in pregnancy. As for FGAs, except safety data are very limited. Aripiprazole can lower serum prolactin in a dose related manner, resulting in reduced lactation
Clozapine 25-900 mg/day	Usual care including routine fetal morphology scan. No association with an	See Antenatal and obstetric care	**RID:** Clozapine = 1.3 to 1.4% **Avoid breastfeeding** - limited safety data.

Constipation is a common adverse effect which can be severe enough to be life-threatening Associated with neutropenia and agranulocytosis → mandatory blood monitoring before dispensing.	↑risk of fetal malformations to date, but less well studied. High risk of maternal weight gain, obesity and ↑ risk of gestational diabetes. Maternal full glucose tolerance test at 24 to 28 weeks gestation (earlier if high risk)	Malformations reported probably relate to maternal obesity or gestational diabetes; such as macrocephaly, shoulder dystocia. Reports of fetal decreased heart rate variability. PNA (see notes above) - ↑risk and severity with higher maternal doses and polypharmacy. - Exclude medical causes of symptoms and give supportive care e.g. swaddling, skin to skin cuddles, or pacifier use for settling, and support for feeding. Theoretical increased risk of sedation, respiratory depression, neonatal seizures, neutropenia, or agranulocytosis	- infant may develop serious adverse effects such as seizures and cardiovascular instability. - theoretical risk of agranulocytosis in the infant.

Mood Stabilisers

Indications: treatment and prophylaxis of mania, Bipolar Disorder, and recurrent depression, aggressive or self-harming behaviour, prevention of depressive episodes associated with Bipolar Disorder. Also see Antipsychotics.

Class and individual dose ranges	Antenatal and obstetric care	New born risks	Breastfeeding
Lithium Lithium Carbonate 400-1200 mg/day. Dose adjusted according to serum levels.	As lithium freely passes across placenta fetal levels are the same as maternal levels. ↑relative risk of Epstein's anomaly but absolute risk low: 10 per 20,000 births compared to background risk of 1 per 20,000 births. Document woman is taking Lithium on morphology scan request. Morphology scan at CWH. Anomaly scan should include detailed fetal cardiac echo (possibly small increased risk of cardiac anomalies). Antenatal care referral and consult perinatal mental health paediatricians. Avoid maternal dehydration, especially if other concurrent illness. Give intravenous fluids early for hyperemesis and promote sleep.	High-risk neonate: must have neonatal review at delivery and 24-hour check. Some infants may be hypotonic and require initial breathing support after birth Risk of infant Lithium toxicity if high maternal levels, or if infant is preterm, dehydrated or has impaired renal function Symptoms of toxicity: - hypotonia, respiratory depression or distress, poor feeding, - cardiac arrhythmia Recommend measuring cord lithium level and repeating at 24-48 hours if >0.5 mmol/L. Support feeding and hydration Ensure infant has new-born screening test (to check thyroid function).	**RID:** Lithium = from 1% to 30% **Breastfeeding on Lithium poses potential risk for the infant** - risk of infant lithium toxicity predominantly in first few days after birth - If mother decides to breastfeed after being informed of potential risks/uncertainty we recommend close infant monitoring supervised by a paediatrician (serum lithium levels on cord blood, day 2, 7and then 3-monthly lithium level, urea, creatinine, electrolytes, thyroid function while breastfed). Additional testing if baby becomes unwell, if maternal levels are high and consider if maternal dose is increased (allow 5 days before testing for steady state

	Monitor maternal serum lithium and creatinine levels monthly until 36 weeks then weekly during pregnancy and within 48 hours postpartum. Consideration should be given to withholding lithium at onset of labour and recommencing soon after birth Maternal thyroid function tests each trimester.		drug level to be reached). Colostrum can be considered in all infants
Sodium valproate (valproic acid) Epilim® 600-2500 mg/day **Sodium Valproate is associated with a high risk of birth defects and developmental problems in children exposed during pregnancy.** **Any women of child bearing age on Sodium Valporate requires a robust contraceptive plan.**	<u>Urgent referral</u> in early pregnancy to antenatal care. Detailed morphology scan at 16- and 20-weeks gestation at CWH through Maternal Fetal Medicine - Document woman is taking Sodium Valproate on any ultrasound requests. Associated with and ↑ risk of fetal malformations that may be dose-related. Folic acid 5 mg daily 3 months pre-conception and throughout pregnancy.	↑ risk of fetal malformations - 10 per 100 exposed births compared to background rate of 2 per 100 births Fetal valproate syndrome: - craniofacial phenotype - major malformations - growth deficiency - neurodevelopmental dysfunction - Neural tube defects - cardiac malformations Possible ↑ risk with dose ≥ 1000 mg/day. Possible association with neonatal afibrinogenaemia and fatal haemorrhage	**RID:** Valproic acid = 1 to 5.6% Breastfeed with caution - there are relatively low levels of valproic acid in breast milk. Long-term adverse effects have not been observed. Monitor infant for sedation or irritability, not waking to feed/poor feeding and weight gain. Based on clinical symptoms some infants may require monitoring of liver enzymes or platelets. There are theoretical concerns of valproic acid-induced hepatotoxicity in the breastfed infant

