PREGNANCY AND BREASTFEEDING
TREATMENT OF PSYCHIATRIC AND SUBSTANCE MISUSE DISORDERS

<table>
<thead>
<tr>
<th>Document lead:</th>
<th>Medicines Information Manager</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ratifying Committee /</td>
<td>Medicines Management Group</td>
</tr>
<tr>
<td>Group:</td>
<td></td>
</tr>
<tr>
<td>Status of document:</td>
<td>Final</td>
</tr>
<tr>
<td>Document Reference:</td>
<td>GD068</td>
</tr>
</tbody>
</table>

Signed:

Dr Maria Clarke, Chair Medicines Management Group

Approval date: June 2017

Essential reading for the following staff groups:

1. All Prescribers
2. All Nurses
3. All Pharmacy staff
   working with women with psychiatric and substance misuse disorders

Following staff groups should be aware exists for references purposes:

1. Managers of services where medicines are prescribed, supplied or administered
2. All staff caring for patients treated with medicines

POLICY IMPLEMENTATION DATE
08/2017

DATE TO BE REVIEWED
08/2020
CONTENTS PAGE

1. Key Points .............................................................................................................. 3
2. Purpose and Scope ............................................................................................... 4
3. Responsibilities .................................................................................................... 6
4. Definitions Used .................................................................................................. 7
5. Procedure .............................................................................................................. 8
   5.1 Prescribing in Pregnancy & Breast-Feeding ..................................................... 8
   5.2 Antidepressants in Pregnancy & Breast-Feeding ............................................. 14
   5.3 Antipsychotics ................................................................................................. 21
   5.4 Anticholinergics .............................................................................................. 27
   5.5 Benzodiazepines & Hypnotics ........................................................................ 28
   5.6 Mood Stabilisers ............................................................................................. 31
   5.7 Rapid Tranquillisation ..................................................................................... 36
   5.8 Medicines fo ADHD ....................................................................................... 36
   5.9 Addictions ........................................................................................................ 38
   5.10 Promoting Parenting ...................................................................................... 48
   5.11 Service Provision ............................................................................................. 49
6. Consultation .......................................................................................................... 50
7. References .............................................................................................................. 50
APPENDIX A .............................................................................................................. 58
APPENDIX B .............................................................................................................. 65
APPENDIX C .............................................................................................................. 72
APPENDIX D .............................................................................................................. 73
APPENDIX E .............................................................................................................. 76

Note that the majority of this document will refer to service users as patients however the term client will be used in sections relating to the treatment of substance use disorders.
1. Key Points

- Treatment decisions during pregnancy and breastfeeding should always be made on a case-by-case assessment, using the most up-to-date evidence and where possible in discussion with the patient. The potential risks of the maternal medication on the foetus/infant should be balanced against the risks of leaving the illness untreated or inadequately treated or the continuation of substance misuse when making this decision.

- The final decision regarding treatment for an individual remains the **clinical responsibility of the prescriber** and should be done in consultation with the patient and with their consent.

- Prescribers should encourage discussion about pregnancy plans\(^1\). When consideration is given to prescribing psychotropics to any woman of childbearing age, appropriate counselling regarding contraception and the risks of pregnancy should be given.\(^1\)

- The aim of prescribing any medication including those for substance misuse during pregnancy should be directed towards the prescribing of the **lowest effective dose** whilst also encouraging compliance with the wider treatment plan and providing adequate monitoring. However, doses so low as to constitute ineffective treatment represent needless exposure by foetus/infant to medication\(^1,3\).

- An integrated care plan should be developed and coordinated by the keyworker detailing all aspects of treatment and interventions, the roles and responsibilities of all individuals involved in the care and who will provide the interventions and agree the outcomes with the woman\(^1\). The care plan, with the clients consent where possible, should be communicated to all professionals involved in the care.

- Healthcare professionals should be given training on mental health problems and substance misuse disorders. Healthcare staff and non-clinical staff such as receptionists should be given training on how to communicate sensitively with women who have mental health disorders or misuse substances.

- Women who are substance users and who attend drug and alcohol treatment programmes are likely to have better antenatal care and better general health than those who do not engage with treatment services. Addiction services should fast-track pregnant women into treatment and engage substance-misusing partners.\(^2\)

- The World Health Organisation stresses the **desirability of breast-feeding** exclusively for at least four to six months. It is therefore important to consider prescribing options that will allow the mother to safely breast-feed.\(^4\) However it is usually inappropriate to withhold treatment to allow breast-feeding to take place.

- Where a woman decides to stop medication in pregnancy and the postnatal period discuss with her the reasons for doing so, her treatment options including, restarting medication, alternative medication and psychological interventions and increasing the level of monitoring and support. Ensure that she is aware of the risks to herself and the foetus or baby when stopping.\(^1\) Ensure both the benefits and risks discussed are fully documented in the patient’s notes.
2. Purpose and Scope

These guidelines provide advice on the associated risks of psychotropic use in pregnancy and breast-feeding and on the risks of harmful use of substances and associated treatment choices in pregnancy to facilitate treatment decisions. However, always consult the most up-to-date information available when deciding on individual treatment as the volume of data for medication use in pregnancy constantly accumulates, and advice may change significantly.

Further general information about the treatment of mental health disorders during pregnancy and breast-feeding can be found within:

- **The British Association of Psychopharmacology consensus guidance on the use of psychotropic medication preconception, in pregnancy and postpartum** (2017). This is a new guidelines in 2017 aimed at building on the NICE guidelines, including specific advice on groups of medicines and the treatment of major mental health conditions during pregnancy, [https://www.bap.org.uk/pdfs/BAP_Guidelines-Perinatal.pdf](https://www.bap.org.uk/pdfs/BAP_Guidelines-Perinatal.pdf)

The guidelines should be read in conjunction with:

- Trust procedures on Child Protection/Safeguarding Children for more information on child protection, safeguarding and promoting the welfare of children.

The guidelines should be read in conjunction with NICE clinical guideline on pregnancy and complex social factors which included women who misuse alcohol and/or drugs (NICE, 2010b), the Confidential Enquiries into Maternal Deaths reports, NICE guidance on smoking, and the Cochrane review on improving pregnancy outcomes by pre-pregnancy health promotion. There are also Cochrane reviews of psychosocial interventions and opioid agonist maintenance treatment for pregnant women.

To discuss treatment options for an individual patient contact the team pharmacist or the Medicines Information Service.

**CONTACT NUMBERS FOR ADVICE:**

- **Coombe Wood Perinatal Psychiatric Services**: 020 8955 4495
- **Westminster Perinatal Psychiatric Service**: 0203 312 1582
- **CNWL Medicines Information Service**: 020 8206 7271 (Monday-Friday, between 9am-5.15pm or email: medinfo.cnwl@nhs.net)
- **UK Teratology Information Service** (UKTIS): 0844 892 0909. UKTIS can provide information on specific medication. Monographs for individual medication are on their website [http://www.uktis.org/](http://www.uktis.org/) (free to register), it is important to check their date.
INFORMATION FOR PRESCRIBERS

- UKMI Question and Answer (Q&A) documents – The United Kingdom Medicines Information (UKMI) network produces guidance on frequently asked questions. For a list of current Q&As see: http://www.ukmi.nhs.uk/activities/medicinesQAs/default.asp
- UKMI Drugs In Lactation Advisory Service provides information on using medicines in lactation http://www.midlandsmedicines.nhs.uk/content.asp?section=6&subsection=17&pageIdx=1
- LactMed: This database contains information on the use of different medicines including psychotropic in breastfeeding. It contains information on the level of such substances in breast milk and infant blood and the possible adverse effect in the nursing infant. This information is updated monthly: http://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f/?./temp/~GU8O2x:1 This is also available as an app.

PATIENT INFORMATION:

All the information below can also be found on the CNWL website: http://www.cnwl.nhs.uk/
All resources are free to access and information is patient friendly.

- Choice and Medication Website: The following website has been developed by specialist pharmacists to provide information on around 20 mental health conditions and over 110 different medicines used to treat these conditions: http://www.choiceandmedication.org/cnwln

- Medicines Helpline: Service users and carers can call the helpline and speak to one of our specialist pharmacists about their medication. Open Monday-Friday, between 9am-5.15pm on 020 8206 7270 email: medinfo.cnwl@nhs.net

- Best Use of Medicines In Pregnancy: This is a new website in 2014 developed by UKTIS to provide information on the use of medication in pregnancy to patients: http://www.medicinesinpregnancy.org/

- Use of Valproate in pregnancy: The MHRA issued a booklet to give to any woman of child-bearing potential prescribed valproate https://assets.digital.cabinet-office.gov.uk/media/54bd3a23e5274a15b3000009/Valproate_booklet_for_patients_Jan_2015.pdf
## 3. Responsibilities

<table>
<thead>
<tr>
<th>Party/person</th>
<th>Key responsibilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Care co-ordinator</td>
<td>• To alert the prescriber as soon as possible where a patient is potentially pregnant or is planning a pregnancy.</td>
</tr>
</tbody>
</table>
| Prescriber | • Consult the most up-to-date evidence when making treatment decisions about medications and evaluate the risks & benefits of medication on a case-by-case assessment.  
• Where possible decisions about medication should be made jointly with the patient and with their consent.  
• Junior doctors should also refer to senior colleagues (Specialist Registrar/Consultant) for advice on psychotropic treatment during pregnancy & breast-feeding.  
• Have pre-pregnancy discussions with patients on choice of psychotropic & implications during pregnancy.  
• Care needs to be shared and clearly communicated to the obstetric team and other healthcare professionals (e.g. GP) involved in patient care.  
• The treatment plan covering pregnancy, delivery and the postnatal period should be clearly documented in the clinical notes.  
• Inform UKTIS of any pregnancy where exposure to medicine (especially where data is limited) has occurred by completing UKTIS form on the website [http://www.uktis.org/](http://www.uktis.org/). |
| Pharmacist | • Advise practitioners on the use of medication during pregnancy and breast-feeding, including the potential risks of the medication as well as any monitoring requirements.  
• Consult current literature when providing information and advice to prescribers.  
• Provide advice on medication in pregnancy & breast-feeding in order to facilitate treatment decisions for individual patients.  
• Provide information & advice about the use of medicines in pregnancy and breastfeeding to patients/carers. If appropriate and with their consent liaise with the relevant clinical team(s) involved in the patients care. |
| Nursing Staff | • To be aware of the risks and benefits of medication during pregnancy & decisions need to be made on an individual basis.  
• Liaise with the prescriber/ pharmacist for advice about the use of medication during pregnancy & breast-feeding.  
• If appropriate inform or refer to relevant clinical team(s) involved in patients care. |
| All staff caring for female patients treated with medicines | • Are aware there are risks with using medication in pregnancy and know how to signpost patients/ carers with questions about the use of medication in pregnancy & breast-feeding.  
• Are aware there are risks with using medication in pregnancy versus the continued use of substances of abuse including alcohol and nicotine, and know how to signpost clients/ carers with questions about the use of medication in pregnancy & breast-feeding.  
• If appropriate inform relevant clinical team(s) involved in patients care. |
4. Definitions Used

**Addictions services** – Substance Misuse services will be referred to Addictions services in this document unless quoting other texts such as NICE Guidelines.

**Antenatal** - relating to the medical care of pregnant women, or to the time before a baby is born

**Ebstein’s anomaly** – a cardiac defect characterized by downward displacement of the tricuspid valve into the right ventricle and variable levels of right ventricular hypoplasia.

**First trimester** - time period extending from the first day of the last menstrual period through 12 weeks of gestation

**Gestational diabetes** – a condition in which women without previously diagnosed diabetes exhibit high blood glucose levels during pregnancy (especially during third trimester).

**Neonate** - a newborn child, especially in the first week of life and up to four weeks

**Neural tube defects** - Neural tube defects are birth defects of the brain and spinal cord. The two most common neural tube defects are spina bifida and anencephaly.

**OST**: Opioid Substitution Treatment

**Persistent pulmonary hypertension (PPHN)** - is defined as the failure of the normal circulatory transition that occurs after birth. It is a syndrome characterized by marked pulmonary hypertension that causes hypoxemia and right-to-left extrapulmonary shunting of blood. PPHN is associated with substantial morbidity and mortality.

**Perinatal** - relating to, or occurring in the period from about three months before to one month after birth

**Perinatal psychiatry**- psychiatric services relating to, or occurring in the period from conception to twelve months after birth

**Postnatal/ Postpartum** - referring to the period of time after the birth of a baby

**Second trimester** - time period extending from the 13th to the 27th week of gestation

**Teratogenesis** - relating to, or causing malformations of an embryo or foetus. Exposure to a teratogen in the first three months is more likely to cause structural malformations and exposure after the first trimester is more likely to cause growth defects

**Third trimester** - time period extending from the 27th week of gestation until delivery

**Client** - Service users or patients engaged in addiction services will be referred to as clients in this document unless quoting other texts such as NICE guidelines.
5. Procedure

Identification of Mental Health Problems & Care Plans

In pregnancy
Protocols for the management of women who are at risk of severe mental illness should be in place in every NHS Trust providing maternity services.\(^{13,14}\) All women should be routinely asked at the beginning of their antenatal care about a past history of or current serious psychiatric disorder.\(^{1,13-16}\)

NICE guidelines (2014)\(^1\) recommend that at a woman’s first contact with services in both the antenatal and postnatal periods, healthcare professionals (including midwives, obstetricians, health visitors and GPs) should ask questions about:
- Past or present severe mental health illness including schizophrenia, bipolar disorder, psychosis in the postnatal period and severe depression.
- Previous treatment by a psychiatrist/specialist mental health team including inpatient care.
- Any severe perinatal mental illness in a first degree relative (mother, sister or daughter).

Women who have a past history of, or current, serious psychiatric disorder, postpartum or non-postpartum, should be assessed by a psychiatrist in the antenatal period and a management plan, taking into account the high risk of recurrence following delivery, agreed and established.\(^{1,13,14,16}\)

For pregnant women with a current or past history of severe mental illness or substance misuse disorder a written care plan covering pregnancy, delivery and the postnatal period should be developed, usually in the first trimester.\(^1\) It should:
- Be developed in collaboration with the woman and her partner, family and carers’ and relevant healthcare professionals.
- Include increased contact with specialist adult perinatal mental health services.
- Be recorded in all versions of the woman’s notes (her own records and maternity, primary care and mental health notes) and communicated to the woman and all relevant healthcare professionals.

The mother’s developing relationship with her foetus/baby and the impact of her illness on the needs/safety of the foetus/baby must be assessed. As with all patients who are parents, if there are other children their needs/safety must also be taken into account\(^{17,18,10,11}\).

Postnatal
Protocols for the detection and management of postnatal depression should be in place in primary care.\(^{1,13}\) After the initial assessment, or for routine monitoring of outcomes, consideration should be given to using self-report measures such as the Edinburgh Postnatal Depression Scale (EPDS), Patient Health Questionnaire (PHQ-9) or the 7-item Generalized Anxiety Disorder scale (GAD-7).\(^1\)

5.1 Prescribing in Pregnancy & Breast-Feeding

5.1.1 Prescribing in Woman of Child Bearing Potential

More than 1 in 6 pregnancies in the general population are unplanned\(^19\), with higher unplanned pregnancy rates in mental health patients. Therefore any exposure to medicine
often occurs unwittingly, before the pregnancy is discovered, in the first trimester when the foetus is most vulnerable. Many women will stop medicines when they find out they are pregnant due to fear of harming their baby leaving them at risk of relapse without removing the risk of harm to the foetus. It is therefore essential to consider the risk of prescribing medicines to all women who may become pregnant along with their future intentions with regards to family planning.5

5.1.2 Prescribing in Pregnancy

**General Prescribing Advice in Pregnancy:**

- Prescribers should encourage discussion about pregnancy plans.1 When consideration is given to prescribing psychotropics to any woman of childbearing age, appropriate counselling regarding contraception and the risks of pregnancy (包括 relapse, risks associated with stopping or changing medication and risk to foetus) should be given.1
- The care of women with a psychiatric or substance misuse disorder during pregnancy and the postnatal period should be the same as for anyone with a psychiatric or substance misuse disorder13. However, treatment decisions need to take into account the impact of the medication on the foetus/infant.13
- Try to avoid medication in the first trimester, unless benefits outweigh risks.20,21
- An integrated care plan should be developed and coordinated by a healthcare professional detailing all aspects of the treatment and interventions, the roles of all individuals involved in the care and who will provide the interventions and agree the outcomes with the woman.1 The care plan, with the patients consent where possible, should be communicated to all professionals involved in the care.
- Prescribers should establish a clear indication for medication (i.e. the presence of significant illness in the absence of acceptable or effective alternatives).13 The severity of mental illness appears to represent an important parameter to take this clinical decision.22
- Where possible use monotherapy in preference to combination treatment.1,23 Choose medicines with profiles that suggest lower risk to the mother and foetus taking into account the woman's previous response to treatment.1,23
- Use the lowest effective dose to achieve remission of maternal symptoms. However, doses so low as to constitute ineffective treatment represent needless exposure by foetus/infant to medication.1,23

**Discussion with patients of Risks and Benefits:**

The risks and benefits will be different in each case depending on the severity of illness and risk of relapse and so need to be assessed on an individual basis in discussion with the patient. Decisions should be based on the latest available information for that medicine.

The pregnancy period is considered to be a window of opportunity to exert change. Nevertheless, it is time limited and services need to ensure prompt, appropriate and effective interventions to prevent irreparable consequences to the foetus. It is important therefore, that services endeavour to be accessible, welcoming, empowering and able to address all the complex issues with which pregnant women may present, as well as their mental health and substance use problems.7

It is paramount that mental health and addiction services offer flexible and closely monitored outpatient interventions in collaboration with the antenatal team.
Any decisions should involve the patient and family where possible after a full discussion of possible risks of exposure to psychotropics to the foetus/infant during pregnancy and breastfeeding weighed against the risks of leaving the maternal mental health disorder untreated and the risks of illicit drug use and withdrawal syndromes for both, mother and foetus and possible long-term neuro-behavioural disturbances for the infant. Decisions should also take into account stage in the pregnancy/gestational age, previous response to other treatments, and severity of illness/risk of relapse for this individual patient.

Clear documentation of the discussion of these risks with the patient and her family are crucial. In some situations a second opinion may be useful. The discussion should cover:

- The background risk of foetal malformations in all pregnancies. There is a background risk of major malformations of between 2 and 3 in 100 and a risk of spontaneous miscarriage between 10 and 20 in 100 in the general population. Over 75% of these malformations are of unknown aetiology; only 1 - 2% are thought to be due to medicines. This background risk may be increased by the presence of a mental disorder. Treatment can reduce the risk, but some psychotropics may increase it. Other factors other than medication may also increase the risk of malformations e.g. blood relation marriages, smoking.

- The potential risks associated with the specific medication(s) prescribed and other treatment options.

- The risk of malformations is increased by some psychotropic medicines, but is often difficult to quantify because of the limited data. The prescriber should acknowledge the uncertainty surrounding the risks with medications – see Table 1.

- The likely benefits of each treatment taking into account the severity of the woman’s illness.

- The risks of not treating the illness (also see section 5.1.4). The risk of relapse or deterioration in symptoms, and ability to cope with untreated or subthreshold symptoms without medication. The mental health of the mother in the perinatal period influences foetal well-being, obstetric outcome and child development.

- A thorough assessment of the benefits and risks of the use or the discontinuation of mind-altering substances should be conducted and a treatment plan should be agreed collaboratively with any pregnant woman presenting for or already in treatment with psychotropic medication.

- Discuss also the potential consequences if a relapse or deterioration in symptoms occurred such as, the possible need for using higher doses (often for prolonged periods) and/or polytherapy.

- The possibility of sudden onset of symptoms particularly in the first few weeks after childbirth.

Table 1: Uncertainties surrounding the risks with medication:

- The risk of malformations is increased by some psychotropic medicines, but the difficulties in assessing the risk with medication in pregnancy for psychiatric illness include the paucity of data and interpretation of exposures are often complicated by other confounders such as concurrent medication, lifestyle (e.g. diet, smoking, illicit substances) use as well as the illness itself.

- Data for many medicines in pregnancy and breast-feeding are derived from small studies, case reports, case series or from preclinical studies in animals (where extrapolation of such studies into human pregnancy is difficult). For more established medicines sometimes larger studies are available, lending to more confidence in the risk assessment.

- It is impossible to be sure that any medicine is ‘safe’ in pregnancy because it is unethical to conduct the randomised placebo-controlled trials that would be necessary to prove the point.
Medication is almost invariably not recommended for use by the manufacturer. Hence the data available to support prescribing decisions in pregnancy are usually of limited quantity and quality. In general data regarding the neurodevelopmental effects of psychotropic medication in pregnancy and breast-feeding are lacking.

