Perinatal Mental Health: Prescribing Guidance for Trust Prescribers and GPs

(Version 3 – January 2015)

Principal Author:
Dr Jenny Cooke – Consultant Psychiatrist, Brighton & Hove Perinatal Mental Health Service

Supported by:
Jed Hewitt – Chief Pharmacist, Governance & Professional Practice

Date of Preparation: October 2014
Date for next full Review: January 2018

This updated guidance was approved by the Trust Drugs & Therapeutics Group in January 2015 and supersedes the 2012 version of the document.

If you require this document in an alternative format, ie, easy read, large text, audio, Braille or a community language please contact the Pharmacy Team on 01243 623349.
(Text Relay calls welcome).
Perinatal Mental Health: Prescribing Guidance


A brief summary of key findings:

- When discussing medication in pregnancy, acknowledge that there is uncertainty surrounding risks.
- Explain the risks of treating versus not treating mental health conditions and the background risk of malformations in women without mental disorder; between 2 and 4 in 100.
- Discuss the risk of relapse. Consider when the last episode was, its severity and the response to treatment.
- Discuss the risks of stopping medicines suddenly. Consider high risk of relapse and risk of withdrawal symptoms.

Prescribing in Pregnancy.

- **Not treating mental health problems in pregnancy carries risks:** Symptoms of depression anxiety or psychosis might result in missed scans and midwife appointments, risky behaviour e.g. self harm, neglect, poor nutrition, smoking, drinking or drug misuse. Remember women will need more medication at higher doses if they relapse and become very unwell.

There is good evidence\(^1,^2\) that maternal anxiety and depression in pregnancy result in childhood emotional and behavioural problems (independent of postnatal factors that influence development of childhood mental ill health). Trying to avoid treatment with psychotropics in pregnancy is not always in the best interests of the patient or the foetus or the wider family.


Some general principles when prescribing in pregnancy:

- Data are often scarce. Often relies on human case reports & pre-clinical animal studies
- Studies are often problematic due to confounders and results need to be treated with caution. Eg. Women on antidepressants in studies are more likely to drink, smoke, not attend antenatal care, have poor nutrition, (prenatally as well as antenatally), and to be on other medication. These factors, and potentially others, may affect intrauterine growth, birth weight and APGAR score
- Need to balance with risks of treating against those of not treating
- Generally use the lowest effective dose for shortest time period
- Where possible, avoid newer drugs that have fewer data on use
Monotherapy is always preferable. Eg. Using more than one antidepressant will increase the risk of cardiac abnormalities
Consider specific trimester risks – usually most risk during first
Ensure adequate foetal screening / infant monitoring is performed
Clearly document all prescribing decisions

Note – Also consider those women who are planning pregnancy. If possible review and rationalise medication prior to actual pregnancy. However, also consider that if a woman who has previously had episodes of severe illness is doing well on a medication and wants to become pregnant or is pregnant it may be preferable to continue that medication unless absolutely contraindicated.

Clearly explain all risks and options to the patient. Ensure that everything is documented and work closely with obstetricians and perinatal psychiatrists to increase monitoring in pregnancy – eg. scans / growth checks / BP monitoring

**Summary Table of Medication Use in Pregnancy**

<table>
<thead>
<tr>
<th>Antidepressants associated with lower risk</th>
<th>Fluoxetine and sertraline (see note below) Tricyclics – amitriptyline and imipramine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antipsychotics associated with lower risk</td>
<td>Olanzapine Quetiapine</td>
</tr>
<tr>
<td>Mood Stabilisers associated with lower risk</td>
<td>Olanzapine Quetiapine</td>
</tr>
<tr>
<td>Hypnotics associated with lower risk</td>
<td>Promethazine</td>
</tr>
</tbody>
</table>

**Antidepressants in Pregnancy**

- Teratogenicity - all carry a small increased risk (1-2%) of birth defects, mainly cardiac. Also risk of reduced intrauterine growth rate (IUGR), low birth weight (LBW) and low APGAR score
- Studies are prone to confounders so results need to be treated with caution
- Remember that risks of not treating depression may outweigh risks of treatment

A recent meta-analysis\(^3\) showed that overall antidepressants do not appear to be associated with an increased risk of congenital malformations, but statistical significance was found for cardiovascular malformations. Given that the relative risks are marginal, they may be the result of uncontrolled confounders. Although the relative risks were statistically significant none reached clinically significant levels.

