

## ANTIDEPRESSANTS IN PREGNANCY & BREASTFEEDING - DELIVER SAFE CHOICES

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- ▶ PROVIDE PRECONCEPTION COUNSELLING FOR YOUNG WOMEN PRESCRIBED ANTIDEPRESSANT MEDICINES
- ▶ DISCUSS NON-PHARMACOLOGICAL INTERVENTIONS
- ▶ CONSIDER ANTIDEPRESSANTS FOR MODERATE TO SEVERE DEPRESSION
- ▶ BE AWARE THAT ALL ANTIDEPRESSANTS CARRY SOME RISK DURING PREGNANCY
- ▶ PROVIDE INFORMATION ABOUT COMPATIBILITY WITH BREASTFEEDING

Mental health problems during the perinatal period are common; antenatal anxiety or depression is experienced by up to 10% of women, increasing up to 16% postnatally. Early intervention produces the best outcomes for mothers and their families.<sup>1</sup> When women first become pregnant, or if they are planning a pregnancy, enquire about any family or personal history of mental illness.<sup>2</sup> All pregnant women should be screened for psychosocial risk factors; mental wellbeing should be considered as important as physical health.<sup>1</sup>

### PROVIDE PRECONCEPTION COUNSELLING FOR YOUNG WOMEN PRESCRIBED ANTIDEPRESSANT MEDICINES

Women who are currently prescribed antidepressants and considering a family should be given preconceptual counselling. It is wise to anticipate potential risks should she become pregnant and proactively discuss these risks with her.<sup>3</sup> Discuss treatment preference, efficacy, tolerability and the risks of continuing or stopping medicines.<sup>2</sup>

The risks of stopping an antidepressant, changing to an alternative, and starting medicines during pregnancy need to be carefully evaluated.<sup>4</sup> Stopping an antidepressant may put the newborn baby at risk if the mother suffers from a relapse and is unable to provide a sufficient level of care to her baby. If women taking antidepressants become pregnant, advise them not to suddenly stop taking their medicine because there is a high risk of relapse (68%).<sup>5</sup> If deemed appropriate withdraw slowly over 1-2 months to reduce the risk of withdrawal symptoms and increase the likelihood of detecting a relapse. If a medicine is working well, it is usually preferable to continue with it rather than risk switching to a medicine that may not be effective. Consider a discussion with, or referral to a maternal mental health (MMH) team.

**Note:** Lithium therapy should always be managed by a specialist service during pregnancy; seek immediate advice from a MMH team for these cases.

### DISCUSS NON-PHARMACOLOGICAL INTERVENTIONS

All women presenting with depression during pregnancy or breastfeeding should be managed on a case-by-case basis.<sup>4</sup> Any treatment offered should involve collaborative decision making with the woman and her partner, including a full discussion of the potential risks and benefits.<sup>1</sup> Take into consideration that the symptoms of depression might hamper decision-making.<sup>3</sup> Enhanced social support and psychological therapy should be considered before prescribing medicines, especially if the symptoms are mild or occur during the first trimester.<sup>2</sup>

Up to 80% of mothers experience the 'baby blues' 3-5 days after giving birth. This is transient and self-limiting, usually dissipating within 10 days.<sup>1</sup> Arrange a plan for follow-up to ensure persistent or worsening symptoms are effectively identified and managed.

**Note:** Worsening depression can lead to increased use of alcohol, illicit substances and smoking.

### CONSIDER ANTIDEPRESSANTS FOR MODERATE TO SEVERE DEPRESSION

If pregnant or breastfeeding women have moderate to severe depression, discuss the risks and benefits of antidepressants, and the risks of no antidepressant therapy.<sup>2</sup> Maternal anxiety and depression can have detrimental effects on foetal and infant development, and on mother-infant attachment.<sup>1</sup> Untreated antenatal depression is associated with low birth weight and poor self-care of the mother and neonate, which may escalate to self-harm and infant neglect.<sup>5</sup> Women already receiving antidepressants who are at high risk of relapse are best maintained on antidepressants during and after pregnancy.<sup>5</sup>

For moderate to severe depression, it is preferable to select antidepressants with the lowest risk profile.<sup>2</sup> (see Table 1) Definitions of pregnancy categories are listed in Table 2.

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**Table 1. Antidepressant Categories for Pregnancy and Breastfeeding<sup>6</sup>**

Medicine	Pregnancy <sup>6</sup>	Breastfeeding <sup>7</sup>
TCAs*	C	Compatible
Citalopram	C	Compatible
Escitalopram**	C	Compatible
Fluoxetine <sup>#</sup>	C	Compatible
Mirtazapine	C	Compatible
Paroxetine <sup>##</sup>	D	Compatible
Sertraline	B	Compatible
Venlafaxine	C	Compatible

**Compatible** - An acceptably low relative infant dose or no significant plasma concentrations or no adverse effects in breastfed infants<sup>7</sup>

\*Imipramine - some consider pregnancy D<sup>6</sup>

†Doxepin - avoid during breastfeeding<sup>7</sup>

\*\*Escitalopram - preferred to citalopram during breastfeeding<sup>6</sup>

<sup>#</sup>Fluoxetine - other SSRIs are usually preferred during breastfeeding<sup>7</sup>

<sup>##</sup>Paroxetine - some consider pregnancy C and the safest SSRI for breastfeeding<sup>6</sup>