There are potential risks to both the mother and foetus/infant from stopping certain medications abruptly. Therefore a pregnant woman should be advised to discuss with their doctor if they are thinking of doing this. When stopping a medicine considerations include:

- Clinical guidance on the specific disorder
- The risk to the foetus/infant as well as to the mother during the withdrawal period.

**Physiological and Pharmacokinetic Changes**

Physiological changes during pregnancy include increased glomerular filtration rate and expansion of plasma volume, which subsequently return to pre-pregnancy states soon after delivery. The physiological changes will be even greater in twin pregnancies. These changes can affect the clearance of many medicines. This may introduce the need for dose increases in the third trimester (usually around week 27 of gestation). Any increases made during pregnancy should be reduced again either near to term, or soon after delivery (see specific guidance for lithium – Appendix A). Dosage changes where possible, should be guided by maternal therapeutic drug monitoring.

If a woman becomes pregnant whilst taking a medicine where there is limited experience in pregnancy, always review the most up-to-date information available when making a decision as to whether it should be continued.

**5.1.3 Exposure to medicines with known teratogenic risk**

Where there are known risks with treatment, detailed ultrasound scanning at about 20 weeks of pregnancy, can give accurate information on gestational age and may detect anomalies while therapeutic abortion is still possible. Liaise with the patients’ obstetrician.

If exposure to a medicine with known teratogenic risk (lithium, valproate or carbamazepine) occurred at the time of conception or in the first trimester, healthcare professionals should:

- Confirm the pregnancy as quickly as possible.
- Offer appropriate screening and counselling about the continuation of the pregnancy, the need for additional monitoring and the risks to the foetus if the woman continues to take the medication.
- Seek advice from a specialist if there is uncertainty about the risks associated with specific medicines.
- Undertake a full paediatric assessment of the newborn infant.
- Monitor the infant in the first few weeks after delivery for adverse medication effects, toxicity or withdrawal (e.g. floppy baby syndrome, irritability, restlessness, increased tone, feeding, sleeping difficulties and rarely seizures). If the mother was prescribed antidepressants in the last trimester, these may result from serotonergic toxicity syndrome rather than withdrawal.
- Stopping a medicine with known teratogenic risk after a pregnancy is confirmed may not remove the risk of malformations.
- Prescribers should inform obstetric team of psychotropic medication use and possible complications.
Teratogenesis - Timing of exposure

Medicines can potentially cause adverse effects at any stage in pregnancy. Exposure to a teratogen in the first three months is more likely to cause structural malformations and exposure after the first trimester is more likely to cause growth defects.21 The embryo is most vulnerable to teratogens during the embryonic phase from days 18 to 55 when the cells differentiate and the major organs are formed. If differentiated cells are damaged they are unlikely to be replaced resulting in permanent malformations.23 The risk of exposure to a teratogen can differ among individuals. Not all foetuses will be affected.21

During the foetal period, from day 56 until birth, organs such as the cerebral cortex and the renal glomeruli continue to develop and remain particularly susceptible to damage. Functional abnormalities such as deafness may also occur.23 Teratogenic effects are usually dose-dependent and the dose response curve is steep i.e. a small increment in dose can result in a large increase in foetal toxicity.21 For example the incidence of neural tube defects with sodium valproate may be dose-related.23

5.1.4 Prescribing in breast-feeding

**General Prescribing Advice in Breastfeeding**

- The World Health Organisation stresses the desirability of breast-feeding exclusively for at least four to six months. It is therefore important to consider prescribing options that will allow the mother to safely breast-feed.4 However it is usually inappropriate to withhold treatment for breast-feeding to continue particularly in patients who are at a high risk of relapse.
- The treatment plan (including potential risks) should be communicated to the GP, health visitor and/or paediatrician.
- Each prescribing decision needs to take account of the risks and benefits to the individual mother and baby, including the indication for treatment, the pharmacokinetic properties of the medication, the age of the baby, clinical status of baby and timing of dosing in relation to infant feeding3,24
- Monotherapy is recommended where possible.
- Choose medicines with profiles that suggest lower risk to the mother and infant.23

Discussion with the patient of risks and benefits:

Psychiatric disorders can have substantial negative physical and psychological sequelae for mother and child. Early diagnosis and treatment interventions are therefore imperative for the health and well-being of the mother and child.4 It is usually inappropriate to withhold treatment to allow breast-feeding where there is a high risk of relapse.

In substance misuse clients, breastfeeding should be encouraged even if the mother continues to use drugs except for cocaine or crack cocaine or a very high dose of diazepam. Methadone is not contra indicated to breastfeeding but the dose should be kept as low as possible while maintaining stability, and the infant should be monitored to avoid sedation.2

In general there is very limited information on breast milk drug excretion with most medicines. Exposure to more than one psychotropic, particularly with medicines with overlapping side effects e.g. sedation, may increase risks.26

Most full term infants have a decreased capacity for drug metabolism until the third week of life. Metabolism and elimination are more efficient in older infants who generally sleep for...
longer intervals, permitting dosing of the mother just after breast-feeding and before the baby’s longest sleep interval.3

Consider additional precautions for preterm, low birth weight or sick infants. Premature infants and sick infants should not routinely be exposed to medications via breast milk26 but cases should be assessed on an individual basis in discussion with the paediatrician (taking into account - gestational age and clinical status of the infant including hepatic, renal and cardiac function), full maternal regimen and timing of dosing in relation to infant feeding.3,27

Monitoring
Infants of mothers who are breast-feeding while taking psychotropic medication should be monitored for adverse reactions. Follow-up of infant’s progress and attainment of developmental milestones is also important.3,4,26 Brain and target cell sensitivity may be greater in younger infants, and so even low serum medication levels in breast-feeding may confer some risk.3 Infant clinical status is the most important parameter to follow.

Parents should be alerted to the side effect profile of medications. Frequent paediatric clinical monitoring (especially in neonates) is important to ensure general health and normal paediatric development5,14,16.

5.1.5 Risks of Leaving an Illness Untreated

The risks and benefits will be different in each case depending on the severity of illness and risk of relapse and so need to be assessed on an individual basis in discussion with the patient. Decisions should be based on the latest available information for that medicine. The mental health of the mother in the perinatal period influences foetal well-being, obstetric outcome and child development.

Risks of Leaving Depression Untreated
There is sufficient evidence to show that leaving severe depression untreated can have adverse effects on the pregnancy outcome, especially if the mother is suicidal, and can adversely affect the mother-child relationship.20,28–32

Persistent depression may affect child development; in a prospective cohort study persistent depression (both pre and postpartum) was associated with developmental delay; the odds ratio was 1.34 (95% confidence interval of 1.11 - 1.62). These findings support the view that the mother's psychological well-being during pregnancy has significant implications for the child's development. Depression has also been associated with preterm delivery28,33

Women who have had a previous episode of depressive illness are at higher risk of further episodes during pregnancy and post-partum. One study found that 68% of women who were well on antidepressant treatment and stopped during pregnancy relapsed, compared with 26% who continued antidepressants. However the authors highlight that these figures may not hold with less severe forms of illness and that the risks and benefits of continuing s during pregnancy, even when a depressive episode has been treated successfully, need careful discussion with affected women.28

Potential risks of not treating the depression include harm to mother through poor self-care, lack of obstetric care or self-harm, or harm to the foetus or neonate.20
Postnatal depression is relatively common, occurring after about 13% of births. It can be severe and may have serious consequences for the woman and her child.31

**Risks of Leaving Schizophrenia Untreated**
Psychiatric illness itself during pregnancy is an independent risk factor for congenital malformations and perinatal mortality. Women with schizophrenia seem to have the highest risk compared to other psychotic illnesses. People with schizophrenia are more likely to have minor physical anomalies than the general population. This background risk complicates assessment of antipsychotic risk.20,24 Adverse outcomes reported in women with schizophrenia include preterm delivery, low birth weight, placental abnormalities, increased rates of congenital malformation, and a higher incidence of postnatal death. Psychiatric illness during pregnancy predicts postpartum psychosis. The postpartum period poses an increased risk of relapse. It has been reported that there is a 20 fold increase in the relative risk of psychosis during the month after childbirth.

**Risks of Leaving Bipolar Affective Disorder Untreated**
In a study34 looking at the risk of bipolar affective disorder (BPAD) relapse during pregnancy in women (n=89) who discontinued therapy versus those who continued mood stabilizer treatment observed the risk of recurrence was twice as likely. The time to first recurrence more than fourfold shorter (and even shorter after abrupt versus gradual discontinuation and the proportion of weeks ill during pregnancy was five times greater in women that stopped treatment. Most relapses were depressive or mixed with the majority occurring in the first trimester. Patients who discontinued treatment spent a greater proportion of the pregnancy in an illness episode compared to those maintained on mood stabilizers. Affective illness may also increase the risk of preterm delivery.20 Maintenance of euthymia during pregnancy is critical because relapse during this period strongly predicts difficulties postpartum. The first month after birth carries a particularly high risk of relapse.20

Risks associated with relapse include poor maternal self-care, poor engagement in obstetric and antenatal care, maternal self-harm, harm to foetus or neonate and possible need of higher doses or polytherapy and hence increased foetal medication exposure should relapse occur during pregnancy. The mother’s mental state should be monitored closely because of the risk of relapse.20

The mental health of the mother in the perinatal period influences foetal well-being, obstetric outcome and child development.20

5.2 Antidepressants in Pregnancy & Breast-Feeding

Refer section 5.1.4 for discussion of some of the known risks associated with depression during the peri- and postnatal period.

5.2.1 Antidepressants in Pregnancy

<table>
<thead>
<tr>
<th>Summary of Advice:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Both depressive symptoms and antidepressant exposure are associated with foetal growth changes and shorter gestations.32</td>
</tr>
<tr>
<td>• There is a lower referral threshold for psychological therapies during pregnancy and breastfeeding and so should be considered1 if there is access to these services and where clinically appropriate.</td>
</tr>
<tr>
<td>• There is considerable evidence that the decision not to prescribe antidepressants to a woman who is moderately to severely depressed or likely to have a recurrence during</td>
</tr>
</tbody>
</table>
pregnancy may generate greater risks to the woman and her foetus that the risks of exposure to the medication.\textsuperscript{35}

- The decision on which antidepressant to prescribe during pregnancy will be based on the individual antidepressant risks and the individual patients clinical needs.
- In patients who become pregnant whilst stable on an antidepressant, it may be appropriate to remain on their current treatment due to the risk of destabilization, especially where there is a known high risk of relapse.\textsuperscript{20} The risk of discontinuing or changing medication, or of reducing the dose, should be carefully weighed against the risk to both mother and child of relapse of the maternal condition. See section 5.1.2 regarding exposure to a medicine with a known teratogenic risk.

- Available data on tricyclic antidepressants (TCAs) in pregnancy do not prove that they are less teratogenic than SSRIs.\textsuperscript{20,36-38} Of the TCAs amitriptyline, imipramine and nortriptyline have been considered appropriate choices in terms of teratogenic risk to the foetus, but these are associated with increased risks of maternal cardiotoxicity, particularly in overdose.

- Data from randomized, controlled trials of antidepressants during pregnancy are lacking, but observational data suggest that selective serotonin-reuptake inhibitors are relatively safe during pregnancy, although increase risks of some maternal and foetal conditions have been reported.\textsuperscript{39} Patients should be educated about the risks, in terms of the absolute risk as well as the risks associated with untreated depression.

- All antidepressants carry the risk of withdrawal or toxicity in neonates. Therefore over the first few weeks post delivery infants should be monitored for signs of withdrawal or toxicity.

- Always consult the most up-to-date information about the medicine when making a risk assessment for an individual patient.

**Tricyclic Antidepressants (TCAs)**

*General advice for TCAs in pregnancy:*

- Amitriptyline, imipramine and nortriptyline are the TCAs of choice in pregnancy however most studies looked at TCAs as a class and the published data on individual TCAs and on the class as a whole is limited.\textsuperscript{38,40}

- Studies conducted to date have shown no increased risk of major malformations after in utero exposure to TCAs.\textsuperscript{20,36,41}

- However, available data on TCA use in pregnancy do not prove that they are less teratogenic than SSRIs.\textsuperscript{42,43}

- TCAs have been associated with an increased risk of pre-term delivery, caesarean section delivery, preeclampsia and low Apgar scores however data is limited and they are yet to be confirmed.\textsuperscript{36,40}

- TCAs which are least anticholinergic such as nortriptyline are less likely to exacerbate orthostatic hypotension, which can occur during pregnancy.

- For patients already stable on TCA, doses may need increasing as the pharmacokinetics of TCAs are altered in pregnant women. Serum levels can be used to guide dosing if necessary.\textsuperscript{36}

- Most TCAs have a higher fatal toxicity index than SSRIs, and so present a higher risk in overdose.\textsuperscript{38}

**Selective Serotonin Reuptake Inhibitors (SSRIs)**

*General advice for SSRIs in pregnancy:*

Data from randomized, controlled trials of antidepressants during pregnancy are lacking, but there is significant observational data available suggest that SSRIs are relatively safe during
pregnancy, although increased risks of some maternal and foetal conditions have been reported, including miscarriage, preterm birth, neonatal adaptation difficulties, neonatal persistent pulmonary hypertension, and cardiac malformations (particularly with paroxetine) and other malformations in neonates.37,39,42,44,45

If a patient becomes pregnant whilst taking an SSRI, a clinical decision should be made in discussion with the patient based on the risks and benefits of continuing treatment during pregnancy for that individual. When weighing up risks, consider stage of pregnancy i.e. greatest risk of teratogenic effects is in the first trimester46 and neonatal toxicity (see 5.1.4) with later stages of pregnancy. Only use where strictly indicated, where the benefits are perceived to outweigh the risks and at the lowest effective dose.

There is some evidence to suggest exposure to more than one SSRI in pregnancy poses a greater risk of septal heart defects47. It would therefore not be advisable to switch between SSRIs during the first trimester.

Persistent Pulmonary Hypertension
SSRIs taken after 20 weeks gestation may be associated with an increased risk of persistent pulmonary hypertension (PPHN) in the neonate.1 PPHN presents as severe hypoxaemia due to pulmonary artery hypertension and is associated with substantial morbidity and mortality. The background rate in the general population is an estimated 1 or 2 cases of PPHN per 1000 pregnancies.
- The observed increase risk is about an extra 3 to 4 cases of PPHN per 1000 pregnancies.48
- The increased risk of PPHN seems to be a class effect of SSRIs and does not differ between specific SSRIs.49
- Other perinatal risk factors for persistent pulmonary hypertension of the newborn include: maternal obesity, delivery by caesarean section, smoker, diabetes and the use of non-steroidal anti-inflammatory drugs during pregnancy.49,50
- Close observation of neonates exposed to SSRIs (or SNRIs e.g. venlafaxine) for signs of PPHN is recommended after birth.48

See end of this section for postnatal withdrawal effects with all antidepressants.

Cardiac Malformations
There is continuing debate regarding the risk of cardiac malformations in foetuses exposed to SSRIs in early pregnancy. Initial evidence suggested that paroxetine use in early pregnancy was associated in some studies with an increased risk of congenital malformations, especially those affecting the heart.42 However, available data are conflicting and the teratogenic potential of paroxetine remains unproven.42 Those studies that do show an increase in risk of cardiac malformation suggest that the absolute risk (0.86-2%) is only slightly raised above the background rate (0.8%).42 Further studies and meta analyses have provided contradictory findings and many of the studies have not been able to accurately confound for factors known to increase the risk of malformations such as smoking, drug and alcohol abuse therefore the risks of the individual SSRIs are difficult to fully establish.51–56 Currently with the evidence available it is not possible to rule out the risk of cardiac malformations. Various reports have been made for the other SSRIs and also for other malformations however there is no clear pattern of malformations identified. It is important to ensure that maternal mental health is treated appropriately.42
The background incidence of congenital cardiac defects in the general population is approximately 1 in 100 pregnancies. This data for SSRIs suggests an increased absolute risk to less than 2 in 100 pregnancies.

Advice for individual SSRIs

- It may not always be appropriate to stop paroxetine in pregnancy depending on the clinical scenario & stage of gestation. The risks and benefits of continuing must be considered on a case by case basis. If an antidepressant is newly indicated during pregnancy than another antidepressant may be more appropriate to initiate.
- Of the SSRIs the most experience is with fluoxetine, although there may be a small increased risk of congenital cardiac defects. Analysis of epidemiological data from seven cohort studies suggest that fluoxetine is not associated with a risk of non-cardiac defects, and that any increased risk of malformations appears to be driven by possible cardiac malformations. The cardiac defects reported in the studies were varied, and ranged in severity from reversible ventricular septal defects to transposition of the great vessels.
- Sertraline is now one of the widest prescribed antidepressants and along with fluoxetine there is growing experience from its use in pregnancy. Overall evidence suggests that sertraline is relatively safe although individual studies and meta analyses have shown a potential increased risk of specific malformations and cardiac malformations. As sertraline is a preferred antidepressant in breastfeeding it is one of the preferred antidepressants for initiation in pregnancy.
- Citalopram and escitalopram are also considered relatively safe in pregnancy and there is growing experience of their use. Again some studies have shown an increased risk for isolated malformations and cardiac malformations however this are not replicated and there is no clear pattern of malformations.

The potential increased risk should be considered in the context of the benefits of treating depression in pregnancy. See section 5.1.4 A detailed ultrasound scan should be considered following first trimester exposure to any SSRI.

A detailed ultrasound scan should be considered following first trimester exposure.

Venlafaxine & Mirtazapine

Venlafaxine should not routinely be initiated in pregnancy as there is insufficient data to assess the risk. However if there are compelling reasons to use e.g. inappropriate to use alternatives or previous history of good response with venlafaxine, the limited data available does not indicate an increased risk of malformation neither the animal reproduction data nor the human pregnancy suggest that venlafaxine is a major risk for congenital malformations. However as with SSRIs it has been associated with low birth weight, prematurity, neonatal serotonin syndrome and respiratory distress. PPHN is an additional potential risk given the related mechanism of action to SSRIs (refer to PPHN section with SSRIs). A single large case-control study reported associations with a number of specific malformations including hypospadias, gastroschisis, cleft palate, limb and heart defects however more information is required to fully confirm and evaluate these findings.

Venlafaxine may be associated with high blood pressure when used at higher doses. It has higher toxicity in overdose than SSRIs and some TCAs, and increased risk of discontinuation symptoms (refer to 5.2.1).
Use of mirtazapine in pregnancy is growing, with data from almost 700 pregnancies, however this information is still limited and therefore it generally would not be considered a first line option until further data is available to assess the risk.\cite{36,62} If there are compelling reasons to use e.g. inappropriate to use or switch to one of the preferred options, the limited data available does not indicate an increased risk of malformations, but as with other antidepressants may be associated with a slight increase in spontaneous abortions and pre-term births.\cite{63}

**Monoamine Oxidase Inhibitors (MAOIs)**

MAOIs should if possible be avoided because of their inherent maternal toxicity and lack of published data on safety in pregnancy.\cite{39}

**Antidepressant Withdrawal (Poor Neonatal Adaption Syndrome) & Postnatal**

**Effects include:**

- All antidepressants carry the risk of withdrawal or toxicity in neonates. Therefore over the first few weeks post delivery infants should be monitored for signs of withdrawal or toxicity.\cite{1}

- TCAs and SSRIs are associated with neonatal withdrawal or toxicity.\cite{32} In most cases the effects are mild and self-limiting; the child rarely has to stay in the neonatal intensive care unit for >5 days.\cite{49,64} In comparison, neonates who experience withdrawal from opiates sometime stay in the hospital for weeks and months.