\(^3\) Grigoriadis et al, Journal of Clinical Psychiatry, 2013, 74(4), 293-308
Do Antidepressants cause autism?
A Swedish study⁴ of 600,000 children found those born to a mother with a history of maternal depression were at higher risk of developing an autistic spectrum disorder, particularly autism without intellectual disability. The association was strongest in those women on antidepressants antenatally, (both SSRIs and other antidepressants). A causal association with antidepressant use in pregnancy could explain 0.6% of ASD cases. However,

- Data could be confounded by indication
- Antidepressant use in pregnancy is an indicator of more severe depression and there is an associated between severe depression and autism
- This study does not provide enough evidence to say we should stop treating moderate to severe depression in pregnancy with antidepressants

⁴, Raj et al, BMJ, 2013, 346:f2059

SSRIs and Persistent Pulmonary Hypertension
One study showed small increased risk of persistent pulmonary hypertension with SSRIs used after 20 weeks, but numbers were small: 6 to12 / 1000 and subsequent large scale studies have failed to reproduce this finding. Overall risks are therefore considered to be smaller than this.

Neonatal Withdrawal
All antidepressants are associated with withdrawal in the neonate but it is usually mild and self-limiting. Withdrawal symptoms are slightly reduced with fluoxetine due to its long half-life. Symptoms include sleeping problems, tremors, constant crying, suckling problems, and myoclonus. Symptomatic treatment is normally not required but the neonate should be kept under observation on a postnatal unit for 48 hours.

Paroxetine
According to NICE, this is the only antidepressant absolutely contraindicated in pregnancy, due to its association with foetal heart defects (first trimester).

Venlafaxine
Although venlafaxine is not recommended by NICE, perinatal psychiatrists and obstetricians use it frequently in treatment-resistant patients. However, blood pressure must be monitored more closely throughout the pregnancy.
Anti-psychotics in Pregnancy

There is more data available for supporting the use of older, first-generation antipsychotics, e.g. chlorpromazine, haloperidol and trifluoperazine, than for newer second generation drugs. However, the United Kingdom Teratolgy Information Service still supports the use of olanzapine and quetiapine. [http://www.uktis.org/](http://www.uktis.org/)

Second generation atypical antipsychotics are associated with low folate levels so during pre-pregnancy counselling, the use of folic acid supplementation (eg. 5mg / day) should be considered / discussed.

Olanzapine is associated with weight gain and gestational diabetes so this needs to be monitored closely during pregnancy.

NICE advises against prescribing clozapine, long-acting antipsychotic injections and anticholinergic drugs. Neonatal toxicity & withdrawal have been reported but again this is very mild and self-limiting.

Mood Stabilisers in Pregnancy

Olanzapine and quetiapine are considered safer options than more traditional mood stabilisers.

Lithium
Wherever possible, use should be avoided, especially in the first trimester and prescribing stopped before conception. Risks include foetal heart defects (incidence raised from 8/1000 to 60/1000) and Ebstein’s anomaly (raised from 1/20,000 to 10/20,000).

Cessation of lithium should be done gradually over at least four weeks. If the woman is not well, switch to an antipsychotic or re-start lithium in the second trimester (if not planning to breastfeed).

If lithium is continued, check serum levels every four weeks aiming for the lower end of the therapeutic range. Higher doses may be needed towards the mid-end of pregnancy therefore check levels every week from week 36 and also check within 24 hours of birth. Birth should take place within hospital.