		Transient neonatal hypoglycaemia Hepatotoxicity PNA (see notes above)	
Carbamazepine Tegretol® 100-1600 mg/day **Carbamazepine is associated with an increased risk of fetal malformations and developmental problems in children exposed during pregnancy.**	Early fetal morphology scan at 16 weeks' gestation to look for NTDs, at CWH. Morphology scan at 20 weeks' gestation at CWH. Document woman is taking carbamazepine on all morphology scan requests. Associated with an ↑ risk of fetal malformations, mainly NTDs, cardiovascular, urogenital malformations, and oral cleft. Folic acid 5 mg daily 3 months pre-conception and throughout pregnancy. Vitamin K, (phytomenadione) oral 10-20 mg/day from week 36 (injection is given orally) Give neonate parenteral vitamin K (phytomenadione) 0.5-1 mg intramuscularly soon after birth.	↑ risk of fetal malformations - spina bifida 1 per 500 exposed births compared to background rate of 1 per 2000 births Mostly NTDs but also: - cardiac malformations - urogenital malformations - oral clefts - minor craniofacial defects - fingernail hypoplasia - developmental delay Increased risk of neonatal haemorrhagic disease → give neonate parenteral vitamin K (phytomenadione) 0.5-1 mg intramuscularly soon after birth. Most neonates have no adverse reactions, but cholestatic hepatitis, seizures and PNA have been reported.	**RID:** Carbamazepine = 1.1 to 7.3% Breastfeed with caution. - Carbamazepine has relatively high levels in breastmilk and breastfed infants can have plasma levels that are measurable but usually below the therapeutic range for carbamazepine. — Long-term adverse effects in the breastfed infant have not been observed. Monitor infant for sedation or irritability, not waking, to feed/poor feeding and weight gain. Depending on symptoms some infants may require monitoring of liver enzymes.

		PNA (see notes above):	
Lamotrigine 25-400 mg/day (monotherapy) 12.5-200 mg/day (with Sodium Valproate) Risk of serious skin reactions and a hypersensitivity syndrome, particularly if dose is increased too quickly.	As lamotrigine freely passes across placenta fetal levels are the same as maternal levels. Detailed fetal morphology scan recommended. Possible ↑ risk of oral clefts but studies are conflicting. Folic acid 5 mg daily 3 months pre-conception and throughout pregnancy. Monitor maternal plasma levels each trimester, and at 37 to 38 weeks gestation (or earlier if there are risk factors for premature labour), then every 1 to 2 weeks for the first 3 to 6 weeks postpartum. Interpret plasma levels cautiously because of changes in protein-binding during pregnancy consult Clinical Pharmacology	Possible ↑ risk of oral clefts if taken during the first trimester but studies are conflicting. If there is a risk, it is likely to be small 1 to 4 per 1000 exposed births. Neonatal plasma levels may reach 60% of maternal plasma levels in the first week. If infant is displaying adverse effects such as apnoea, rash, drowsiness, or poor sucking then plasma neonatal levels should be checked, and infant should be reviewed by a paediatrician.	**RID:** Lamotrigine 7.6 to 18% (variable) Breastfeed with caution. - Neonates are at risk of high lamotrigine plasma levels, as maternal plasma and milk levels can rise dramatically in the immediate postpartum period if maternal dosage is not reduced to the pre-pregnancy dosage. - One case report of severe apnoea in an infant exposed to lamotrigine via breastmilk and in utero. Due to risk of Stevens Johnsons syndrome, if rash occurs check infant Lamotrigine levels and pause breastfeeding until cause can be established. Monitor infant for sedation or irritability, not waking to feed/poor feeding and weight gain. Depending on symptoms some infants may require monitoring of liver enzymes.