- Poor neonatal adaptation syndrome occurs in 10-30% of infants who are exposed at term to SSRIs-SNRIs.\cite{49,64}

- Tapering of psychotropics approximately 2 weeks before estimated delivery has been suggested to reduce risk of neonatal complications however no clear advantage for the newborn has been demonstrated.\cite{20,38,65} Given the lack of evidence of benefit of the strategy, unpredictability of expected delivery dates and the risk of relapse during this period we would not recommend this practice.\cite{64}

- Medicines that have shorter half-lives such as venlafaxine and paroxetine may be associated with an increased risk of withdrawal effects, and possibly an increased severity.\cite{1,22}

- Short-term neonatal withdrawal symptoms associated with TCA near to the time of delivery such as jitteriness, hyperexcitability, myoclonus, convulsions and suckling problems, have been reported especially in premature or smaller than average infants.\cite{36,38}

- Short term neonatal symptoms associated with use of SSRIs near to the time of delivery include jitteriness, irritability, tremor, constant crying, shivering, hypotonia, suckling and sleeping difficulties. More severe reactions such as respiratory distress and convulsions have been infrequently reported. Some of these symptoms may be due to serotonin stimulation rather than withdrawal. Symptoms usually resolve within 1 week but in some cases may last longer.\cite{32}

- Neonatal haemorrhage has been reported as a possible complication of maternal use of SSRI treatment, although there is a distinct lack of data to evaluate risk. Caution may be advisable in women with concurrent diseases or other conditions that may increase the risk of bleeding.\cite{32}

**Antidepressants and spontaneous abortion**

There is less information regarding spontaneous abortions, as administrative databases generally do not record this outcome.
Two studies using different methodologies, one a teratogen information service study and the other a case control from a prescription database, found a similar increased risk of spontaneous abortion (relative risk 1.63 and odds ratio 1.61).43,66

Antidepressants and foetal growth and preterm birth

Several studies reported a small, but statistically significant increase (1 week early, < 37 weeks) in the incidence of premature births of women exposed to antidepressants late in pregnancy.67,68

In the cases of low birth weight, small for gestational age, spontaneous abortion, foetal growth, intrauterine death and preterm birth although the evidence does not suggest any major increase in risk, data is too limited to rule out an increased risk.36,37,42,45

5.2.2 Antidepressants in Breast-feeding

- The following are recommendations for healthy full term infants. It is usually not advisable for premature, ill or low birth weight infants to be exposed to psychotropics via breast milk - always seek additional advice/information.
- Where mothers have been successfully maintained on an antidepressant throughout pregnancy the same medication should usually be continued in the postpartum period.40 This may also limit withdrawal effects in the neonate.
- SSRIs sertraline and paroxetine are among the first line choices for the management of depression in breastfeeding mothers.31,69,70
- Citalopram and fluoxetine are present in breast milk at relatively high levels and so are not the preferred SSRIs in breast-feeding.
- Infants exposed to SSRIs via milk should be monitored for sedation, poor feeding and behavioural effects.
- TCAs are usually compatible with breast-feeding except doxepin.26
- Experience of the use of reboxetine, venlafaxine, mirtazapine and duloxetine in lactation is very limited and they are not considered as first line antidepressants in breastfeeding women.
- MAOIs should be avoided in lactation.

SSRIs
Sertraline and paroxetine are among the first line choices for the management of depression in breastfeeding mothers.31,69,70 SSRIs are the antidepressant group for which the most data exist for use in lactation, although data is still limited.

Infant ingestion via milk is lowest for sertraline and highest for fluoxetine.31 Limited data on effects of SSRI exposure via breast milk on weight gain and infant development are encouraging. Co-therapy with sedating agents is best avoided. Citalopram and fluoxetine are present in breast milk at relatively high levels and so are not the preferred SSRIs in breast-feeding.26 Although each case should be assessed on an individual basis as it may not always be appropriate or necessary to change the antidepressant, but close monitoring of the infant would be advisable.

Infants exposed to SSRIs via milk should be monitored for sedation, poor feeding and behavioural effects.
TCAs
TCAs are usually compatible with breast-feeding except doxepin. First line choices of the TCAs include imipramine and nortriptyline, if clinically appropriate as these are less sedating, and are present in breast milk at relatively low levels. Risks can be further minimised by using a single daily dose and breastfeeding immediately before medication administration. For very young infants feeding frequently, it may be possible to reduce medication exposure by substituting with one bottle feed at the time when peak plasma medication levels occur in the mother. Infants should be monitored for sedation, poor feeding or other behavioural changes.

Other Antidepressants
Experience of the use of MAOIs, reboxetine, venlafaxine, mirtazapine and duloxetine in lactation is very limited and they are not considered as first line antidepressants in breastfeeding women. MAOIs should be avoided in lactation. There is absence of data on use in lactation and potential to cause serious interactions with some foods and medicines.

Limited data indicate that reboxetine, duloxetine and mirtazapine pass into milk in small amounts and estimated infant intake via milk has been calculated at values of up to 2% of the weight adjusted maternal dose. Values for venlafaxine are higher at 3.5 – 9.2%.

Venlafaxine via breast milk may attenuate neonatal withdrawal symptoms where the medicine is used close to term.

Apart from two cases of reduced weight gain with venlafaxine, no adverse effects have been reported for infants exposed to reboxetine, duloxetine, mirtazapine or moclobemide. Use of other sedating agents in the mother should be avoided since sedation may be additive.

Other resources for antidepressant use in breastfeeding
The following UKMI Q&As are available:
- Management of depression in breastfeeding mothers – are tricyclic antidepressants safe?
- Management of depression in breastfeeding mothers – are selective serotonin reuptake inhibitors (SSRIs) safe?
- Management of depression in breastfeeding mothers – Are reboxetine, venlafaxine, duloxetine, mirtazapine and MAOIs safe?
- Management of depression in breastfeeding mothers – Are St. John's Wort and other complementary therapies safe?

The full list of UKMI Q&As are available here: http://www.ukmi.nhs.uk/activities/medicinesQAs/default.asp

5.2.3 Neurodevelopmental Effects
- There is limited data addressing possible neurodevelopmental delay in antidepressant exposed infants. It is therefore difficult to make an evaluated assessment of risk.
- A study on 80 preschool children exposed to antidepressants did not indicate any adverse effects on neurodevelopment, measured using indicators such as global IQ, language and behaviour.
- Four studies including nearly 100 mother/infant pairs with third trimester exposure to SSRIs have not revealed any long-term effects whereas two studies found subtle effects on motor movement control, the clinical implication of which are unknown. None of the studies found any influence on cognitive, emotional or behavioural development.
A population based case control study found an increased risk of autism spectrum disorders in children exposed to both SSRIs and TCAs in utero however the absolute risk was low and was not thought to have contributed significantly towards the dramatic increase in prevalence of these disorders. Further studies and analyses have shown contradictory findings, although one large cohort study found no association with antidepressants and autism but instead linked them with the development of ADHD. It is thought that major depression itself may be the major contributing factor in studies which have shown an increase in autism. The link between antidepressants and autism remains to be fully established.

5.2.4 St. John’s Wort and other complementary therapies

Use of these herbal products and nutritional supplements is often perceived by patients to be a safer or more natural alternative to conventional antidepressants. Of these complementary remedies, the strongest evidence base for benefit in depression exists for St. John’s Wort.

Although there is some evidence that St John’s Wort may be of benefit in treating mild to moderate depression, NICE advises that it should not be prescribed or recommended for use by patients because of uncertainty about appropriate doses, variation in the nature of preparations and potential serious interactions with other medicines such as oral contraceptives, anticoagulants and anticonvulsants.

Pregnancy and Breastfeeding

Women who are Pregnant or breastfeeding should be advised not to self-medicate with St. John’s Wort or other complementary therapies.

Pregnant or breastfeeding women should be advised not to self-medicate with herbal products such as St John’s Wort, Gingko biloba or Valerian because of the lack of data to support safe use at this time. Some evidence exists to support the safe use of St John’s Wort during breastfeeding but further data are needed to confirm these preliminary findings.

- Minor side effects of colic, drowsiness and lethargy have been described in breastfed infants whose mothers were taking St. John’s Wort.
- Infants exposed to St John’s Wort during breastfeeding should be monitored for adverse effects, particularly sedation and poor feeding.
- Due to lack of data to support safe use in lactation, nutritional supplements tryptophan in dose exceeding the maximum recommended daily intake of 220 mg and S-adenosylmethionine are best avoided in breastfeeding mothers.

5.2.5 Male Fertility and Antidepressant Medication

- Animal data have shown that citalopram, paroxetine and fluoxetine may affect sperm quality. Impact on human fertility has not been observed so far.
- Human case reports with some SSRIs have shown that an effect on sperm quality is reversible.
- Animal data did not show an effect of sertraline on fertility parameters.

5.3 Antipsychotics

Refer to section 5.1.4 for discussion of some of the known risks associated with schizophrenia and bipolar affective disorder during the peri- and postnatal period.

- The risks and benefits will be different in each case depending on the severity of illness and risk of relapse and so need to be assessed on an individual basis in
discussion with the patient. Decisions should be based on the latest available information for that medicine.

- NICE (2014)\(^1\) advise that if a pregnant woman is stable on an antipsychotic and likely to relapse without medication she should be advised to continue the antipsychotic.
- Overall the evidence available for antipsychotics as a group do not suggest any increased risk of malformations therefore where indicated, treatment with antipsychotics should continue during pregnancy.

### 5.3.1 General information for Antipsychotics in Pregnancy

Progress of pregnancy in patients with psychotic disorders should be monitored closely for normal foetal development and to detect relapse or other pregnancy complications. Data relating to antipsychotics and pregnancy are poor. A Cochrane review (2004) suggests insufficient data on which firm conclusions about treatment options can be made.\(^86\)

Women taking antipsychotics associated with hyperprolactinaemia (e.g. first generation antipsychotics, risperidone, paliperidone, amisulpride) who are planning a pregnancy should be advised that raised prolactin levels reduce the chances of conception. If levels are raised consider an alternative medication.\(^1\)

Consider potential for hypotension with prescribed antipsychotic. Maternal orthostatic hypotension could decrease placental blood flow, with potentially damaging effects to the foetus.\(^24\) Consider potential for sedation and anticholinergic effects with prescribed antipsychotic. Sedation may worsen the fatigue in pregnancy; and the anticholinergic side effects of constipation and hypotension may also be worsened.

A recent study showed that gestational diabetes was more than twice as common in women who used antipsychotics compared with women who did not.\(^57\) The study looked at data for women (n=358,203) who gave birth in Sweden between July 2005 and December 2009. The women taking antipsychotics were placed into two groups according to whether they were taking 1) olanzapine and/or clozapine (absolute risk 4.1%) or 2) other antipsychotics including first or second generation (absolute risk 4.4%).\(^57\) The two groups were compared with pregnant women who were not taking antipsychotics (absolute risk of 1.7%). There have been reports of low birth weight following exposure to antipsychotics however there are confounding factors such as smoking that may increase this risk.\(^87,88\) Conversely there have been reports of an increased incidence of being large for gestational age babies.\(^89\) Increased weight gain together with poor folate intake can lead to an increased risk of folate deficiency and subsequently an increased risk of neural tube defects. All patients should be advised to take standard folate supplementation (400micrograms daily), those at high risk of neural tube defects, including those who are obese ( BMI >30kg/m\(^2\)) have diabetes, or are on anticonvulsants (see section 5.6.1) should be advised to take folic acid 5mg daily.

### All pregnant women prescribed an antipsychotic should

- Be advised about diet and monitored for excessive weight gain in line with the NICE guideline\(^90\) on weight management in pregnancy: [http://www.nice.org.uk/guidance/ph27](http://www.nice.org.uk/guidance/ph27)
- Be monitored for gestational diabetes in line with the NICE guideline\(^91\) on diabetes in pregnancy: [http://www.nice.org.uk/guidance/cg63](http://www.nice.org.uk/guidance/cg63)
- Be advised to take folic acid supplements (400 micrograms daily). Those at particular risk should have supplementation with 5mg folic acid\(^34\) 6 weeks prior to conception until the 12\(^{\text{th}}\) week of pregnancy.
Conventional antipsychotics

<table>
<thead>
<tr>
<th>General Advice for First Generation Antipsychotics in Pregnancy:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• NICE (2014) guidance on antenatal mental health advises that if a woman becomes pregnant whilst stable on an antipsychotic and is likely to relapse without medication, she should be advised to continue the antipsychotic.</td>
</tr>
<tr>
<td>• There is limited data on which to base the risk assessment with the conventional antipsychotics, and so it remains uncertain whether they are entirely without risk. However, the wide use of these medicines over several decades suggests that if there is a risk it is likely to be small. Haloperidol and the phenothiazines were previously considered to be the antipsychotics of choice in pregnancy but there is also growing evidence for the use and safety of second generation antipsychotics in pregnancy.</td>
</tr>
<tr>
<td>• Consider risk for extrapyramidal side effects with first generation antipsychotics and possible need for additional potentially teratogenic medications (i.e. anticholinergics, refer to section 5.4.1) to manage side effects.</td>
</tr>
</tbody>
</table>

Advice for individual first generation antipsychotics is as follows:

- **Haloperidol:**
  The published epidemiological data, combined with the follow-up data provided by the UK Teratology Information Service (UKTIS), do not demonstrate an increase in risk of congenital malformations or spontaneous abortion following haloperidol exposure however this data is limited. There is no specific pattern to malformations reported in infants exposed to haloperidol in pregnancy.

- **Phenothiazines:**
  Chlorpromazine and trifluoperazine are among the antipsychotics of choice to start in pregnancy and are considered by many to be of low risk however their potential for causing hypotension and anticholinergic effects means they must be used with care.

Data for the use of phenothiazines in pregnancy mainly relates to their use in hyperemesis gravidarum at lower doses than those used in the treatment of psychosis.

Although one survey found an increased incidence of defects with chlorpromazine, other reviewers have concluded that the phenothiazines are not teratogenic and that because of its extensive clinical experience, chlorpromazine is among the treatments of choice if antipsychotic therapy is required during therapy. Close to term both the mother and neonate should be monitored carefully due to its potential to cause maternal hypotension and neonatal withdrawal effects. Most of the evidence with trifluoperazine suggests that it is not associated with an increased risk of malformations.

There is very limited documented evidence of the use of antipsychotic depots in pregnancy therefore they are best avoided where possible, given the potential for accumulation and toxicity in the neonate. Where a patient is stable and responding well to a depot antipsychotic and there is a history of non-compliance it can be continued.

Consider risk for extrapyramidal side effects (EPSE) especially with high potency first generation antipsychotics (e.g. haloperidol and trifluoperazine) and possible need for additional potentially teratogenic medications to manage side effects (i.e. anticholinergics, refer to section 5.4).
Second generation antipsychotics

**General Advice for Second Generation Antipsychotics in Pregnancy:**

- Of these there is more experience with olanzapine or quetiapine during pregnancy.\(^{95–97}\)
- Given the growing evidence for the safe use of the second generation antipsychotics during pregnancy although previously haloperidol and the phenothiazines were the antipsychotics of choice in pregnancy, second generation antipsychotics with the most experience may now be considered as alternatives. The risks of destabilization and maternal relapse should be taken into account before switching.
- A detailed ultrasound scan should be considered following first trimester exposure with a second generation antipsychotic.
- Second generation antipsychotics are known to be associated with weight gain which can increase risks for both mother and baby, such as the baby being at higher risk of neural tube defects.
- Obesity is associated with high rates of obstetrical complications including gestational diabetes, pre-eclampsia and caesarean delivery. Consider increased risk with olanzapine and clozapine compared to other antipsychotics.\(^{24}\) Other side effects of second generation antipsychotics include diabetes and sedation, which confer significant risk factors in pregnancy.
- Inform obstetrician regarding risk of metabolic adverse effects, and need for close monitoring of weight and blood glucose throughout pregnancy.

Advice for individual second generation antipsychotics is as follows:

- **Olanzapine**
  A review by the UK Teratology Information Service (UKTIS)\(^{95}\) advises that the current available data for olanzapine do not suggest a substantially increased risk of congenital malformations or spontaneous abortion and no pattern of malformations have been observed. However the available data are too limited to be certain about the risks. Some recent case reports have suggested a potential teratogenic effect of olanzapine, however an increased risk of congenital malformations has not been observed in systematic epidemiological studies and causality cannot be determined. A global safety surveillance database now has evidence of over 600 pregnancies during which olanzapine was used. The frequency of outcomes including major malformations, prematurity and spontaneous abortion did not differ from outcome rates reported in the general population.\(^{98}\)
  Other risks include an increased risk of intensive care neonatal admissions and gestational diabetes has also been reported during treatment with olanzapine.\(^{88}\) In addition weight gain associated with olanzapine treatment can increase the risks for both mother and baby, such as the baby being at higher risk of neural tube defects.\(^{99}\)

- **Quetiapine**
  A review by the UKTIS\(^{97}\) advises that the current available data for quetiapine do not suggest a substantially increased risk of congenital malformations or spontaneous abortion and no pattern of malformations have been observed. However the available data are too limited to be certain about the risks. Quetiapine is one of the second generation antipsychotics with the most experience in pregnancy.

- **Risperidone**
  A review by the UKTIS\(^{96}\) states that there are limited data available on which to base an assessment of the risk of risperidone in pregnancy. These data do not suggest a significantly
increased risk of congenital malformations or spontaneous abortions following exposure to risperidone but are too limited to exclude any increase in risk.

- **Aripiprazole**
  The data for aripiprazole in pregnancy are very limited. The data available do not suggest a significantly increased risk of congenital malformations or spontaneous abortion following exposure but are too limited to exclude any increase in risk.\(^{100}\) A single study did show an increase risk of low birthweight and pre-term delivery.\(^{100}\)

- **Clozapine**
  Ideally clozapine should not be initiated in pregnancy. If a woman prescribed clozapine becomes pregnant, consider switching to another antipsychotic, although it is acknowledged that this may not be a viable clinical option for the mother and on the balance of risk and evidence available, clozapine should usually be continued.\(^{20}\) A review by UKTIS\(^{101}\) states there are limited data on which to base an assessment of the safety of clozapine in pregnancy. These data do not suggest a significantly increased risk of congenital malformations or spontaneous abortion following exposure but are too limited to exclude any increase in risk. There are a small number of perinatal/ neonatal seizures, gastroesophageal reflux, sedation and cardiovascular instability reported with foetal exposure to clozapine\(^{27}\). Additional concerns include theoretical risk of agranulocytosis in the infant. The possible risks of agranulocytosis with foetal clozapine exposure warrants monitoring of white blood cell count (WBC) in newborn.\(^{102}\)

Withdrawal and Postnatal effects following antipsychotic exposure include:
- A perinatal syndrome has been reported in infants born to mothers taking first generation antipsychotics. Symptoms include respiratory depression, difficulty in feeding, floppy infant syndrome, hypertonicity, sluggish primitive reflexes, neonatal restlessness, tremor, poor suckling, and abnormal movements. These are fairly rare and generally resolve within days\(^{102}\). Withdrawal effects in the neonate have also been reported with second generation antipsychotics.
- In 2011 the FDA released a safety alert notifying healthcare professionals that the pregnancy section for all antipsychotics should state the potential risk for abnormal muscle movements (extrapyramidal side effects) and withdrawal symptoms in newborns whose mothers were treated with these medicines during the third trimester.\(^{103}\)
- Observation of the neonate for at least 2 days is advisable where antipsychotics have been used up to delivery.
- To reduce the risk of neonatal adaptation disorders, dose reduction or even treatment interruption in the days’ immediately preceding delivery can be discussed with the patient if the clinical course allows. Although this will not always be clinically appropriate. The postpartum period represents a high risk so if dosage reductions are made, the pre-pregnancy dosage should be started immediately after delivery to prevent a relapse at this vulnerable stage.\(^{104}\)

5.3.2 Antipsychotics in Breast-feeding

<table>
<thead>
<tr>
<th>General Advice for Use of Antipsychotics in Breastfeeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>- There is limited data(^*) on the use for all antipsychotics in breastfeeding(^4) and data is often conflicting so all decisions need to be made on an individual case basis with the benefits of breastfeeding being weighed against the potential risks of the medication.</td>
</tr>
</tbody>
</table>
Of the second generation antipsychotics the most data is with olanzapine however quetiapine, has a shorter half-life and is recommended as the preferred second generation in breastfeeding in a number of sources.4,20,40

Infants exposed to antipsychotics through breastfeeding should be regularly monitored for side effects such as sedation, muscle rigidity or tremors as well as achievement of developmental milestones.

Treatment with antipsychotic combinations should usually be avoided (or stop breastfeeding) where possible. Developmental decline in infants nursed by mothers treated with antipsychotic combinations (haloperidol and chlorpromazine) has been reported.

*Data for antipsychotics in breastfeeding at present is limited to a hand-full of case reports and at best small studies in which patient numbers are usually less than ten. Decisions should be based on the latest available information for that medicine.

Advice for individual antipsychotics is as follows:

- **Haloperidol** is secreted into breast milk20. Limited data suggests that maternal doses of haloperidol monotherapy up to 10 mg daily produce low levels in milk and do not affect the breastfed infant105. Very limited long-term follow-up data indicate no adverse developmental effects when haloperidol is used alone.105 Developmental decline in infants nursed by mothers treated with antipsychotic combinations of haloperidol and chlorpromazine have been reported105.

- Of the second generation antipsychotics the most data is with olanzapine and so it is one of the preferred second generation antipsychotics in breastfeeding.4,20 Limited information indicates that maternal doses of olanzapine produce low levels in milk. In most cases, short-term side effects have not been reported, but sedation has occurred.69,106 Monitor the infant for drowsiness and developmental milestones, especially if other antipsychotics are used concurrently.71 In a recent study no increase in adverse long-term outcomes in olanzapine-exposed breastfed infants were found.107 The study supported the continuation of breastfeeding in women treated with olanzapine. However advised, until additional long-term studies are available, infants exposed to olanzapine through breast milk should be followed up.