Sodium Valproate
This drug is absolutely contraindicated in pregnancy and should also be avoided in all women of child bearing potential. There is a high risk of neural tube defects, (risks raised from 6/10,000 to 100-200/10,000). It can also affect intellectual development of child in up to 30% of exposures. (Valproate syndrome).
Carbamazepine
NICE recommend that this drug is not routinely prescribed during pregnancy due to the risk of neural tube defects (risk raised from 6/10,000 to 20-50/10,000). It has also been linked to other major malformations, gastrointestinal tract problems and cardiac abnormalities.

Lamotrigine
NICE recommend that this drug is not routinely prescribed during pregnancy. Risk of oral cleft is around 9/1000.

Use of benzodiazepines in pregnancy
NICE recommends that these drugs only be used short-term, if considered necessary for extreme anxiety and agitation. They are associated with cleft palate and with other malformations including Ebstein's anomaly. Maternal use of a benzodiazepine during pregnancy is also associated with an increased risk of preterm delivery. Floppy baby syndrome in neonate and neonatal withdrawal are also possible.

Use of (other) hypnotics in pregnancy
NICE suggest the use of low dose chlorpromazine or amitriptyline in response to serious and chronic problems. However, many perinatal psychiatrists prefer to use a sedating antihistamine, e.g. promethazine. Z-drugs are not recommended by NICE but zopiclone is used by some perinatal psychiatrists for short-term use.

Prescribing in Breast Feeding
NICE Clinical Guidelines advise that breast-feeding should not be discouraged. Rather, wherever possible, the safest treatment available should be used so that breast-feeding can still take place.

Summary Table of Medication Use in Breast-feeding

<table>
<thead>
<tr>
<th></th>
<th>Breastfeeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressants associated with lower risk</td>
<td>Sertraline (first-line choice) Paroxetine Imipramine Nortriptyline</td>
</tr>
<tr>
<td>Antipsychotics associated with lower risk</td>
<td>Sulpiride Olanzapine Quetiapine</td>
</tr>
<tr>
<td>Mood Stabilisers associated with lower risk</td>
<td>Olanzapine Quetiapine (Valproate)</td>
</tr>
<tr>
<td>Hypnotics associated with lower risk</td>
<td>Promethazine</td>
</tr>
</tbody>
</table>
It must be noted that for most drugs there are very little data on levels in breast milk and safety in breast-feeding and therefore recommendations in reference texts are often based on just a small number of case reports.

Similarly, there is no clear evidence or information for the vast majority of drugs on the timing of feeds with regard to timing of doses, or on whether milk at certain times of day should be discarded.

Based on various information sources, the following drugs (in particular) should be avoided in breast-feeding or if unavoidable used with caution:

Antidepressants:
- Citalopram
- Clomipramine
- Dosulepin
- Doxepin - avoid
- Duloxetine
- Escitalopram
- Fluoxetine
- MAOIs
- Mirtazapine
- Reboxetine
- Venlafaxine

Antipsychotics:
- Aripiprazole
- Clozapine - avoid
- Paliperidone
- Pimozide
- Risperidone

Mood stabilisers:
- Lithium – avoid (very high levels possible in breast milk and in infant serum).
- Lamotrigine – avoid (as above. Also risk of serious dermatological problems in the infant – eg. Stevens-Johnson syndrome.

Hypnotics:
- Zopiclone – avoid (high levels possible in breast milk)
- Benzodiazepines – avoid long-acting or in high dose
Good sources of Information on prescribing in pregnancy and breastfeeding:

- Iphone app: Lactmed – free to download.
- Summaries of Product Characteristics (or contact the individual drug manufacturer) [http://www.medicines.org.uk/emc/](http://www.medicines.org.uk/emc/)
- The Maudsley Prescribing Guidelines
- Psychotropic Drug Directory – Stephen Bazire

Other references:


Fluoxetine: Possible small risk of congenital cardiac defects. MHRA Drug Safety Update (2010), 3(8), 4-5