Anxiolytics and Hypnotics

Indications: short term relief of severe anxiety, Panic Disorder resistant to antidepressant therapy, insomnia (short term use), acute behavioural disturbance, symptoms of Post-Traumatic Stress Disorder

Class of drug and individual dose ranges	Antenatal and obstetric care	New born risks	Breastfeeding
Benzodiazepines **Long-acting** Diazepam 2-60 mg/day Nitrazepam 5-10 mg/day Clobazam 5-60 mg/day Clonazepam 1-8 mg/day Diazepam is the most studied benzodiazepine in pregnancy and breastfeeding. **Short-acting** Lorazepam 1-4 mg/day Oxazepam+ 10-120 mg/day Temazepam+ 10-30 mg/day Triazolam 0.125-0.25 mg/day + metabolites of Diazepam	Usual care including fetal morphology scan. Possible ↑ risk of oral cleft but studies are conflicting. Lower risk with intermittent (PRN) use. Lorazepam associated with anal atresia causality not established. Lower risk with intermittent (PRN) use. For women taking benzodiazepines regularly, consider tapering the dose near term.	Benzodiazepine use during pregnancy has been associated with intrauterine growth restriction and small for gestational age, but reports confounded by maternal anxiety and substance use. Regular maternal use during the third trimester can cause neonatal hypotonia and breathing difficulty at birth or NA (see notes above) - Withdrawal symptoms may be delayed several days after the birth and last for 2-3 weeks - ↑risk and severity with higher maternal doses and polypharmacy (particularly antidepressants)	**RID long-acting:** Diazepam = 0.88 to 7.14% Nitrazepam = 2.9% Clobazam = 4.3 to 11.5% Clonazepam = 2.8% **RID short-acting:** Lorazepam = 2.6 to 8.5% Oxazepam = 0.28 to 1% Temazepam = undetectable Triazolam: unknown (not studied) Intermittent (PRN) use of short-acting benzodiazepines: - breastfeeding could be considered if mother wishes to and no contraindications. Regular use or intermittent use of long-acting benzodiazepines: - caution with breastfeeding as infant adverse effects (sedation, mild jaundice, apnoea, and hypotonia) have been reported. Monitor infant for sedation, slowed breathing rate, not waking to feed/poor feeding, and weight gain.

Zopiclone 3.75-7.5 mg/day	Usual care including fetal morphology scan. No association with an increased risk of fetal malformations to date. For women using regularly consider tapering the dose near term.	Possible ↑ risk of preterm birth (up to 2 weeks) and low birth weight but may be confounded by maternal anxiety and substance use. NA (see notes above) - Symptoms can occur within first 24 hours or be delayed to several days after the birth and last for 2-3 weeks - ↑risk and severity with higher maternal doses and polypharmacy (particularly antidepressants)	**RID:** Zopiclone = up to 3.2% Consider breastfeeding if mother wishes to no contraindications - Caution with high doses and/or regular use - Limited safety information. Monitor infant for sedation, slowed breathing rate, not waking to feed/poor feeding and weight gain.

Attention Deficit Hyperactivity Disorder (ADHD) medications

Class of drug and individual dose ranges	Antenatal and obstetric care	New born risks	Breastfeeding
CNS stimulants Methylphenidate Doses vary, see NZF.	Usual care including routine fetal morphology scan. Consider foetal echocardiography Limited safety data. Possible ↑ risk of fetal cardiac malformations. Possible ↑ risk of spontaneous abortion. Possible ↑ risk of preeclampsia. Monitor heart rate and blood pressure.	Regular maternal use during the third trimester can cause "floppy infant syndrome" or NA (see notes above).	**RID:** < 1% Long-term neurodevelopmental effects have not been studied. Monitor infant for weight loss, poor feeding, poor sleeping patterns, agitation and irritability.
Non-CNS stimulants Atomoxetine Doses vary, see NZF.	Usual care including routine fetal morphology scan. Limited safety data (less than methylphenidate) Possible ↑ risk of spontaneous abortion.	Limited safety data.	**RID:** unknown (expected to transfer into breast milk). Limited safety data. Long-term neurodevelopmental effects have not been studied. Monitor infant for sleeplessness, hyperactivity and poor feeding.

Supporting material

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