- Limited information indicates that maternal quetiapine oral doses of up to 400 mg daily produce low levels in milk, equivalent to be less than 0.5% of the weight adjusted maternal dose.108,109 Quetiapine has a short half-life compared to many of the second generation antipsychotics and therefore there is reduced risk of accumulation in the neonate and for that reason it is considered by some sources to be the preferred second generation in breastfeeding.26 There is little published experience with quetiapine during breastfeeding and little long-term follow-up data, which should be taken into account when making the risk assessment.108

- Limited information indicates that maternal risperidone doses of up to 6 mg daily produce low levels in milk.110 There is little published experience with risperidone during breastfeeding and little long-term follow-up data, which should be taken into account when making the risk assessment.

- It is not recommended to breast-feed whilst taking clozapine mainly due to the risks of agranulocytosis, and reported cases of accumulation of clozapine in breast milk.26

### 5.3.3 Neurodevelopmental Effects

- The few small studies examining the long-term neurobehavioral effects in children exposed to first generation antipsychotics in utero have reported no behavioural or intellectual abnormalities.24,25,111
- There are no studies available on the neurobehavioural effects of second generation antipsychotics.\textsuperscript{24,111}
- In a recent study among 6-month-old infants, a history of intrauterine antipsychotic exposure, compared with antidepressant or no psychotropic exposure, was associated with significantly lower scores on a standard test of neuromotor performance.\textsuperscript{75}
- Normal development following foetal exposure to clozapine has been reported in seven subjects evaluated up to 5 years of age. There is a report of a child born prematurely with several anomalies and delayed development at 7 months.\textsuperscript{24,111}
- Very limited long-term follow-up of infants exposed to olanzapine indicates that infants generally developed normally, but combinations of antipsychotic agents can negatively affect development.\textsuperscript{106} Two cases of normal development have been reported following foetal exposure to olanzapine; one of these reported delayed motor development at 7 months that resolved at 11 months.\textsuperscript{24}
- There are two cases of normal development up to 1-year postpartum following foetal exposure to risperidone.\textsuperscript{24}
- There is one case of normal development at 6 months following foetal exposure to quetiapine.\textsuperscript{40}

5.4 Anticholinergics

- Given the lack of evidence for the safety of anticholinergics in pregnancy it is advisable not to routinely prescribe anticholinergic medications for the treatment of extrapyramidal side effects of antipsychotics in pregnancy or breastfeeding, except for short-term use; instead adjust dose and timing of the antipsychotic or switch to another medicine to avoid side effects.

5.4.1 Anticholinergics in Pregnancy

There are few data available on the potential reproductive toxicity of procyclidine in human pregnancy.\textsuperscript{112} The outcome data that are available suggest that procyclidine use during pregnancy could be associated with a small increase in the risk of congenital malformation, although no specific pattern of malformations has been identified. The possibility remains that this apparent increase in risk could result from other factors, including underlying disease or concurrent therapy.\textsuperscript{113}

One study that assessed benztropine and trihexyphenidyl (benzhexol) in pregnancy, and found a possible association between the use of these medications and malformations.\textsuperscript{94} Based on a small number of exposures with benztropine, there may be a possible association with cardiovascular defects.\textsuperscript{94}

A Collaborative Perinatal Project monitored 50,282 mother-child pairs, 401 of who used atropine in the first trimester. No association with malformations was found. However when anticholinergic agents were grouped together, a possible association with minor malformations was found.\textsuperscript{113}

Chronic use of anticholinergics or use near term (including procyclidine) has been associated with neonatal withdrawal adverse effects and so they should be gradually withdrawn before delivery.
5.4.2 Anticholinergics in Breast-feeding

With short-term use the infant should also be monitored for untoward signs and symptoms, particularly for anticholinergic adverse effects such as tachycardia and changes in temperature. Constipation and urinary retention may occur in infants with repeated doses. Long term use of an anticholinergic might reduce milk production or milk letdown, but a single dose is not likely to interfere with breastfeeding.

No information is available on the use of orphenadrine, procyclidine, trihexyphenidyl or benztropine during breastfeeding.

Neonates and young infants are more sensitive to the effects of anticholinergics and the potential hazard would be greater in this age group.

5.5 Benzodiazepines & Hypnotics

5.5.1 Pregnancy

General advice for prescribing in Anxiety

- Where clinically justifiable, use of benzodiazepines in the first trimester may be considered, ideally following discussion with the patient of the possibility of risk.
- It is imperative that the lowest effective dose is used and only for as long as considered clinically necessary.

Benzodiazepines

Please refer to Section 5.8.6 for use of benzodiazepines in addiction services

Where clinically justifiable, use of benzodiazepines, in particular diazepam, in the first trimester may be considered, ideally following discussion with the patient of the possibility of risk. It is imperative that the lowest effective dose is used and only for as long as considered clinically necessary.

NICE advise not to routinely prescribe benzodiazepines to pregnant women, except for short-term management of extreme anxiety and agitation. They advise to consider gradually stopping benzodiazepines in women who are planning a pregnancy, pregnant or considering breastfeeding.

Studies investigating the teratogenicity of benzodiazepines are conflicting as to whether a possible association with increased risk of congenital malformation, specifically of orofacial clefts, exists. Older studies suggest possible increased risks of congenital malformation, including orofacial clefts and cardiac malformations. More recent, better designed studies, have failed to identify such associations.

If benzodiazepines do cause birth defects the risk appears to be low. The potential effects of diazepam use at any stage of pregnancy on foetal neurodevelopmental outcome is unknown.

In light of conflicting data concerning the risk of congenital malformation, detailed foetal ultrasound scans may be considered following first trimester exposure.

There are no data available relating specifically to the risk of spontaneous abortion (SA) following diazepam exposure in pregnancy, and although an increased risk of spontaneous
abortion following exposure to benzodiazepines as a group has been reported, these data are considered too limited and confounded to be certain that a clinically relevant increased risk of spontaneous abortion exists.\textsuperscript{115}

Abrupt discontinuance of chronic benzodiazepine use should be avoided as severe withdrawal symptoms (physical and psychological) may occur in the mother. Consideration should also be given to the risk of substitution with other substances (e.g. alcohol) if benzodiazepines are discontinued.\textsuperscript{94}

General advice for prescribing in Sleep Disorders

<table>
<thead>
<tr>
<th>For women with a severe or chronic sleep problem, where a hypnotic is indicated, promethazine should be considered.\textsuperscript{1}</th>
</tr>
</thead>
<tbody>
<tr>
<td>There are few data available on the use of zopiclone or zolpidem in pregnancy and they should therefore not routinely be used in pregnancy.\textsuperscript{116}</td>
</tr>
</tbody>
</table>

Zopiclone and Zolpidem

There are few data available on the use of zopiclone in pregnancy. Based on animal data and limited data of human exposure in pregnancy zopiclone does not appear to increase the risk of malformations although a small study has provided evidence of an association between maternal zopiclone use and pre-term delivery but the data is too limited to be certain that a true association exists.\textsuperscript{116} Although there is insufficient information to establish its safety, and it should therefore not routinely used in pregnancy.\textsuperscript{116}

Similarly the data on the use of zolpidem in pregnancy is limited although there is more experience with zolpidem than zopiclone. Based on the limited data of human exposure in pregnancy zolpidem does not appear to increase the risk of malformations. Associations between in-utero zolpidem exposure and increased risks of preterm delivery and low birth weight have been reported however the available data is limited and conflicting therefore a link between zolpidem and reduced intrauterine growth remains to be established.

As with all centrally acting medication, zopiclone, and zolpidem may be associated with withdrawal effects in the neonate – see below. A detailed ultrasound scan should be considered following first trimester exposure.

Promethazine

NICE (2014)\textsuperscript{1} guidance on antenatal mental health advises pregnant women with a mental disorder who have sleep problems should initially be given general advice about sleep hygiene. For women with serious and chronic problems, promethazine may be considered.\textsuperscript{1}

The published data, in combination with many years of clinical experience of promethazine use for a number of indications, do not indicate an increased risk of congenital malformations following exposure to promethazine in pregnancy.\textsuperscript{117} This includes studies which have looked at maternal overdoses and found no increased risk of malformations. There is a theoretical risk of neonatal withdrawal symptoms following use near to term.\textsuperscript{38}

Withdrawal and Postnatal Effects

Third trimester exposure of benzodiazepines and use close to term has been associated with ‘floppy infant syndrome’ which, includes symptoms such as hypotonia, lethargy, suckling difficulties, apnoea and hypothermia. Neonatal withdrawal symptoms (e.g. intrauterine growth retardation, tremors, irritability, hypertonicity, diarrhoea, vomiting, vigorous suckling), have also been reported.\textsuperscript{94}
Observation of the neonate for respiratory depression, withdrawal symptoms or adaptation problems is recommended when benzodiazepines have been used up to delivery.38

5.5.2 Breast-feeding

- Generally benzodiazepines are not ideal for breastfeeding mothers due to their relatively long half-lives and the development of dependence. Shorter acting benzodiazepines e.g. lorazepam are deemed safer provided their use is short-term or intermittent, low dose and after the first week of life. Lorazepam appears to be excreted in breast milk at relatively low levels.69
- If treatment is strictly indicated, the 'Z-' hypnotics (see below regarding individual medicines) may be used in breastfeeding if it is short term and intermittent use and the baby is healthy and full-term.118
- Generally, it would be wise to discourage bed sharing (mother and infant) when the mother has taken a sedative or hypnotic medication.

Benzodiazepines
Generally benzodiazepines are not ideal for breastfeeding mothers due to their relatively long half-lives and the development of dependence. Shorter acting benzodiazepines e.g. lorazepam are deemed safer provided their use is short-term or intermittent, low dose and after the first week of life. Lorazepam appears to be excreted in breast milk at relatively low levels.26,69

All benzodiazepines should be used with caution taking into account that neonates metabolise benzodiazepines more slowly. Long-acting benzodiazepines e.g. diazepam should be avoided as they could potentially accumulate in the breastfed infant following prolonged administration, leading to possible sedation and increased risk of apnoea.

Try and avoid breastfeeding at peak benzodiazepine plasma concentrations (which is around 2 hours for lorazepam) to minimise exposure.69

Repeated doses of benzodiazepines during breast-feeding can produce lethargy, sedation, poor suckling and weight loss.27 If repeated administration is needed or prolonged use is required review care plan/ risk assessment.

Monitor infant for adverse effects such as sedation, nausea, reduced suckling, and other signs of toxicity. If such symptoms occur breast-feeding should be discontinued and immediate advice sought.

Zopiclone and Zolpidem

Insomnia: If treatment is strictly indicated, the 'Z-' hypnotics (zopiclone, and zolpidem) may be used in breastfeeding if it is short term and intermittent use and the baby is healthy and full-term.118

However it should be borne in mind that there is only limited information on breast milk levels for all of the Z drugs, and as with exposure to any psychotropic via breast milk the infant should be monitored carefully.118

Advice for individual z drugs include:
- Zaleplon was previously recommended in breastfeeding due to its short half life however it was discontinued and is no longer available in the UK.
- **Zolpidem** has a longer half-life (than zaleplon) of 2 to 5 hours; with rapid absorption. There has been one report of adverse effects with its use in a breast-fed baby (the mother was also taking regular sertaline 100mg at night). Zolpidem will generally be preferred over zopiclone due to its shorter half-life.

- **Zopiclone's** half-life is about 4 to 5 hours; absorption is rapid. There have been no published reports of concern via milk.

These medicines are rapidly absorbed and excreted; exposure can thus be minimised by feeding immediately before taking a dose and then avoiding feeding at peak maternal plasma concentrations, (or using a formula feed or expressed milk) where this is possible.

Promethazine

There is no published evidence of the use of promethazine in breastfeeding, although there is many years of experience of it being used without reported problems. It is also used safely in many paediatric conditions. As with all hypnotics sedation may occur in the infant, so breastfeeding should be avoided if the infant is at risk of apnea. Promethazine is a phenothiazine derivative and dopamine antagonist it may possibly interfere with lactation particularly after repeated use. It has a long half-life: of 5-14 hours.

**Monitoring includes:**
- The baby should be monitored for excessive drowsiness, and the possibility of additive effects with other CNS-active medicines should be considered.
- Generally, it would be wise to discourage bed-sharing (mother and infant) when the mother has taken a hypnotic.

5.5.3 Neurodevelopmental Effects

Very few studies have focused on the development of behavioural toxicity, and the data is controversial.

Two studies that focused on this area failed to find any long-term detrimental effects of diazepam exposure on postnatal development. However another study found that prenatal exposure to benzodiazepines caused a general delay in mental development up to 18 months of age. Another study reported that in approximately 550 children who were followed up to 4 years of age, prenatal benzodiazepine exposure was not associated with adverse effects on neurobehavioral development or IQ.

5.6 Mood Stabilisers

<table>
<thead>
<tr>
<th>Summary of Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>NICE¹ advise that if antimanic medication is needed during pregnancy, low dose antipsychotics are the preferred treatments in pregnancy, where clinically appropriate.</td>
</tr>
<tr>
<td>Exposure to mood stabilisers, such as carbamazepine, lithium and sodium valproate, in early pregnancy increases the risk of congenital malformations¹²² and may affect the neurodevelopment of the infant.</td>
</tr>
<tr>
<td>The risk increases with the use of more than one mood stabiliser, therefore combinations of mood stabilisers should be avoided.¹²²</td>
</tr>
<tr>
<td>All women prescribed antiepileptic drugs should be prescribed a daily dose of 5mg folic acid from pre-conception until the end of the first trimester.¹²²</td>
</tr>
<tr>
<td>Abrupt cessation increases risk of relapse of the mothers’ illness; therefore where possible gradually withdraw over 2 to 4 weeks.¹²²</td>
</tr>
</tbody>
</table>
5.6.1 Mood Stabilisers in Pregnancy

Lithium
Refer to Appendix A: ‘Guidelines for the use of Lithium in Pregnancy and the Postpartum Period’ for advice on lithium in pregnancy.

Valproate
Valproate is known to be teratogenic. There is a 2-3% reported incidence of spontaneous malformations (all types) in new-born babies in Europe. Detecting a medication-induced increase in incidence is very difficult, but it is estimated that valproate increases the incidence of congenital malformations by 2-4 fold.

If valproate exposure occurs in pregnancy a referral to the obstetrician should be made to arrange additional monitoring required including a detailed ultrasound scan (refer also to section 5.1.2).

Valproate should not routinely be used in women of child bearing age, NICE (2014) advises against its use in women of child bearing potential for any indication. NICE set a quality standard that valproate should not be prescribed for women of child bearing potential for a mental health condition. The MHRA strengthened the warnings related to any products containing valproate or valproate derivatives following a Europe wide review. Children exposed in utero to valproate are at a high risk of serious developmental disorders (in up to 30-40% of cases) and/or congenital malformations (in approximately 10% of cases) The MHRA advises that valproate should not be prescribed to female children, female adolescents, women of childbearing potential or pregnant women unless other treatments are ineffective or not tolerated.

If there is no effective alternative, explain risks and importance of using adequate contraception. Women who could become pregnant should be given information on the risks to an unborn child should she become pregnant and take valproate. The patient should be advised to urgently consult their doctor if they are planning a pregnancy or become pregnant. Resources for patients and professionals including a patient information leaflet is available here: https://www.gov.uk/government/publications/toolkit-on-the-risks-of-valproate-medicines-in-female-patients


Do not prescribe valproate to women younger than 18 years (increased risk of unplanned pregnancy in this group). The risks with valproate include:

- The risk of neural tube (spina bifida, anencephaly) defects is increased 20 fold by valproate to around 100-200 in 10,000.
- A syndrome that includes oral cleft and other congenital malformations are also described with valproate.
- Effects on the child’s intellectual development (see section below).
- Polycystic ovary syndrome in women younger than 18 years.
- The risk of teratogenicity with valproate is estimated to be around three times higher than with other mood stabilizing agents such as carbamazepine and lamotrigine.
• The risk of malformations has been shown to be substantially higher in women who previously had a pregnancy that resulted in foetal malformation whilst taking valproate and remain on valproate in subsequent pregnancies.38,128,129

• If a woman on maintenance valproate treatment becomes pregnant (unplanned), and remains mentally stable, consideration should be given to stopping the valproate and if appropriate, using an alternative medicine (such as an antipsychotic). If there is no alternative to valproate then the following is advised:
  o Folic acid 5mg/day supplementation should be prescribed.
  o Limit the dose to a maximum of 1gram/day, as higher doses are associated with a greater incidence of congenital malformations, notably spina bifida.34
  o Avoid peaks in valproate levels by using slow release formulations and dividing the daily dose. E.g. if the total daily dose required is 800mg per day, prescribe Epilim Chrono® 400mg BD (twice a day).130
  o Monitor maternal valproate levels throughout the pregnancy (at least once in each trimester).124
  o Sodium valproate has been associated with neonatal syndrome, hepatic toxicity and hypoglycaemia.122

Carbamazepine
Carbamazepine should not be routinely prescribed for women who are pregnant because of the lack of evidence of efficacy and the risk of neural tube defects in the foetus.1 The risk of neural tube defects is raised from 6 in 10,000 to around 20 to 50 in 10,000. Other major foetal malformations include gastrointestinal tract problems and cardiac abnormalities131.

Carbamazepine is teratogenic in humans with malformations reported following in utero exposure including neural tube defects, hypospadias, cardiac, renal or respiratory defects and microcephaly.131 Exposure to antiepileptic polytherapy regimens which contain carbamazepine may further increase the risk of major congenital malformation. Due to inconsistencies in investigation methods, it is currently difficult to state an estimated percentage of the risk however the risk appears to be dose related132 and is significantly less than with valproate. More recent studies have suggested that overall risk of major malformations with carbamazepine, apart from NTDs, is one of the lowest compared to other antiepileptics and to healthy controls.133

If a woman who is taking carbamazepine for a psychiatric condition is planning a pregnancy or has an unplanned pregnancy, this should usually be withdrawn because of the risk of neural tube defects and other malformations in the foetus. If appropriate an alternative medicine (such as an antipsychotic) should be considered.

If carbamazepine exposure occurs in pregnancy a referral to the obstetrician should be made to arrange additional monitoring required including a detailed ultrasound scan. Carbamazepine has been associated with neonatal hepatic toxicity.124,131

Lamotrigine
The evidence for the safe use of lamotrigine in pregnancy is growing and it could be considered as an option in patients for whom antipsychotics are not suitable however consideration has to be given to its slow titration schedule which exposes the foetus to sub-therapeutic concentrations of the medication. It is one of the antiepileptics of choice in pregnancy.38
If a woman who is taking lamotrigine is planning a pregnancy or has an unplanned pregnancy, the clinician should consider the risk/benefit of continuing lamotrigine. If the decision is to stop lamotrigine an alternative medication may need to be considered. If therapy with lamotrigine is considered necessary during pregnancy, the lowest possible therapeutic dose is recommended.\textsuperscript{13}

Post marketing data from several cohort studies and prospective pregnancy registries have documented outcomes in over 7500 women exposed to lamotrigine monotherapy during the first trimester of pregnancy.\textsuperscript{13,134} Overall, these data do not suggest a substantial increase in the risk for major congenital malformations.\textsuperscript{13,134} Although a possible association between first trimester lamotrigine use and orofacial clefting in the infant has been identified in one study, further studies have failed to provide evidence of such a link. Animal studies have shown developmental toxicity\textsuperscript{13,134}

There have been reports of decreased lamotrigine plasma levels during pregnancy,\textsuperscript{13} which may in turn reduce the therapeutic effect. After birth lamotrigine plasma levels rapidly return to pre-pregnancy levels, and so if the dose has been increased during pregnancy there is a risk of dose-related adverse events.\textsuperscript{1,13,38} Efficacy should therefore be closely monitored for during pregnancy. If it is necessary to increase the lamotrigine dose during pregnancy then this should be reviewed soon after birth with a view of reducing to the pre-pregnancy dose. Taking lamotrigine serum levels before, during and after pregnancy can help to guide these decisions. In addition, dose-related undesirable effects should be monitored after birth.\textsuperscript{13}

If lamotrigine exposure occurs in pregnancy a referral to the obstetrician should be made to arrange additional monitoring required including a detailed ultrasound scan. Lamotrigine has been associated with neonatal hepatic toxicity.\textsuperscript{124} Lamotrigine also carries the risk of dermatological problems (notable Stevens-Johnson syndrome) in the infant if taken while breast-feeding.\textsuperscript{135}

5.6.2 Mood stabilisers in Breast-Feeding

- NICE (2014)\textsuperscript{1} advises that if a prophylactic agent for Bipolar Affective Disorder (BPAD) is needed whilst breast-feeding that the first choice should be an antipsychotic (but not clozapine). Women already taking prophylactic antipsychotic medication should be encouraged to breastfeed unless they are taking clozapine.\textsuperscript{1}
- Further advice should be sought for women taking carbamazepine, lithium, or clozapine prior to initiating breastfeeding.
- If a woman is on combination therapy or if there are other risk factors, such as premature birth, specialist advice should be sought prior to breastfeeding.\textsuperscript{136,137}
- All infants should be monitored for sedation, feeding difficulties, adequate weight gain, and developmental milestones. Infants should also be monitored for unwanted effects associated with the antiepileptic, particularly with newer antiepileptics.\textsuperscript{136}

Lithium

**Lithium should not routinely be prescribed for women who are breastfeeding.**\textsuperscript{1} Women who wish to breast-feed should be advised not to breast-feed if taking lithium and offered a prophylactic agent that can be used when breast-feeding.

Lithium is secreted into breast milk and levels achieved are approximately 40-50\% of maternal serum levels.\textsuperscript{138,139} Although a recent review suggests that the plasma levels in breastfed infants may be as low as 25\% of the maternal plasma levels.\textsuperscript{139} There have been
reports of lithium toxicity in breast-feeding infants, including cyanosis, electrocardiogram abnormalities and hypotonia. This toxicity is felt to be due to the relatively immature kidney function in neonates and is especially likely to occur during times of dehydration (e.g. infection).

A number of studies of lithium suggest that lithium administration is not an absolute contraindication to breastfeeding if the physician monitors the infant closely for elevated plasma lithium and monitored for toxicity.69 The decision should be made on a case by case assessment after carefully assessing the risks and most up-to-date information.

Valproate
Valproate concentrations in breast milk are low. Breast-feeding would appear to be relatively safe27,40,69 although with a small but finite risk of haematological effects.40 A detailed risk assessment should be carried out before it is decided to breast-feed. Closely monitor the infant for liver and platelet changes.

Given the concerns for prospective pregnancies, the woman must be adequately counselled on the use of appropriate contraceptive methods if valproate is used in breastfeeding.

Please refer to section 5.6.1 regarding the use of valproate in women of childbearing age.

Carbamazepine
Carbamazepine concentrations in breast milk appear to be low from the limited data available. Transient hepatic toxicity such as hyperbilirubinaemia and raised GGT have been reported in neonates exposed to carbamazepine during breast-feeding. A detailed risk assessment should be carried out before it is decided to breast-feed. Closely monitor the infant for liver and platelet changes.40

Lamotrigine
NICE (2014)1 no longer advises against the use of lamotrigine in breastfeeding women. There is a theoretical risk of dermatological problems in the infant, such as Stevens–Johnson syndrome however no cases have yet been reported in breastfed infants. Lamotrigine breast milk concentrations are high, as is the relative infant dose however very few adverse reactions have been reported in breastfed infants.27,109,135 There are single case reports of withdrawal syndrome when breastfeeding was stopped suddenly and of severe apnoea. The risk to the breastfed infant is highest in the neonatal period because of reduced capacity for glucuronidation, relatively low plasma protein binding and altered maternal pharmacokinetic parameters in the postpartum period when the medicine has been used in pregnancy.135 The decision should be made on a case by case assessment after carefully assessing the risks and most up-to-date information. Where the mother decides to continue breastfeeding the infant should be monitored for adverse effects from lamotrigine. If a rash occurs in the infant breastfeeding should be withheld until the cause of the rash is established.

5.6.3 Neurodevelopmental Effects
In a follow-up study of children included in the Register of Lithium Babies, 60 children exposed to lithium either during the first trimester or throughout pregnancy did not differ behaviourally from their non-exposed siblings. In another study, the attainment of major developmental milestones for 22 lithium-exposed subjects was similar to that for non-exposed comparison subjects.140 This was confirmed in a recent study with 15 children that
concluded children developed normally after being exposed to lithium in utero and that no major developmental problems had evolved.\textsuperscript{141}

Valproate carries a risk of effect on the child’s intellectual development and polycystic ovary syndrome in women younger than 18 years. Developmental delay characterised by low verbal IQ have been described in a number of reviews of the evidence of infants exposed to valproate in utero, although the relative risks have not been determined. More recently it has been shown that children born to mothers who take valproate during pregnancy have an increased risk of lower cognitive test scores than children exposed to other anti-seizure medications during pregnancy (FDA safety announcement 2011).\textsuperscript{142} This conclusion is based on the results of epidemiological studies that show children born to mothers who took valproate sodium or related products throughout their pregnancy tend to score lower on cognitive tests (IQ and other tests) than children born to mothers who took other anti-seizure medications during pregnancy.\textsuperscript{125} There is increasing evidence that valproate is linked to further developmental delays, and autism in children exposed to valproate \textit{in utero}.\textsuperscript{38}

It is recommended that the increased likelihood of neurodevelopmental disorders should be communicated to women for whom sodium valproate is a treatment option.\textsuperscript{143}

There is limited data on long term neurodevelopmental outcomes for \textit{carbamazepine}. However, six studies found no impairment of cognitive functions in children exposed to carbamazepine monotherapy.\textsuperscript{144}

A study failed to demonstrate harmful effects of breastfeeding during antiepileptic (Including valproate, lamotrigine and carbamazepine) therapy on cognitive outcomes in children previously exposed in utero.\textsuperscript{145}

5.7 Rapid Tranquillisation

NICE (2014)\textsuperscript{1} guidelines advise that a pregnant woman requiring rapid tranquillisation should be treated according to guidelines on the short-term management of disturbed behaviour, but\textsuperscript{1}:

\begin{itemize}
  \item A pregnant woman should not be secluded following rapid tranquillisation\textsuperscript{1}.
  \item The restraint procedures should be adapted to avoid possible harm to the foetus.
  \item When choosing an agent for rapid tranquillisation, consider an antipsychotic or a benzodiazepine with a short half-life and use the lowest effective dose.
  \item The woman’s care during the perinatal period should be managed in close collaboration with a paediatrician and an anesthetist.\textsuperscript{1}
\end{itemize}

Refer also to the CNWL Rapid Tranquillisation Guidelines available on Trustnet

5.8 Medicines for ADHD

Treatment of adolescent girls and adults with Attention Deficit Hyperactivity Disorder (ADHD) has resulted in increasing exposures of babies to the medicines used to treat ADHD during pregnancy and breastfeeding. The decision to treat ADHD in a pregnant or lactating woman should be carefully considered until further information on the use of stimulants and atomoxetine is available and the consequences of untreated maternal illness have been evaluated.
5.8.1 Treatment of ADHD in Pregnancy

- There is limited information on the use of stimulants or atomoxetine to treat ADHD in pregnancy and there is also limited information on the course of ADHD symptoms through pregnancy.
- Patients with ADHD may undertake more risky behaviours when untreated therefore their individual risk needs to be considered when making prescribing decisions.
- The majority of data is for methylphenidate which does not suggest significant teratogenicity however there may be neonatal withdrawal reactions should the medicine be used to term.
- Much of the data on pregnancy exposure with stimulants comes from illicit use therefore may not be comparable to those using prescribed stimulants to treat ADHD.
- Consideration can be given to use of medication intermittently to reduce exposure to the foetus.

Stimulants in pregnancy

The majority of data in pregnancy is for methylphenidate, although much of the older data comes from illicit use of methylphenidate often with other substances therefore may over-estimate any risks.\textsuperscript{146} Whilst the data is limited, that which is available for methylphenidate does not suggest that there is an increased risk of major malformations.\textsuperscript{146,147} Pre-term delivery and growth restriction have been reported following the abuse of methylphenidate\textsuperscript{147} and miscarriage has been linked with methylphenidate but may be related to ADHD itself.\textsuperscript{6}

There is limited evidence on the long term neurodevelopmental effects of patients treated with stimulants in pregnancy.\textsuperscript{147}

Neonatal withdrawal symptoms should be expected following the use of stimulants in pregnancy and the baby should be monitored for any adaptation problems. Where possible consideration should be given to withdrawing the stimulant in the latter stages of pregnancy to reduce withdrawal in the infant.\textsuperscript{147}

Atomoxetine use in pregnancy

Atomoxetine is a selective noradrenaline re-uptake inhibitor with properties similar to NRI antidepressants. There is very limited evidence of the use of atomoxetine in pregnancy therefore it should be used cautiously until further information is available.\textsuperscript{148}

5.8.2 Treatment of ADHD in Breast-feeding

- There is limited information on the use of stimulants or atomoxetine to treat ADHD in a breast-feeding woman and there is also limited information on the course of ADHD symptoms in the post natal period.
- Methylphenidate appears compatible with breastfeeding however the dose should be kept low both to limit the exposure to the baby and also as high doses may interfere with lactation.

Stimulant use in Breastfeeding

If treatment of ADHD is indicated in a breast-feeding woman, methylphenidate is the preferred agent. There is limited information on the use of stimulants in breast-feeding.
however evidence that is available shows that only low levels of methylphenidate are excreted into breast milk.26

Longer acting stimulants such as lisdexamfetamine may lead to accumulation in the breastfed infant and therefore ideally should be avoided.26

Infants exposed to stimulants via breastfeeding should be monitored for signs of CNS stimulation (decreased appetite/weight gain, sleep disturbances, irritability).26

Atomoxetine use in Breastfeeding
There is limited evidence on the use of atomoxetine in breastfeeding and due to its longer half life there is potential for accumulation of the medicine in the breastfed infant. Atomoxetine use should be avoided in breastfeeding where possible, if atomoxetine is used in breastfeeding the infant should be monitored for decreased appetite/weight gain, sleep disturbances and GI symptoms (pain, vomiting, constipation).26

5.9 Addictions

The following is a general description of some of the effects in pregnancy and breastfeeding of the most frequently misused substances.

The use of alcohol, nicotine and illicit substances is likely to result in risks to the mother and the foetus, be that experimental, recreational, occasional, problematic or dependent use. These risks include direct toxicity and withdrawal syndromes for both, mother and foetus and possible long-term neuro-behavioural disturbances for the infant.

Any decisions should involve the woman and family where possible after a full discussion of possible risks of exposure to prescribed medicines to the foetus/infant during pregnancy weighed against the risks of illicit drug and alcohol use and withdrawal syndromes for both, mother and foetus and possible long-term neuro-behavioural disturbances for the infant.

Decisions should also take into account stage in the pregnancy/gestational age, previous response to other treatments, and severity of illness/risk of relapse for this individual client NICE Guidelines7 recommend that Mental Health Addictions services should work with local antenatal services and other local agencies, including social care and third-sector agencies to coordinate antenatal care by, for example:

1. jointly developing care plans across agencies
2. including information about opiate replacement therapy in care plans
3. co-locating services
4. Offering women information about the services provided by other agencies.

Early information-sharing between the GP, maternity and addiction services is essential. All women who are substance users (including alcohol) should have integrated specialist care that includes professionals in addiction, child safeguarding, specialist midwifery and obstetrics.7

Enabling pregnant substance users to access antenatal care is vital. In 2006–2008, 11% of all maternal deaths were in substance misusers and 44% of substance-misusing women received no/little antenatal care. Some 31% of maternal deaths from suicides were in substance misusers.149
The aim of prescribing medication for substance misuse during pregnancy should be directed towards the prescribing of the lowest possible dose that will provide benefit with minimal risk, and encouraging compliance with the wider treatment plan and providing adequate monitoring.

Women using illicit drugs and alcohol tend to use multiple substances, including nicotine and each drug carries its own characteristic and individual effects on the mother and on the foetus.

In general, women are encouraged to discontinue alcohol and drug use during pregnancy because of the associated risks, but this may prove very difficult for those who use alcohol or drugs dependently.

5.9.1 Cannabis (hash, resin, marijuana, weed, skunk, dope)

**Pregnancy**
Cannabis is one of the most extensively used substances by pregnant women however is commonly used alongside other substance, particularly tobacco which makes it difficult to evaluate the potential teratogenic effects of cannabis alone. Although the active component of cannabis, Delta 9-Tetrahydrocannabinol (THC), crosses the placental barrier, no direct teratogenic effects have been described in association with its use in pregnancy. However, cannabis can decrease uteroplacental perfusion and foetal growth; affect the processing of information, memory and executive function and impair the regulation of emotional behaviour later in life.

Cannabis hyperemesis syndrome is a syndrome which presents with cyclic vomiting and compulsive bathing seen in people heavily using cannabis and has been reported in pregnant women. Given that it shares features with hyperemesis gravidarum it may be underdiagnosed and should be considered in women who chronically use cannabis.

**Breastfeeding**
Although published data are limited, it appears that active components of cannabis are excreted into breast milk in small quantities. Cannabis use should be minimized or avoided by nursing mothers because it may impair their judgment and child care abilities. Breastfeeding can mitigate some of the effects of smoking and little evidence of serious infant harm has been seen, it therefore maybe preferable to encourage mothers who use cannabis to continue breastfeeding while minimizing infant exposure to cannabis smoke and reducing cannabis use.

Cannabis should not be smoked by anyone in the vicinity of infants because the infants may be exposed by inhaling the smoke. Some evidence indicates that paternal cannabis use increases the risk of sudden infant death syndrome in breastfed infants.

5.9.2 Cocaine (white, powder, crack, rock, paste)

**Pregnancy**
Cocaine causes acute vasoconstriction which may cause foetal haemorrhage and hypoxia. Its use is contraindicated in pregnancy. Cocaine use during pregnancy has been associated with increased risk of spontaneous abortion, placental abruption, premature labour, intrauterine growth retardation and Sudden Infant Death Syndrome (SIDS). The teratogenicity of cocaine is not confirmed, however malformations observed in infants after
Prenatal cocaine exposure include microcephaly and malformations of the skeletal system, nervous system, gastrointestinal tract, genitourinary system and cardiovascular system.\textsuperscript{158–160} Exposure in late pregnancy may lead to neonatal withdrawal in the infant.\textsuperscript{159}

**Management**
The Department of Health guidelines recommend offering psychological approaches including family intervention to pregnant women misusing stimulants.\textsuperscript{2} Substitute prescribing is not recommended.\textsuperscript{149} There are however uncertainties over which psychological intervention is most effective during pregnancy.\textsuperscript{149} The client’s mental state after the discontinuation of cocaine should be closely and regularly monitored, in order to detect and manage possible psychiatric symptoms. These symptoms may appear as a natural reaction to the discontinuation of the drug after a prolonged and/or heavy period of use, in which case they will improve rapidly, or may reflect a more formal psychiatric disorder.

Contrary to general fears, sudden discontinuation of cocaine has only beneficial effects on both the mother and the baby. The main difficulty is for the client to break her cycle of misuse.

**Breastfeeding**
Cocaine is excreted in the breast milk at a high milk/plasma ratio. For this reason, breastfeeding is not recommended if the mother continues to use this drug. Significant agitation in the breastfeeding infant of cocaine using mothers has been reported.\textsuperscript{2,161} Cocaine should not be used by nursing mothers or smoked (such as with "crack") by anyone in the vicinity of infants because the infants can be exposed by inhaling the smoke. Selected mothers with a history of cocaine abuse who are not currently using cocaine can breastfeed their infants. Among these mothers, some authors have proposed that breastfeeding be discontinued only for those infants who test positive for cocaine exposure.

---

5.9.3 Amphetamines (speed, uppers)

**Pregnancy**
Amphetamines cross the placental barrier. In elevated doses and frequent use, they are associated with embryo toxicity and risk of miscarriage, intrauterine growth retardation, prematurity and low birth weight.\textsuperscript{162–164}

**Management**
The Department of Health guidelines recommend offering psychological approaches including family intervention to pregnant women misusing stimulants.\textsuperscript{2} Substitute prescribing is not recommended.\textsuperscript{149} There are however uncertainties over which psychological intervention is most effective during pregnancy.\textsuperscript{149}

**Breastfeeding**
In dosages prescribed for medical indications, some evidence indicates that amphetamine might not affect nursing infants adversely. The effect of amphetamine in milk on the neurological development of the infant has not been well studied. It is possible that large dosages of amphetamine might interfere with milk production, especially in women whose lactation is not well established.\textsuperscript{165}
5.9.4 Ecstasy (3,4-methylenedioxymethamphetamine, MDMA, MDEA, MDA)

**Pregnancy**
Information of its effects if used during pregnancy is scarce, possibly because its use tends not to be continuous or dependent. In principle, similar effects and repercussions to amphetamines are to be expected. Women should be advised to avoid the use of ecstasy if pregnant or planning to become pregnant.\(^{166,167}\)

**Management**
The Department of Health guidelines recommend offering psychological approaches including family intervention to pregnant women misusing stimulants.\(^2\) Substitute prescribing is not recommended.\(^{149}\) There are however uncertainties over which psychological intervention is most effective during pregnancy.\(^{149}\)

**Breastfeeding**
Use while breastfeeding is contraindicated.\(^{69}\)

5.9.5 Opiates (Heroin, opium, morphine, methadone, codeine, buprenorphine)\(^{2,168–171}\)

**Pregnancy**
No evidence of teratogenesis has been associated with opiates or heroin use, but evidence of foetal growth retardation, increased perinatal mortality and morbidity and increased risk of sudden infant death syndrome (SIDS) have been reported.\(^{168–171}\) Because of heroin’s short half-life, frequent episodes of withdrawal of various degrees of intensity are likely. These are associated with spasm of the smooth muscle and uterine contractions, which can affect the pregnancy in 2 ways:

- Increase the risk of precipitating delivery or abortion
- Decrease in the blood supply to the placenta, increasing the risk of foetal suffering and affecting foetal growth.

Stabilising the pregnant woman not only reduces the risks to the foetus, but it also facilitates the cessation of the use of other illicit drugs and the reduction of harm and crime\(^2\).

The neonate of an opiate user may experience withdrawal symptoms of varied degree or intensity, depending on the level and time during pregnancy of the maternal drug use, the half-life of the opiates used and the degree of maturity and health of the newborn. Withdrawal symptoms in the neonate appear sooner in the case of opiates with shorter half-life, such as heroin and opium, and when the amount of drug used is high. However, there is no clear relation between the intensity of the neonatal abstinence syndrome (NAS) and the maternal methadone dose at delivery.

**Prescribed Opioids and Pain relief in pregnancy**\(^{172}\)

There are conflicting opinions as to the safest and most effective regimens for treatment of pain during pregnancy. Severe or chronic pain, if left untreated or inadequately treated, can have adverse effects on both mother and foetus. As the foetus is totally reliant on the mother for its oxygen and nutrient supply during pregnancy, prolonged or serious events, such as pain that causes interference with the functioning of the maternal cardiovascular system, may have secondary adverse effects on the developing foetus.
Where possible non-pharmacological measures should be employed before drug therapy is considered. If non pharmacological measures are not effective then the client should be treated as for the non-pregnant patient, where pain medication is initiated at the step in the analgesic ladder appropriate to the level of pain as dictated by a pain scale considering the risk and safety of the use of individual medicines in pregnancy.

Management
Opioid substitution therapy (OST) depend on the general principles. Maintenance, at a dose that stops or minimises illicit use, is most appropriate for ensuring continuity of management of pregnancy and aftercare. OST carries a lower risk to the foetus than continued use of illicit drugs and is associated with improved compliance with antenatal care, reduced maternal morbidity and improved neonatal outcomes. Improvements in perinatal outcomes were similar for methadone and buprenorphine in a prospective observational study.

If illicit opiate use continues, strenuous efforts should be made to stabilise the client on a prescribed opioid, which may involve increasing its doses.

**Buprenorphine** may be associated with less neonatal abstinence syndrome than methadone and increased birth weight.

The use of injectable drugs, in particular illicit drugs, is not advisable during pregnancy. For those women on an injectable opiate maintenance regime, it is recommended to switch to an oral regime, in order to reduce the risk of complications associated with injecting and problems with dose management and administration during delivery.

Care Planning
Most pregnant women fear the idea of babies being born ‘addicts’. The clinician must clarify the difference between the concepts of addiction and dependence, in relation to the newborn. Where the mother may have an addiction, the baby will be born dependent on a substance and not necessarily addicted.

A treatment plan that is clear but flexible should be established as soon as the initial assessment has taken place. A wide range of possible treatment options, including maintenance, dose increase, and reduction and splitting should be considered. If detoxification is realistic and safe, this goal should be supported. See below for further information.

Consider the frequency of installment collections. The practical difficulties in attending pharmacy especially during latter part of pregnancy or in the event of pregnancy related illness need to be weigh up clinical risk of less frequent installments.

Many pregnant women choose a withdrawal regimen, but withdrawal during the first and third trimester should be avoided.

There should be close liaison with antenatal services. Refer to section 5.10 for further information on care planning.

**Opioid Substitution treatment (OST) Initiation**
Starting substitute prescribing requires careful assessment and urine evidence of the use of opiates. It is normally preferable to initiate methadone than buprenorphine for those whose drug use includes regular use of illicit or prescribed methadone, as well as heroin. This is
because the partial agonist activity of buprenorphine may trigger unnecessarily intense withdrawal symptoms.

The required evidence of withdrawal symptoms still applies, although the presence of these symptoms should not be demanded to be excessive, i.e. feelings of discomfort, in order to avoid foetal suffering. The first dose still needs to remain within safe guidelines, (see the Trust Guidelines on the pharmacological management of opioid misuse for further information) but the monitoring needs to be more frequent and proactive. Further dose increases should not be delayed by waiting for objective withdrawal symptoms. The titration to the appropriate dose needs the close collaborative effort of the woman, medical and nurse/key worker.

Prescribing oral solution of methadone (1mg/1ml) may prove difficult for pregnant women, especially towards the end of the pregnancy or for those experiencing nausea and vomiting, in particular, if the sickness is moderate to severe and the dose of methadone is high. In this case splitting the dose and changing the time of administration may be helpful. Alternatively, prescribing a different formulation, such as methadone tablets or concentrate (10mg/1ml) for a limited period of time can also be considered, being mindful of the greater potential for misuse of these formulations.

Maintenance
If a woman who is stabilised on methadone or buprenorphine for treatment of opioid dependence becomes pregnant, therapy should be continued. The most appropriate dose of the opiate substitutes methadone or buprenorphine needs to be negotiated with the pregnant woman against the experience of symptoms of withdrawal from opiates and should aim at the highest dose that is necessary, but the lowest possible to stop withdrawal symptoms and provide comfort.

Detoxification
If a decision to withdraw is achieved, a detoxification plan can be arranged provided that the regime chosen does not provoke withdrawal symptoms. Withdrawal in the first trimester is associated with an increased risk of spontaneous miscarriage. Withdrawal of methadone or buprenorphine may be undertaken gradually during the second trimester; for example, the dose of methadone may be reduced by 2–3 mg every 3–5 days. For Buprenorphine, 1–2 small doses reductions may be undertaken per week. 0.8 mg have been managed comfortably in specialist services.

If illicit opioid use occurs, the client should be re-stabilised at the optimal maintenance dose and consideration should be given to stopping the withdrawal regimen. Further withdrawal of methadone or buprenorphine in the third trimester is discouraged because maternal withdrawal symptoms, even if mild, is associated with foetal distress, stillbirth, and the risk of neonatal mortality. For this reason, any withdrawal regimes in the third trimester should be well-planned and carefully monitored.

The decision to detoxify should depend on the client's aim, the opioid dose and the length of time available between decision-making and delivery date. Ideally, detoxification should be reached well in time before the expected delivery date. Reduction regimes should also be carefully monitored and halted 2-3 weeks before the expected delivery date, so that the woman can direct her attention towards preparing for the delivery.
Preterm and postnatal consideration

Drug metabolism can be increased in the third trimester; it may be necessary to either increase the dose of methadone or change to twice-daily consumption (or a combination of both strategies) to prevent withdrawal symptoms from developing.

The neonate should be monitored for respiratory depression and signs of withdrawal if the mother is prescribed high doses of opioid substitute. Signs of neonatal withdrawal from opioids usually develop 24–72 hours after delivery but symptoms may be delayed for up to 14 days, so monitoring may be required for several weeks. Symptoms include a high-pitched cry, rapid breathing, hungry but ineffective suckling, and excessive wakefulness; severe, but rare symptoms include hypertonicity and convulsions.

It is important to recognise the risk of accidental opioid overdose in clients who stop or reduce opioid misuse in pregnancy but start misusing opioids again after childbirth.1

Breast-feeding

Methadone is the mainstay of the treatment of opioid drug dependence and breastfeeding has benefits to an infant who has been exposed in utero to maternal opioids. There is less evidence and experience for the use of buprenorphine, which is considered compatible with breastfeeding for short-term use.26 The dose of methadone should be kept as low as possible in breast-feeding mothers and the infant should be monitored for sedation (high doses of methadone carry an increased risk of sedation and respiratory depression in the neonate).

Buprenorphine is excreted in low concentrations in breast milk and has low oral bioavailability; however, neonates should be monitored for drowsiness, adequate weight gain, and developmental milestones.

Increased sleepiness, breathing difficulties, or limpness in breast-fed babies of mothers taking OST should be reported urgently to a healthcare professional.

5.9.6 Benzodiazepines (benzos, downers) in substance misuse

Refer to section 5.5 for general information on the use of benzodiazepines in pregnancy and breastfeeding.

Pregnancy

Abrupt withdrawal of diazepam is not recommended as this may destabilise the maternal condition, or potentially lead to self-administration of other medications, or drugs of abuse like alcohol, which may confer a significant risk miscarriage and/or foetal distress.

Signs of intoxication in the newborn include low APGAR scores, slow reflexes, hypotonia (floppy baby), hypothermia, a feeble cry and poor sucking. In severe cases, respiratory depression may be observed.

The newborn may experience withdrawal symptoms, which can be severe, protracted and prolonged, lasting as long as 3 months after delivery.176

Withdrawal symptoms in the newborn differ from those of adults and are less specific. (See Neonatal Abstinence Syndrome, section below). For these reasons, self-medication for sedation purposes during pregnancy should be strongly discouraged.
Management

Ideally it is recommended to avoid starting benzodiazepine treatment during pregnancy unless there is a clinically compelling reason or it’s for the treatment of alcohol withdrawal, to reduce larger doses and ideally to detoxify. There is little advantage for the pregnant woman and her baby to remain on these drugs and the long-term use of benzodiazepines is not recommended.

In some instances, initiating benzodiazepines is unavoidable because of clinical risk associated with illicit use. In these cases it is advisable to transfer any benzodiazepine to an equivalent dose of diazepam, because of its long half-life and then reduce the dose slowly. Detoxification can be done at any time during the pregnancy, at a pace that depends on the individual case and the amount of benzodiazepines being used. Avoid rapid withdrawals as this may precipitate labour.

Please refer to the Trust’s guideline, Pharmacological Management of Benzodiazepine Dependence in clients 16 years and over for further information on prescribing.

There is a difference between therapeutic and dependent use of benzodiazepines. When used as part of the treatment for a medical or a mental health condition, consideration must be given to the effects on the pregnancy of not having the treatment, beyond the problem of withdrawals.

Breastfeeding

Breastfeeding whilst on benzodiazepines, especially higher doses (>10 mg daily), is not advisable, because the drug is present in the milk, at a high plasma/milk ratio. For lower doses, the balance between the risks and benefits of continuing prescribing whilst breastfeeding should be carefully determined.

Where possible use short-term, intermittent dosing to reduce infant exposure.

Monitor the infant closely for drowsiness, poor feeding and adequate weight gain. The associated use of benzodiazepines and opiates carries an increase in the risk of overdose.

5.9.7 Tobacco

Pregnancy

Tobacco use and exposure through passive smoking during pregnancy is associated with an increased risk of intrauterine growth retardation, cleft lip and/or palate, ectopic pregnancy, spontaneous abortion, premature delivery, perinatal mortality and poor postnatal development. Carbon monoxide (CO) crosses the placenta and reaches up to 15% higher concentration in the blood of the foetus than in the mother’s.

Nicotine is a powerful vasoconstrictor. As such, it increases the blood pressure and heart rate, reduces the uterine blood flow and causes a generalised reduction of blood flow and oxygen to the foetus, increasing its heart rate and oxygen demands, in short, increasing the risk of foetal suffering.

Tobacco smoke is immunotoxic and can interfere with the production of antibodies. For this reason, Zanardo et al 2005 suggest that breast-feeding could be non-protective against infection among the neonates nursed by smoker in comparison with non-smoker mothers.
Management
Pregnant women should be encouraged to stop smoking, be offered information on the potential effects of tobacco smoking on the pregnancy and the baby and on the benefits of abstinence. The first choice treatment for tobacco use cessation during pregnancy would be through cognitive behavioural therapy (CBT). In non-pregnant populations, CBT combined with nicotine replacement therapy (NRT) has been shown to increase rates of tobacco use cessation.180

Concerns exist over the efficacy and safety of NRT in pregnancy. An advantageous risk vs. benefit ratio has not, as yet, been adequately proven, however use of NRT may be preferable to continued foetal exposure to the many harmful constituents of tobacco smoke. The available data which investigate pregnancy outcomes, although limited, do not yet provide substantial evidence of an increased risk of adversity when NRT has been used during pregnancy. Should CBT measures fail to control a client’s urge to use tobacco, NRT could be considered provided concomitant tobacco use is kept to an absolute minimum. When NRT is indicated it should be used at the lowest effective dose which controls symptoms of withdrawal and cravings.180

UKTIS does not currently have any specific guidelines relating to the use of electronic cigarettes in pregnancy. The exact content of electronic cigarette fluid may vary considerably (both in terms of the nicotine concentration and the product excipients, which are likely to be solvent / hydrocarbon based). This is further confounded by the fact that the manufacture of electronic cigarette fluid is not regulated by the MHRA and therefore it cannot be considered equivocally to standard nicotine replacement therapies.183

5.9.8 Solvents
The inhalation of solvents may reduce the oxygen supply to the foetus and cause cardiac arrhythmias in the mother. The use of solvents may also cause facial abnormalities similar to those seen in fetal alcohol syndrome and their use is linked to low birthweight.184,185 They can cause an abstinence syndrome in the neonate of heavy using mothers. Clients should be advised to stop using solvents and be supported with psychosocial interventions.

5.9.9 Alcohol186,187
Prenatal exposure to alcohol has been associated with an increased risk of spontaneous abortion. Alcohol is a known teratogen which easily crosses the placenta. When consumed in pregnancy, may impair development of the foetal nervous system. This can result in cognitive deficits and behavioural problems in the offspring, as well as perturbing foetal growth and organ formation. The extent and severity of these effects depends on several factors including the amount of alcohol ingested during the pregnancy, the gestational age at which the foetus was exposed and co-ingestion of other teratogenic substances.

The characteristic Foetal Alcohol Syndrome (FAS), reported with chronic high (>5 units/day) maternal alcohol consumption during pregnancy, is characterised by pre and postnatal growth retardation characteristic facial features including midfacial hypoplasia, microcephaly, thin upper lip, small palpebral fissures, flat maxillary area and under developed philtrum; and central nervous system abnormalities manifested as developmental delays, intellectual deficits and behavioural problems.186

The less severe Foetal Alcohol Spectrum Disorder (FASD) has been reported at any level of maternal alcohol consumption. Features include structural malformations, respiratory
dysfunction, vision and hearing problems, and mental, behavioural and/or learning disabilities.

There is no conclusive evidence to indicate a safe exposure level during pregnancy. Adverse effects from acute exposure to alcohol or binge drinking (>5 units on one occasion) are difficult to predict, with outcome depending on timing of exposure, genetic differences in alcohol metabolism (in both the mother and the foetus), and other associated compounding risk factors such as maternal lifestyle.186

Management

NICE187 recommends that alcohol should be avoided completely during the first three months of pregnancy due to the risk of miscarriage. While a safe level of alcohol consumption has not been established,149 the Department of Health and NICE recommend that women who choose to drink should limit their alcohol consumption to no more than one - two units once a week. Pregnant women should be advised to avoid alcohol altogether in the first trimester as it may be linked with an increased risk of miscarriage.187 There is limited evidence that binge drinking five or more standard drinks in a single episode, may be associated with neurodevelopmental harm to the baby.149

Alcohol withdrawal symptoms can increase the risk of miscarriage or foetal suffering, pharmacological detoxification should be offered when significant and as part of a relapse prevention plan. The appropriate but minimal necessary amount of benzodiazepines should be given preferably in an inpatient setting under specialist supervision.1 It is paramount that addiction/mental health services offer flexible and closely monitored assisted alcohol withdrawal in collaboration with antenatal team (preferably in an inpatient setting) to pregnant women who are dependent on alcohol.1 For the alcohol dependent client who does not want assisted alcohol withdrawal, services should work with an aim to help her reduce her alcohol intake.1

The BNF188 recommends using benzodiazepines in pregnancy with caution. The benzodiazepine of choice for alcohol detoxification remains chlordiazepoxide or diazepam, although any long-acting benzodiazepine is effective. The advised regime is 4 divided doses in a daily reducing schedule and the dose should be determined following assessment. For further advice on prescribing benzodiazepines in alcohol withdrawal, see the CNWL guideline: Prescribing for Alcohol Withdrawal and dependence in patients 18 years and over.189

Medicines available to help maintaining abstinence, such as disulfiram, acamprosate and naltrexone or nalmefene are not recommended for use during pregnancy or breastfeeding as there is no clinical data to support their use in pregnancy. They should only be used in pregnancy after a careful benefit/risk assessment. The following are recommendations for specific relapse prevention medication.149

- Acamprosate: Animal studies have shown evidence of malformations but there is very limited information from humans.190 Contraindicated in lactating women
- Naltrexone: Not recommended during breastfeeding
- Nalmefene: Not recommended during pregnancy

5.9.10 Neonatal Abstinence Syndrome with substance misuse

When a woman uses opiates, benzodiazepines, alcohol or barbiturates regularly during pregnancy, it is possible that her newborn may experience symptoms of withdrawal from these substances. Withdrawal symptoms in the newborn are less specific to the class of drug
used and differ from the withdrawal symptoms seen in adults on account of its immaturity. Withdrawal symptoms translate the irritability of the central, gastro intestinal and autonomic nervous systems in response to the abrupt cessation of the sedative effects of the drugs mentioned above.\(^{191}\)

- **Central nervous system symptoms** include tremor, easy startling, excessive crying, hyperactive reflexes, hyperactivity (excessive movement, inability to settle or sleep), scratching, hyper tonicity (stiff muscles), high pitch cry and seizures.
- **Gastrointestinal symptoms** include excessive sucking and appetite but inability to suck and swallow effectively, regurgitation and vomiting, loose, frequent stools and diarrhoea.
- **Autonomic symptoms** include sneezing, yawning, hiccoughs, nasal stuffiness, tachypnoea, respiratory depression, temperature instability, sweating, dehydration and tachycardia.

The onset, duration and severity of the newborn’s withdrawal symptoms vary widely and depend on factors such as the type of drug, the amount and duration of use by the mother, the gestational age and metabolic capacity of the newborn and the timing and amount of mother’s last dose before delivery. Withdrawal symptoms can start a few hours after birth, more likely if the mother has been using a short acting drug, such as heroin or lorazepam, or as protractedly as 2 weeks, more likely associated with the use of longer acting drugs, such as methadone, buprenorphine or diazepam. Management needs to be provided by the paediatric/neonatal team.

In newborns of opioid using mothers, there does not appear to be a direct relationship between the maternal dose/amount of opioids and the development of withdrawal symptoms in the newborn and although most newborns display some degree of withdrawal symptomatology, it is not unusual to see minor withdrawal symptoms in babies born to mothers on a high dose of methadone and vice versa. Therefore, it is not advisable to make specific assumptions or to counsel prior to delivery, as to the exact effect of the mother’s opioid dose on her newborn. The advice should include the variety of possible outcomes, in relation to withdrawal symptoms.

5.9.11 Care Planning
For information on care planning for a pregnant client please refer to Appendix B.

5.10 Promoting Parenting
Those working with pregnant and postpartum women must keep the needs of not only the mother but also her baby and other siblings in mind. They have a duty to enable women to retain their parenting role\(^8\) and a duty to safeguard and promote the welfare of children.\(^{17,18}\) They should:

- Promote and enable support from the woman’s existing social network.
- Work closely and co-operatively across agency boundaries (primary care, maternity, mental health, social services, home start, sure start, voluntary sector) to provide support to women in their mothering roles.
- Provide support to women in their mothering role by facilitating their access to community based support services (e.g. Newpin, Sure Start).
- Ensure children are safely looked after if their mother is admitted to inpatient care, that contact is maintained and that children are able to visit their mother.
- Ensure discharge/rehabilitation planning incorporates consideration of woman’s parenting role and the well-being of her children.\(^{15}\)
• Provide family friendly visiting areas in inpatient care, crèche facilities for outpatient appointments and times that are convenient for child care arrangements.
• Explore a woman’s need for respite from her child/children or residential crisis support where they can stay together.\textsuperscript{15}

If you have concerns about a child’s welfare, The Department of Health’s best practice guidance makes the following recommendations (15.3.1- 15.3.6):\textsuperscript{17}
• Discuss concerns with your manager, or designated health professional and/or other senior colleagues.
• If, after this discussion, you still have concerns, and consider the child and their parents would benefit from further services, consider which agency, including another part of your own, to whom you should make a referral.
  o If you consider the child is or may be a child in need, you should refer the child and family to social services.
  o In general, seek to discuss your concerns with the child, as appropriate to their age and understanding, and with their parents and seek their agreement to making a referral to social services unless you consider such a discussion would place the child at risk of significant harm.
  o If you make your referral by telephone, confirm it in writing within 48 hours. Social services should acknowledge your written referral within one working day of receiving it, so if you have not heard back within 3 working days, contact social services again.
  o If you have concerns that an unborn child may be at future risk of significant harm, it may be necessary for social services to convene an initial child protection conference prior to the child’s birth.

5.11 Service Provision
5.11.1 Integrated strategy
It is recommended that in every locality there should be a Perinatal Mental Health Strategy Group. There should be integrated protocols for all women suffering mental health problems during pregnancy and following delivery ensuring that women are speedily identified and appropriately treated at the level of care, primary, secondary or tertiary, required for their best treatment.\textsuperscript{13}

A shared, inter-agency approach to risk management, contingency planning and identifying and supporting the needs of children is recommended.\textsuperscript{15} In each locality there should be a policy involving Obstetricians, Paediatricians, Midwives, Substance Misuse Services, General Practice and Social Services, for the management of drug misusing mothers.\textsuperscript{14}

5.11.2 Specialist Perinatal Mental Health Provision
• All Mental Health Trusts should provide a Consultant Psychiatrist with a special interest in Perinatal Psychiatry and a specialist multidisciplinary community team which is available to all Maternity Trusts.\textsuperscript{13,14}
• The Royal College of Psychiatry is compiling a comprehensive document on the competencies and requirements for perinatal psychiatrists – refer to the website for further details http://www.rcpsych.ac.uk/members/sections/perinatal.aspx
• Whenever possible referral to perinatal services and/or infant mental health services should be made.
  o Coombe Wood Perinatal Psychiatric Service
  o Westminster Perinatal Psychiatric Service
Women suffering from serious mental illness postpartum requiring admission to a psychiatric unit should not be admitted to a general psychiatric ward and separated from their baby, but to mother and baby facilities separate from those for other patients with particular regard to their physical and safety needs, and ideally should be admitted to a specialist Mother and Baby Unit.\textsuperscript{1,13,14,17}

According to NICE guidelines\textsuperscript{1} clinical networks should be established to provide:

- a specialist perinatal service in each locality, to provide direct services, consultation and advice to maternity services, other mental health services and community services access to specialist advice on the risk and benefits of psychotropic medication during pregnancy and breast-feeding
- clear referral and management protocols pathways of care for service users, with defined roles and competencies for all professional groups involved.

6. Consultation

Specialist consultants in psychiatric perinatal and postnatal services have been consulted in the development of this guideline. It has been circulated to members of the medicines management group (MMG) and has been ratified by the MMG.

7. References

23. UKMII: What you should think about when prescribing to pregnant women?
61. UKTIS. Use of Venlafaxine in pregnancy, February 2016.
62. UKTIS. Use of Mirtazapine in pregnancy, September 2015.
71. UKMI. Management of depression in breastfeeding mothers – Are reboxetine, venlafaxine,
duloxetine, mirtazapine and MAOIs safe?


81. UKMI. *Management of depression in breastfeeding mothers – Are St. John’s Wort and other complementary therapies safe?*


92. UKTIS. *Use of Haloperidol in Pregnancy.* August 2014.


95. UKTIS. *Use of Olanzapine in Pregnancy.* January 2015.

96. UKTIS. *Use of Risperidone in Pregnancy.* January 2015.

97. UKTIS. *Use of Quetiapine in Pregnancy.* January 2014.


100. UKTIS. *Use of Aripiprazole in Pregnancy*. March 2015.


111. eMedicines Compendium. Kemadrin Tablets 5mg (Aspen). Last updated on eMC 06.11.2014.


125. UKTIS. *Use of Sodium Valproate in Pregnancy*. May 2015.


142. FDA. FDA Drug Safety Communication: Children born to mothers who took Valproate products may have impaired cognitive development. (2011).
166. UKTIS. Use of MDMA (ecstasy) in Pregnancy. October 2016.
168. UKTIS. Use of_codeine or dihydrocodeine in Pregnancy. October 2015.
183. CNWL. Personal communication with the United Kingdom Teratology Information Service, Feb 2015.
186. UKTIS. Use of Alcohol In pregnancy. July 2011.
190. UKTIS. Use of Acamprosate in pregnancy, December 2015.
GUIDELINES FOR THE USE OF LITHIUM during PREGNANCY AND POSTPARTUM

1 INTRODUCTION

The lifetime prevalence of bipolar affective disorder is approximately 1% in both men and women. In women the illness is most prevalent in the child-bearing years. While lithium has been used during pregnancy there is a small but significant teratogenic risk to a potential foetus. There is also a risk of lithium toxicity to both mother and newborn with use in later pregnancy which, can be minimised by close and careful monitoring of lithium treatment. This guidance aims to review those risks, presents a protocol in algorithmic form for dealing with a prescription of lithium during pregnancy, discusses practical issues pertaining to dosage and lithium monitoring and the management of lithium toxicity.

2 LITHIUM IN PREGNANCY

2.1 Lithium should not be routinely prescribed for women, particularly in the first trimester of pregnancy (because of the risk of cardiac malformations in the foetus). However if after risk assessment a clinical decision is made to start lithium in pregnancy a baseline foetal echocardiography ultrasound scan should be considered before initiating lithium.

2.2 There is a possibility that lithium may lower fertility.

2.3 Teratogenicity:
- Lithium is associated with an increased risk of congenital malformations and other toxic effects in the foetus and neonate.
- Lithium increases the risk of foetal heart defects to around 60 in 1000, compared with the risk of 8 in 1000 in the general population. Specifically lithium has been associated with an increased risk of Ebstein's anomaly (characterized by downward displacement of the tricuspid valve into the right ventricle and variable levels of right ventricular hypoplasia) is 10-20 times higher than expected, however the absolute risk remains small (0.05 -0.1%) and has not been replicated in all studies. Lithium may increase the risk of neural tube defects. Pre-conceptual folate supplementation is recommended.
- Lithium may increase the risk of neural tube defects. Pre-conceptual folate supplementation is recommended.

2.4 Continuing Lithium in Pregnancy

2.4.1 If a woman who is taking lithium becomes pregnant:
- The NICE guidelines (2014) suggest that in some women it is possible to discontinue lithium during the first trimester if the woman is well and not at a high risk of relapse. Lithium should be tapered off slowly and it should be explained that this may not remove the risk of cardiac defects in the foetus.
- If the woman is not well or is at risk of relapse, the following options should be considered;
  - continuing with lithium if there is a high risk of relapse (see below).
stopping lithium and restarting it in the second trimester if the woman is not planning to breast-feed and her symptoms have responded better to lithium than to other medication in the past, or

- switching gradually to an antipsychotic.

However, UKTIS state that there are conflicting opinions as to whether the pregnant woman should be changed to an antipsychotic or to stop the lithium after pregnancy is confirmed and restart it in the second trimester.

2.4.2 Dosing advice

- If it is decided that a woman should continue taking lithium during pregnancy, treat with the lowest dose with a maximum daily dose below 1g if possible.
- Lithium entirely readily crosses the placenta and foetal serum concentration is similar to that of the mother. Therefore, dividing the daily dose (ideally no more than twice daily) is recommended to reduce peak levels of lithium and the potential for adverse effects to the foetus.
- Following a single dose of lithium, plasma levels peak at 2-4 hours before falling to half of the peak after about 6 hours.
- Some data suggests a maximum single dose of 300mg however others feel that the size of the dose is irrelevant and it is more important that serum monitoring reflects an appropriate therapeutic level. When faced with this decision, it should be noted that there is probably little to be gained from using a regime of more than twice daily dosing, because of adherence problems and difficulties interpreting serum monitoring (should be done 12 hours post-dose), hence it is reasonable to use a single dose slightly above 300mg.

2.4.3 Monitoring

- Scan:
  Detailed foetal ultrasound scanning (level III) and foetal echocardiography should be offered (recommended at around weeks 6 and 18, to screen for Ebstein’s anomaly).

- Lithium Levels & Urea and Electrolytes:
  - Too low a concentration of lithium resulting in inadequate therapy can be as harmful as too high a concentration hence adjustment of the dose may be required for adequate control.
  - In the third trimester the use of Lithium may be problematic because of changing pharmacokinetics.
  - Pregnancy increases glomerular filtration rate and plasma volume, tending in turn to increase lithium clearance and necessitating increased doses to maintain serum level.
  - Paradoxically it is important to be aware of the tendency to sodium depletion and selective resorption of lithium at the proximal tubule can increase lithium levels. Hyperemesis, fever, reduced fluid intake or dietary restriction of salts can all raise lithium levels. Various medications including thiazide diuretics, angiotensin converting enzyme (ACE) inhibitors and non-steroidal anti-inflammatory drugs have a similar effect.
  - As a result of changes in fluid balance, serum lithium levels, urea and electrolytes and creatinine should be checked every 4 weeks, then weekly from the 36th week and a lithium levels should be done every 2 days perinatally. A lithium level should also be taken within the first 24 hours after childbirth; the dose should be adjusted to keep serum levels towards
the lower end of the therapeutic range, and the woman should maintain adequate fluid intake.\(^1\)

- If there is risk of premature labour e.g. if the patient is carrying multiple babies; serum lithium levels, urea and electrolytes and creatinine should be checked more frequently.

- Prior to onset of labour, it is recommended to either withdraw lithium temporarily or reduce the dosage by 25% - 50\(^{138}\) on the estimated day prior to delivery. After delivery, renal function rapidly returns to the pre-pregnant state and postpartum diuresis results in a significantly decreased volume of distribution. As a result lithium concentrations rise and there is a risk of toxicity for both mother and neonate.

- Women taking lithium should deliver in hospital, and be monitored during labour by the obstetric medical team in addition to usual midwife care.\(^1\) Monitoring should include fluid balance, because of the risk of dehydration and lithium toxicity (in prolonged labour, it may be appropriate to check serum lithium levels and consider the use of intravenous fluids to maintain adequate hydration).

- There should be at least one check of thyroid function mid-late pregnancy\(^{138}\) and supplements given as necessary.

2.4.4 Communication

- Care needs to be shared and clearly communicated to the consultant obstetrician\(^{193}\) with clear written documentation in patient’s mental health notes, maternity notes and hand-held notes of treatment plan covering pregnancy, delivery and the postnatal period (which should include details of lithium monitoring, when to stop lithium prior to or at delivery and monitoring advice).\(^1\)

3 LITHIUM POSTNATALLY

3.1 Risks to Mother

3.1.1 The mother’s mental state should be monitored closely because of risk of relapse. The postpartum period carries high risks (30-50%) of acute recurrence of mania and depression.

3.1.2 Postpartum affective and psychotic episodes can be very severe and often require emergency psychiatric intervention to avoid injury or suicide to the mother and abuse or infanticide of the newborn.

3.1.3 In general, postpartum relapse of mania and depression can be reduced five-fold when lithium is given shortly before birth (week 36) or within 48 hours of delivery (if this is done follow guidance as for section 2) and continued into the postpartum period, compared with women who do not receive postpartum lithium therapy. Should this be done, it is important to ensure the woman is medically stable (once the fluid balance is established)\(^1\) and to decrease the lithium dosage by about 25% - 30%.\(^{139,194-196}\)

3.1.4 Therefore to avoid relapse, consider reinstating lithium in women with bipolar illness who have been well during pregnancy without pharmacotherapy.

3.1.5 Consider augmenting treatment with an antipsychotic if a woman maintained on lithium is at high risk of a manic relapse in the immediate postnatal period.

3.1.6 Under normal circumstances, lithium levels, urea and electrolytes and creatinine should be checked daily during the first few days postpartum until patient’s clinical state is stable. These checks should be repeated 5-7 days after any dose change.
Once the lithium dose and patient’s clinical state is stable, recheck after a month. The patient should be advised to maintain adequate levels of hydration. A repeat thyroid function test in the puerperium is also advisable.\textsuperscript{193}

3.2 Risks to Neonate

3.2.1 Problems with lithium toxicity occur in the newborn at lower serum levels compared to adults.\textsuperscript{46}

3.2.2 The risk of neonatal toxicity is highest shortly after birth because of the very abrupt change in maternal clearance. Abnormal irritability follows lithium withdrawal.\textsuperscript{46}

3.2.3 It is recommended to undertake a full paediatric assessment of the newborn infant and monitor the infant for 10 days after birth for adverse medication effects, lithium toxicity or withdrawal (e.g. floppy baby syndrome, irritability, restlessness, feeding and sleeping difficulties).

3.2.4 Beyond the first trimester exposure lithium is associated with problems including neonatal toxicity e.g. goitre, hypotonia, cyanosis, ‘floppiness’, poor thermoregulation and low APGAR scores. Appropriate neonatal support should be readily available. Cases of cardiac arrhythmias, neonatal hypothyroidism, nephrogenic diabetes insipidus, gastrointestinal bleeding, seizures and shock have also been described.

3.2.5 Most of these toxic effects are self-limiting, returning to normal in 1-2 weeks. This corresponds with the renal elimination of lithium from the infant. The serum half-life of lithium in newborns is prolonged, averaging 68-96 hours, as compared with the adult value of 10-20 hours. Two cases of nephrogenic diabetes insipidus persisted for 2 months or longer.\textsuperscript{197,198}

3.2.6 Lithium is secreted into breast milk and levels achieved are approximately 40-50% of maternal serum levels.\textsuperscript{139} There have been reports of lithium toxicity in breast-feeding infants, including cyanosis, electrocardiogram abnormalities and hypotonia. This toxicity is felt to be due to the relatively immature kidney function in neonates and is especially likely to occur during times of dehydration (e.g. infection). Women who wish to breast-feed should be advised not to breast-feed if taking lithium and offered a prophylactic agent that can be used when breast-feeding. The first choice should be an antipsychotic (but not clozapine).\textsuperscript{1}

4 LITHIUM TOXICITY

4.1 Signs and Symptoms

4.1.1 The onset of symptoms may be delayed for up to 24 hours especially in lithium naïve patients.\textsuperscript{138}

4.1.2 Early symptoms of lithium toxicity are non-specific and may include apathy and restlessness which could be confused with mental changes arising from patient’s depressive illness or bipolar affective disorder. Other signs of lithium toxicity include similar drowsiness, tremor, tinnitus, nystagmus, slurred speech, diffuse gastrointestinal symptoms, polyuria and polydipsia\textsuperscript{188}, and are similar to common side-effects of maintenance therapy.

4.1.3 In mild cases withdrawal of lithium and administration of generous amounts of sodium salts and fluid will reverse the toxicity.\textsuperscript{197}

4.1.4 Major acute lithium toxicity is typically seen at serum levels above 2.0mmol/l and requires urgent treatment. Signs include clouding of consciousness, cerebellar and extrapyramidal signs, seizures, anorexia, vomiting, diarrhoea, cardiac arrhythmias, hypotension, circulatory collapse and myocardial infarction. The ECG may show T wave inversion and ST segment depression.\textsuperscript{198} Symptoms do not necessarily
correlate with lithium concentrations, toxicity has been reported at therapeutic
terminology and negligible symptoms at high levels.

4.2 Treating Lithium Toxicity
Prompt treatment of lithium toxicity is essential because of the mortality and risk of
permanent neurological or renal damage, occurring in 10% of cases. Treatment
is supportive and there is no specific antidote.

4.2.1 In the Mother
- Specialist information and advice on the treatment of poisoning should be sought
  from the UK National Poisons Information Service (Refer to Appendix B for contact
  number).
- Treatment is supportive with special regard to electrolyte balance, renal function,
  and control of convulsions.
- If patient is still on lithium, stop immediately.
- Contributory medicines such as thiazide diuretics, angiotensin converting enzyme
  (ACE) inhibitors and non-steroidal anti-inflammatory drugs should be stopped.
- Monitor ECG in symptomatic patients.
- Gastric lavage is only indicated in acute overdose. Symptoms may progress
despite stopping lithium because of the long elimination half-life, tissue binding and
intracellular accumulation of lithium.
- Control convulsions with intravenous diazepam if they are isolated.
- If they are more frequent it may be necessary to intubate, paralyse and ventilate
  the patient.
- Sodium and water balance should be restored. A forced diuresis should only be
  used in the situation in which there is a reduced glomerular filtration rate secondary
to hyponatraemia after a brief period of intoxication with a lithium level of less than
2.5 mmol/l. In most cases it should not be used. Monitoring is necessary to ensure
that the serum concentration decreases to 1 mmol/l within 30-36 hours of
starting treatment, otherwise haemodialysis should be instituted.
- Haemodialysis is the treatment of choice in severe lithium intoxication because it
clears up to 100 ml/min of blood, but peritoneal dialysis (clearance 15ml/min) may
also be used. Lithium is the most dialysable toxin known, having a low
molecular weight and negligible protein binding. Indications for haemodialysis are
lithium levels above 3.5 - 4.0mmol/l or an unstable clinical picture. At
equivocal levels of 2.0 - 4.0mmol/l it is important to determine the rate of lithium
elimination. This can be done by plotting three or more serum concentrations on a
logarithmic scale against time at 3-hourly intervals. If this predicts that the lithium
concentration will not decrease below 0.6 mmol/l in less than 36 hours,
haemodialysis is indicated.
- Dialysis should be repeated until the serum level is <1mmol/l 6-8 hours after the
end of treatment.
- Serum lithium levels demonstrate a rebound effect after dialysis that illustrates the
redistribution of the lithium from the intracellular compartment to the extracellular
compartment. This redistribution may require repeated or prolonged dialysis
sessions in order to prevent serum lithium levels from increasing to toxic
concentration.
- Bosinski et al, 1998 reports two cases of rebound toxicity occurring following
haemodialysis. In one case there was a very significant rebound to predialysis
levels after 9-15 hours and in another it happened after 7 hours. This illustrates the
speed at which it can occur and hence the importance of close monitoring of patient's lithium levels and clinical symptoms post dialysis.

- It has been reported that rebound in serum lithium levels is common after acetate dialysis due to intracellular accumulation, but this is less of a problem with bicarbonate dialysate.201
- Clinical improvement generally takes longer than reduction of serum lithium concentrations regardless of the method used.

4.2.2 In the Neonate

- Treatment is supportive with special regard to electrolyte balance, renal function, and control of convulsions.
- The neonate may have lithium toxicity even though the mother is not affected and has a normal or low plasma lithium level.202
- Treatment of poisoning in the neonate needs to be provided on a neonatal unit and additional advice can be sought from the UK National Poisons Information Service (see Appendix B for contact number)
SUMMARY OF MANAGING LITHIUM IN LATE PREGNANCY

Continue lithium:

a. Minimum effective dose with a maximum daily dose below 1g if possible;
b. Two divided doses and a suggested maximum single dose of 300mg if possible;
c. Monitor lithium levels, U&Es and creatinine every 4 weeks, then weekly from 36th week, every 2 days perinatally and within 24hrs after childbirth and adjust dose to keep serum lithium levels towards lower end of normal range;
d. There should be at least one check of thyroid function mid-late pregnancy and supplements given as necessary;
e. Detailed foetal ultrasound scan/echo (level III) at around weeks 6 and 18;
f. Shared care with obstetricians with clear written documentation in patient's mental health notes, maternity notes and hand-held notes of treatment plan covering pregnancy, delivery and the postnatal period;
g. Counsel patient that hyperemesis, fever, infection, reduced fluid intake or dietary restriction of salts can all raise lithium levels and should any of these apply to contact to team immediately to monitor serum lithium level. Advise about maintaining adequate hydration/ toxicity & signs/ medication with may contribute to toxicity.

Peri-natally:

a. Once labour begins, either withdraw lithium temporarily or reduce the dosage by 25% - 50%;
b. Monitor lithium levels, U&Es, creatinine and fluid balance during labour and delivery;
c. Monitor baby for neonatal toxicity, check for congenital defects and goitre.

Post-natally:

a. Closely monitor maternal mental state because of risk of relapse of mania or depression;
b. Check mother and neonate for lithium toxicity and if necessary treat accordingly (Refer to section 4);
c. Consider starting or restarting lithium in the mother at a reduced dose as soon as fluid balance is established. Monitor lithium levels, U&Es and creatinine daily for first few days until patient’s clinical state is stable, 5-7 days after any dose change then after 1 month;
d. Monitor thyroid function in the mother and neonate;
e. Consider augmenting lithium treatment with an antipsychotic if woman at high risk of a manic relapse in immediate postnatal period:
APPENDIX B

The Care Pathway and Case Management of Pregnant Clients

1.1 Access to services

- Access to services for pregnant women and their partners needs to be prioritised and all referral avenues facilitated, i.e., self, GP, Social Services, antenatal clinics, Health Visitors and other Addictions Services. Bear in mind that the women may be anxious about the attitudes of health care staff and the potential role of social services. They may also be overwhelmed by the involvement of multiple agencies.

- These women need supportive and coordinated care during pregnancy. Particular attention should be paid to:
  - integrating care from different services
  - ensuring that the attitudes of staff do not prevent women from using services
  - ensuring women are given evidenced based information about their treatment options so they may make informed decisions.
  - addressing women's fears about the involvement of children's services and potential removal of their child, by providing information tailored to their needs
  - addressing any health issues or concerns e.g. blood born virus screening and testing, poor nutrition
  - addressing family relationship and personal safety issues or concerns
  - addressing housing problems
  - addressing women's feelings of guilt about their misuse of substances and the potential effects on their baby.

- The Addictions professional needs to be more proactive and more flexible in trying to engage a pregnant woman presenting to services and may need to use other settings, such as antenatal clinic, for that purpose.

- Clinics should ensure that pregnancy testing is available, to establish or confirm pregnancy when necessary. Confirmation should also be sought from the woman’s GP.

- The approach and attitude of the service and professionals are vital in the delivery of care and ensuring good outcomes. Efforts must be made to encourage women to engage with other agencies and to maintain good liaison. Services must be well coordinated and pay attention to effective and prompt interdiscipline and interagency communication by:
  - jointly developing care plans across agencies
  - including information about opiate substitution therapy in care plans
  - co-locating services
  - monitoring attendance at appointments
  - offering women information about the services provided by other agencies.
  - progress is tracked through the relevant agencies involved in her care
  - notes from the different agencies involved in her care are combined into a single document
  - there is a coordinated care plan.

- It is likely that pregnant women who are misusing substances are leading chaotic lifestyles. The actual or perceived treatment demands and the involvement of more than one service can be anxiety provoking and overwhelming, in particular the expectations of services such as Family and Children Social Services. The woman should have a named midwife or doctor who has specialised knowledge of, and experience in, the care of women who misuse substances, and provide a direct-line telephone number for the named midwife or doctor.

- The earlier the engagement in service the better the outcome. Equally, prioritising pregnant women and their partners into treatment will improve outcomes.
• It is important to be explicit and clear from the beginning about the practical meaning of concepts like confidentiality, multidisciplinary teams and multiagency work.
• During pregnancy, it can be challenging both to advocate successfully for clients and to share appropriate information. Further guidance on this can be found within the Children's Act 2003 and Every Child Matters and CNWL Safeguarding Children and Young People policy.
• Multiple agencies need to become involved, i.e. antenatal/obstetric clinic, neonatology, GP, other medical services, Addictions services, social services, housing services, etc. Out of concern for the welfare of and to protect the newborns and children of women who are unstable in their drug use, Family and Children Services need to become involved. This is done through each agencies Safeguarding systems and procedures.

1.2 Assessment
• The assessment of a pregnant client should not differ from that of any other client.
• It should be multi-disciplinary, thorough and continuous throughout the pregnancy.27
• It should involve the assessment of:

1. Drugs and alcohol use:
   - Alcohol use
   - Tobacco/nicotine products including e-cigarettes
   - Illicit drug use and novel psychoactive substance
   - Mode of administration: Injected, smoked, oral
   - Prescribed and not prescribed medication.
   - Use of over the counter medication
   - Storage of all medicines
   - Current contact with drug/alcohol services
   - Current treatment and care goals
   - Previous contact/treatment with drug/alcohol services

2. Mental health issues:
   - Current and past mental health problems associated with pregnancy, including hospital admissions
   - and treatment
   - Current and past anxiety related problems
   - Current & past history of low mood, depression and/or self harm, suicidality
   - Current and past history of psychotic disorders
   - History of eating disorder
   - Low self-esteem/worth
   - History of physical, emotional or sexual abuse
   - Bereavement
   - Women’s perception of her own circumstances, needs and coping ability
   - Worries or concerns about pregnancy

3. Physical health:
   - Previous pregnancies and obstetric history
   - General Health Status
   - Dental Health
   - Exposure to blood borne viruses
   - Sexually transmitted infection
   - Complications from injecting
   - Accidents or injuries
4. Safeguarding:
   - History of previous or current contact with children and families social services
   - Care of existing children
   - History any children not in the care of the client
   - Parenting skills
   - Relationship with partner, family, friends
   - Contact with other health and social care
   - Previous history of childcare problems

5. Social functioning:
   - Housing situation
   - Financial situation
   - Employment or training and education issues
   - Workers
   - Difficulty getting registered with a GP

6. Offending history
   - Legal situation
   - Current and previous charges
   - Current court cases
   - Community Service
   - Probation orders
   - Court drug treatment orders

7. Strengths, needs, and risks:
   - Obstetric/gynaecological
   - Maternal Health
   - Domestic Abuse
   - Any current concerns for personal safety
   - Impact of drug culture environment
   - Social Isolation/unsupported pregnancy

Undertaking joint home visits with social worker or health visitor is a useful way to further assess any support needs the pregnant woman may have. If the substance misuse practitioner has any concerns during or following a home visit this should be discussed at the MDT or with the Line manager as soon as possible. Discussion on safe storage of all types of medications needs to be addressed not only at the home visit but checked at each subsequent appointment.

1.3 Formulation of Care Plan
An individual care plan can only be formulated after a comprehensive assessment has been completed and all relevant information from the other agencies such as maternity services, supporting the pregnant woman has been corroborated. The care plan should include:

- Addressing the urgent initial needs.
- Treatment goals for the drug and alcohol problem that are safe and realistic.
- Safeguarding risks and management plan
- Consideration for the relevant aspects of the woman’s physical and psychological health.
- Social functioning goals and support.
- A strategy to minimise criminal involvement and offending.
1.4 Urgent Initial Needs
- Regardless of the nature of the substance misuse problem, any pregnant woman accessing the Addictions Treatment Services should be considered in ‘urgent need’ and should take priority for assessment and engagement into the service.
- If the client has not been in contact with other services, referral to the antenatal service is an immediate priority and must be included in all care plans.
- Women have a choice as to where they would like to receive their antenatal care.
- Most hospitals have midwives allocated to respond to this client group. Depending on local policy/practice, referrals can be made directly or through the GP.
- If the woman does not have a GP, registering with one is a priority.
- Appropriate treatment should be commenced as soon as possible.
- Urgent need may also include social aspects such as finances and housing for which help from other agencies may be needed.

1.5 Drugs and alcohol treatment goals
- Like all service users, pregnant women vary widely in their presentation and have different treatment goals. Pregnant women are likely to feel concerned, guilty and/or anxious about the potential harm of their substance misuse to their baby. Therefore, information on the potential risks of the use of psychotropic substances during pregnancy should be provided and delivered clearly and sensitively.
- Goals (i.e. no or minimal drug use of either licit, illicit or prescribed) must aim for best possible outcome for mother and baby, but also be realistic and pragmatic about what can be achieved. It is helpful to work with the understanding that for some pregnant clients harm minimisation is a more realistic goal.
- With respect to prescribed opiates such as methadone or buprenorphine, both maintenance and detox are possible. Some women will choose to remain on a maintenance dose, whereas others may feel motivated to reduce and attempt to detox. Whilst it is important to support the woman in her goal, it is also necessary to remain vigilant and be prepared to change the treatment plan, as often women find reductions harder than anticipated. They should not be pressured into a reduction of their opiate dose or abstinence, although this may have been the initial treatment aim.
- Safe storage of medication: Any change to collection of medicines must be within a framework of considering if the decision could have an impact on other children within the home. The rationale for change in collections of prescribed medication should be documented in the pregnant woman’s notes. Safe storage information leaflets must be given and a discussion held eliciting the pregnant women’s understanding of the importance of safely storing medicines. Equally if there are concerns medicines are not being stored safely this is an indication to review collection from the local pharmacy and consider increasing supervised consumption following discussion in the MDT
- Life post birth must be addressed before delivery. Understandably, women may have doubts, worries and anxieties in relation to how they feel they might cope. Pressures at this time can destabilise and facilitate relapse.
- Urine toxicology screening becomes a much more necessary and useful treatment tool for client engagement during pregnancy. The frequency of urine testing may needs to be decided by the MDT, in order to provide a clear indication of current drug use to the staff, as well as clear boundaries and containment to the client.
Urine monitoring is only part of the treatment process, but not the treatment in itself. However pregnant women that are non-compliant with staff, requests for urine screening must be addressed at each occurrence and discussed with the MDT.

It is worth noting that urine test results are often relied upon quite heavily by other agencies, such as Family and Children Services. They are often used as evidence in court proceedings. Bear in mind that they do have a margin of error and this should be pointed out in any report, especially if a result is at odds with the clinical presentation. Part of the role of the Addictions professional is to ensure that a balanced and accurate picture of the woman’s engagement in services and treatment progress is given to these agencies, including urine monitoring within a multifaceted treatment package.

Substance misuse management during pregnancy is a fine balance between what is comfortable and realistic for the woman and what is necessary to ensure the best outcome for the baby.

1.6 Physical and Psychological Health

- General health issues that are made evident in the assessment need to be addressed. As standard practice, all pregnant women are offered testing for Hep B and HIV as part of their antenatal screening. Testing for Hep C is recommended for all drug users, in consideration of the possibility of vertical infection transmission and for the purpose of breastfeeding and immunisation of the baby.
- Care plans need to include efforts to increase awareness around healthy eating, smoking cessation and the advantages of the use of folic acid. NICE recommends the use of folic acid prior to pregnancy and up to 12 weeks into the pregnancy, to prevent possible neural tube defects. 167
- Addictions professionals need to have an awareness of potential pregnancy symptoms and complications, such as morning sickness, constipation, heartburn, fatigue, pre-eclampsia, and that these are considered in the care plan. If concerns or doubts about the progress or state of the pregnancy arise during treatment, women need to be referred to seek appropriate advice, either from antenatal services or Accident and Emergency.
- Mental health concerns should be clearly identified and addressed in the care plan. These need to be discussed within the Multidisciplinary Team and a clear strategy agreed as to how and by whom the treatment is to be monitored and how often this is to be reviewed during the pregnancy.

1.7 Social Functioning

- Issues such as housing may become more urgent when a client becomes pregnant. Present housing arrangements may no longer be suitable and she may need further support to try to solve her housing difficulties.
- In assessing the relationship with the woman’s partner, it is important to explore issues related to domestic abuse, as it is not uncommon that this begins or escalates during pregnancy. Abuse may take the form of physical, sexual or psychological abuse. In more extreme cases, the perpetrator may seek control over the victim, which may result in her isolation from the outside world. In addition to the distress involved, domestic abuse can cause miscarriage, premature delivery, low birth weight, placental abruption, stillbirth and maternal death. 203
- The Addictions Treatment Services or Health Services may be the victim’s only point of contact and chance to disclose their experience.
- Practitioners should be aware that domestic abuse can exist prior to or start in pregnancy and they should prepare themselves to support victims and be able to use other resources than the usual to help manage the problems.
• Practitioners should undergo training and seek support from more experienced staff if they feel ill-equipped to deal with this aspect of care.

1.8 Criminal Involvement and Offending
• If a pregnant client has a history of offending or outstanding legal issues, she may be at risk of imprisonment. It is important that this is taken into consideration when drawing a management plan, as this might impact on the pregnancy. For example, if a pregnant opiate user is arrested, the prescribing of opiates and avoidance of withdrawal symptoms become an important issue.
• It may be useful for women to carry a letter with prescribing information and service contact information.

1.9 Co-ordinate Delivery of Treatment and Other Services
• The role of the Addictions professional is to offer a high level of support.
• Maternal health pathways suggest a minimum of fortnightly key work sessions throughout the pregnancy, but according to need, clients are seen on a weekly basis and some even more frequently.
• It is worth noting than a pregnant woman may have a number of other appointments to attend; therefore, flexibility is needed and close liaison with other professionals in order to maximise and facilitate compliance.
• Effective care of pregnant women who misuse substances requires a multi-agency approach, with Antenatal and Family and Children Services being key partner agencies.
• When thresholds for Safeguarding child concerns have been met, a pre-birth case conference needs to take place. In cases where there are no child protection concerns, but the family meets the threshold for a child in need assessment, a network meeting prior to birth needs to be organised. In both these cases Family and Children Services will be the lead agency and coordinate the case.
• When the client does not meet either of the above thresholds, it is good practice to have a pre-birth planning meeting, between weeks 28 and 32. Although any professional can take the lead in the organisation of this meeting, it is midwives who are in a better position to do this.
• The rationale for this meeting is to:
  1. Ensure that a birth plan is in place.
  2. Ensure that antenatal services are aware of substance misuse problems and/or prescribing issues (drug, dose etc.), so that once a woman is admitted onto the ward the correct prescribing can be provided and the Addictions service’s contact details are clear on discharge. It may be useful to write details of the current prescribing in her handheld antenatal notes, or provide a letter with these and the chemist’s details. However, not all women may want this information written in their hand held notes as unintended others may read them, i.e. family.
  3. Give the mother an opportunity to meet the health visitor.
  4. Ensure that there will be support for the client following the birth of the baby, and establish the role of each professional.
  5. To clarify possible Child Protection concerns.
• In a “routine” pregnancy, antenatal appointments take place every four weeks after week 12, every two weeks from week 32, and every week during the last three or four weeks. Women with substance use issues generally receive a higher frequency of antenatal care, and it is important to clarify this point with the client’s midwife. Antenatal clinics may carry out urine toxicology screening. Keyworkers should maintain liaison with
midwifery services to ensure attendance at appointments and that scans and tests have been completed. Linking collections of prescriptions to appointments may be a useful strategy to ensure contact is maintained with the pregnant woman.

- Addictions services should offer weekly to two weekly follow up appointments to monitor the pregnant woman’s progress. However if clinically indicated this may need to be increased.

1.10 Care plan review

- Women's goals and treatment aims may change throughout the pregnancy. Therefore, care plans need to be reviewed regularly and frequently, in order to provide the necessary adjustments in response to the rapid pace of change of this period.
- The dose of opiates, for example, may need to be adjusted. As the pregnancy progresses, some women may find that what once was a comfortable dose, no longer holds them, or they feel unable to continue with their dose reduction. Other women experience an increase in drowsiness and may require their dose to be reduced. Issues such as this highlight the need for regular review of care.

1.11 Aftercare/After Birth

- Even with good antenatal liaison, the postnatal period can be difficult. Challenges include preventing the risk of mixed advice. Breastfeeding is often one such example.
- All prescribed and non-prescribed drugs, hepatitis B and C should be taken into account when advising on breastfeeding.
- Wherever possible, this client group should be encouraged and supported to breastfeed, carefully considering the risks versus the benefits of this.
- The role of the Addictions practitioner is vital when liaising with the ward, to ensure that the woman receives the appropriate medication and to reinforce awareness of her care plan.
- The postnatal period can be very stressful, especially if baby is displaying signs of withdrawal. This period is difficult and is often a time when women experience lapses.
- The care plan must be sensitive to changing support needs. It may be beneficial to include home visits, as it may prove unrealistic to expect the women to attend the clinic regularly.
- The postnatal period is a good time to encourage women to think about their sexual health, contraception and smear tests.
- Also during this period, there is readjustment of the hormonal system, which has been associated with changes in mood in the mother. Therefore, it is necessary to monitor mood closely and be alert to the appearance of postnatal blues and/or depression.
- It is useful to review how medication and/or illicit drugs, if these are being used, are stored. Although small babies are not mobile, it is not long before they are able to start exploring their surroundings.

All clients, women and men, should be asked about and informed of the risk of unforeseen drugs overdose in young children, even those who do not have children, as they may come into contact with children of friends and family.
COOMBE WOOD PERINATAL MENTAL HEALTH SERVICES

Coombe Wood perinatal inpatient unit is available for CNWL patients.

- Coombe Wood Perinatal Services comprises of three components:
  - the inpatient treatment unit
  - the parenting assessment service
  - perinatal community service.

- Coombe Wood Perinatal Mental Health Unit can accommodate up to 10 parents and 11 babies.
- The Inpatient Treatment service can accommodate up to eight mothers who are experiencing moderate to severe mental health difficulties together with their babies of up to 18 months of age – one bed can also be offered to a pregnant woman who is in the last trimester of pregnancy (this is decided on an individual case basis & being compliant with the protocol.
- This service provides treatment to mothers who suffer from treatable mental health problems in the postnatal period and have a baby under the age of 18 months. The aim of joint admission is to facilitate bonding with the baby.
- The Parenting Assessment Service uses up to 2 beds for 6 week Residential Parenting Assessment of parent(s) with their children. There are two family rooms available for assessment of couples.
- The Perinatal Community Mental Health Service provides community based assessment and treatment for women with moderate to severe mental health difficulties during the late antenatal or postnatal period who are registered with a GP in Brent or Harrow.
- Referrals to the inpatient, parenting assessments, and perinatal community service are made directly to the Unit on 020 8955 4495.

WESTMINSTER PERINATAL PSYCHIATRIC SERVICE

- The Mother and baby unit is centrally funded and women from all areas can access beds
- The Perinatal Mental Health Team at St Mary’s has been operative since 2009 and we offer a wide range of hospital and community based clinical interventions, training, supervision and education and
- Women can be referred for preconception advice
- Experienced in providing advice to patients with a serious mental illness and complex medical problems in collaboration with the obstetric teams at St Mary’s
- Can be contacted on 0203 312 1582

USEFUL CONTACTS NUMBERS FOR ADVICE

- Coombe Wood Perinatal Psychiatric Services: 020 8955 4495
- Westminster Perinatal Psychiatric Services: 0203 312 1582
- The CNWL Medicines Information Service: 020 8206 7271 (advice on medicines in pregnancy and lactation)
- UK National Poisons Centre: 0844 892 0111
Equality Impact Assessment

1. What is the name of the Policy, Service Development, Business Plan, Strategy or Organisational Change being assessed?

**Procedure:** Pregnancy and Breast-feeding Psychotropic Prescribing Guideline

2. Briefly describe the aim of the Policy, Service Development, Business Plan, Strategy or Organisational Change that is being Impact Assessed. What needs or duties are it designed to meet? What are its intended outcomes?

This guideline aims to help facilitate the decision making when selecting a psychotropic in pregnancy, and includes general treatment principles and factors to take into account when undertaking risk assessment as well as information on individual psychotropics. The latest information available in the literature should always be consulted when making treatment decisions. The guidelines incorporate recommendations outlined by the NICE Clinical Guideline No. 192 on Antenatal and Postnatal Mental Health, April 2014. The guideline does not provide treatment recommendations for individual patients as choice of psychotropic may be influenced by individual patient factors, comorbidites, physical conditions.

3. Does this development have an impact on information quality, information security and/or information compliance, including staff or patient privacy? **Yes** or **No**

**No**

4. If yes, have you completed an information governance impact assessment form or otherwise contacted the Information Governance team? **Yes** or **No**

**N/A**

For the purposes of this assessment, the relevant protected characteristics are: **Age, disability, gender reassignment, pregnancy and maternity, race/ethnicity, religion or belief, gender/sex, sexual orientation.**

**MEETING THE GENERAL DUTIES**

5. How does the service / policy / procedure / development **contribute in a positive way to**:

(a) eliminating discrimination, harassment, victimisation and any other conduct that is prohibited by or under the Equality Act 2010;

(b) advancing equality of opportunity between persons who share a relevant protected characteristic and persons who do not share that characteristic.

(c) fostering good relations between persons who share a relevant protected characteristic and persons who do not share that characteristic.

**Race / Ethnicity**

The procedure states that it seeks to ensure that all service users are treated in compliance with The Equality Act 2010. Staff working within this procedure will have due regard to avoiding discrimination and providing equality of opportunity regardless of the patient’s age, disability, gender, race/ethnicity, religion, belief or sexual
orientation to enable them to have a positive experience of their care e.g. information will be tailored to specific needs. Clinical decisions will be based on the patient's needs and reflect any known specific conditions which might impact on their response to treatment with medicines.

Disability
As above
Gender
As above
Gender Re-assignment
As above
Sexual Orientation
As above
Religion or Belief
As above
Age
As above
Pregnancy and Maternity
As above
Marriage and Civil Partnership (applies to a. above only)
As above

ADVERSE IMPACT
6. Is there any evidence that the subject of this EHRIA could affect people having a protected characteristic disproportionately, thus leading to an adverse impact? The disproportionate effect or adverse impact might be actually happening or have the potential to happen.

What evidence have you analysed to inform your conclusion? For example, evidence might be from equalities data on patients accessing/not accessing the service, findings from patient or staff surveys, service user complaints, staff grievances, concerns from local or national pressure groups or public concern in the local or national media.

Race / Ethnicity

There are no known reasons or evidence which indicates that any specific characteristics of service users might lead to an adverse impact of this procedure.
HUMAN RIGHTS

7a. How does the subject of this EHRIA contribute to encouraging respect for human rights?

This procedure aims to provide equitable treatment for all service users taking into account any individual needs and as such respects their human rights.

7b. Is there any evidence that the subject of this EHRIA is at risk of unlawfully restricting an individual’s human rights?

No

CONSULTATION

8. Have you consulted representatives from groups having protected characteristics (staff, service users, carers, other stakeholders or expert groups) as part of your assessment? Please give details of who have you consulted, the method used, the results of the consultation, how the results have been used and where they have been published.

The Medicines Management Group has multidisciplinary membership including primary care representatives.

RESPONDING TO ADVERSE IMPACTS / BREACHES IN HUMAN RIGHTS

9. Can any identified adverse impacts relating to Equality or breaches in Human Rights be justified? If they cannot be justified, how do you intend to deal with it?

None are anticipated. The MMG would be responsible for considering and agreeing any required action.

MONITORING

10. Provide information on how you intend to monitor for actual adverse impact in the future.

Direct reporting to MMG or analysis of any incidents or errors through the incident reporting system.

Equality and Human Rights Impact Assessment Action Plan

The following actions will be undertaken as a result of the Equality and Human Rights Impact Assessment to address identified adverse impact:

<table>
<thead>
<tr>
<th>Adverse impact identified</th>
<th>Action to be taken</th>
<th>Timescale</th>
<th>Responsible manager</th>
</tr>
</thead>
<tbody>
<tr>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

To be signed by the manager undertaking the full assessment.
Name: Nicola Carson  
Designation: Medicines Information Manager  
Date: 13.6.2017

To be countersigned by the Senior Manager, i.e. Service Head, Line Manager, Director, as appropriate.
Name: Caroline Parker  
Designation: Consultant Mental Health Pharmacist  
Date: 07.08.2017
## Document Review History

<table>
<thead>
<tr>
<th>Date of Review</th>
<th>Reason for Review</th>
<th>Version Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>April 2015</td>
<td>Two previous pregnancy guidelines Pregnancy and Breastfeeding - Psychotropic Prescribing Guideline and Pregnancy and Breastfeeding: substance misuse prescribing guidelines combined. Updated the psychotropic guideline, which was due for routine review and combines it with the substance misuse guideline which was approved at the February MMG. Main changes to the mental health sections: Each Section reviewed and updated following review of the literature and new NICE guideline on antenatal and postnatal mental health. For antidepressants and antipsychotics there are no longer specific recommendations for first line medications (sections 5.2 and 5.3), Sodium valproate: updated in light of NICE and MHRA guidance, no longer recommended in women of child bearing potential (section 2, and 5.6) Lamotrigine is a treatment option and no longer contraindicated by NICE in pregnancy (section 5.6) Promethazine has been added and is recommended for the treatment of insomnia in pregnancy (section 5.3) Resources for patients and professionals have been updated (section 2) Zaleplon and zolpidem added (section 5.3) Inclusion of the Westminster Perinatal service ( sections 2, 5.10 and appendix c)</td>
<td>1.0.0</td>
</tr>
<tr>
<td>June 2017</td>
<td>Routine review Addition of a section on pre-pregnancy planning Addition of the BAP consensus guidelines produced in 2017 on management of perinatal mental health: <a href="https://www.bap.org.uk/pdfs/BAP_Guidelines-Perinatal.pdf">https://www.bap.org.uk/pdfs/BAP_Guidelines-Perinatal.pdf</a> Change to the section on SSRIs Consolidated into one section to bring together the conflicting information on risk of cardiovascular malformations Updated section on SSRI and link to autism Addition of the MHRA resources on use of sodium valproate in women of child bearing age Zaleplon removed as no longer available in the UK Addition of a section on ADHD Information on Hyperemesis cannabis syndrome added</td>
<td>2.0.0</td>
</tr>
</tbody>
</table>