### ALL ANTIDEPRESSANTS CARRY SOME RISK DURING PREGNANCY

Depressive symptoms during pregnancy are associated with foetal growth changes and pre-term birth. The risks associated with antidepressants may include congenital abnormalities, pre-term birth, neonatal withdrawal symptoms, persistent pulmonary hypertension of the newborn (PPHN) and neurobehavioural effects.<sup>7</sup>

Involve the family as appropriate and consider consulting with, or referring to a MMH team or other available psychiatric service for advice.<sup>2</sup>

For newly diagnosed depression in pregnant women, consider treatment options that are most compatible with breastfeeding. Sertraline or escitalopram are currently the most preferred SSRIs to use during pregnancy and breastfeeding. Venlafaxine and paroxetine have a relatively higher risk of neonatal withdrawal,<sup>6</sup> so should only be considered if the patient has not tolerated or not responded to safer options.

#### Birth defects

There is conflicting information about the risk of birth defects following antidepressant use during pregnancy, and most malformations have no known cause.<sup>3</sup> Individual studies mostly demonstrate no statistically significant

increase in the overall risk of any malformation with antidepressants. The studies that do show an increased risk of cardiac malformation suggest an absolute risk of 0.86-2%, compared to the background rate of 0.8%.<sup>8</sup>

Some studies suggest that SSRIs, particularly high dose paroxetine in the first trimester may be associated with congenital heart defects. Note that these include anomalies such as small ventricular septal defects which often close during childhood.<sup>9</sup>

#### Neonatal withdrawal

If antidepressants are used late in pregnancy, there may be a risk of neonatal withdrawal.<sup>2</sup> Symptoms include behavioural changes and irritability which are generally self-limiting and can also be linked to nicotine exposure and maternal depression itself.<sup>2,10</sup> Venlafaxine and paroxetine have a relatively higher risk of neonatal withdrawal, so should only be considered if the patient has not tolerated or not responded to safer options.<sup>6</sup>

Neonatal withdrawal symptoms should be discussed with the mother in advance; the postnatal midwife (and Plunket nurse) should also be informed.

#### Pregnancy-induced hypertension (PIH)

Antidepressants, in particular paroxetine, have been associated with pregnancy induced hypertension (PIH).<sup>11</sup> Other risk factors for hypertension should also be considered, including smoking, obesity, alcohol, lack of exercise, and untreated depression.

#### Persistent pulmonary hypertension

All SSRIs have been associated with persistent pulmonary hypertension of the newborn (PPHN) if taken late in pregnancy (after 20 weeks gestation). This potentially life-threatening neonatal syndrome is very rare. In the general population PPHN occurs in around 2 per 1000 live births. When expectant mothers are exposed to SSRIs during pregnancy this risk increases to 3 per 1000.<sup>12</sup>

**Note:** There is some evidence to suggest that all women with depression, regardless of SSRI use, are more likely to give birth to infants with PPHN.<sup>13</sup>

#### Post-partum haemorrhage

There is some evidence to suggest that SSRIs decrease platelet function and potentially increase the risk of bruising and bleeding.<sup>5</sup> Observational studies suggest that SSRIs may

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be associated with post-partum haemorrhage, although the absolute increased risk is likely to be low,<sup>14</sup> and the evidence is mixed.<sup>5</sup>

### Overdose risks

Although TCAs have been widely used by pregnant women over many years and are generally considered safe for the foetus, they are often considered second-line because of poor tolerability (eg sedation and constipation) and poor outcome in case of maternal overdose.<sup>2</sup>

### PROVIDE INFORMATION ABOUT COMPATIBILITY WITH BREASTFEEDING

If an antidepressant has been used successfully during pregnancy, for many women it is most appropriate to remain on the same medicine post-partum, rather than changing medicines at a time when they are at their most vulnerable. The amount that an infant is exposed to via breastmilk is less than in-utero, and continuing with the same medicine while breastfeeding may also minimise withdrawal symptoms in the infant.<sup>5</sup> It is advisable to closely observe new mothers for symptoms of depressive relapse post-partum, even if no alterations are made to their medicines.

The extent of exposure to the infant depends on many factors, including protein binding (to maternal plasma) and lipophilicity. Sertraline, escitalopram, paroxetine, nortriptyline and imipramine have low to undetectable infant serum levels when the mother is breastfeeding, with no reports of short term adverse events.<sup>15,6</sup> These options may be preferable if the mother is initiating an antidepressant post-partum.

**Note:** Escitalopram is generally preferred to citalopram because there are lower serum levels detected in breastfed infants.

Fluoxetine is considered the least preferred SSRI for breastfeeding, especially for newborn infants because it has the highest infant serum levels.<sup>6</sup> Paroxetine is considered the safest SSRI for breastfeeding, but may be less favourable during pregnancy.<sup>6</sup> The long term consequences of exposure to SSRIs via breastmilk to infant neurobehavioural development are unknown.<sup>16</sup> With all medicines, it is advised to prescribe the lowest effective dose possible to breastfeeding women.<sup>5,17</sup>

The most amount of experience with breastfeeding is with TCAs, and with the exception of doxepin, they are generally considered to be compatible.<sup>18</sup> TCAs have a very low transfer

into breastmilk compared with other antidepressants.<sup>8</sup> SSRIs are often preferred for depression, but TCAs are a useful option if women have not responded well. Discuss with a MMH team if there are any concerns. It is necessary to weigh potential risk against the known benefits of breastfeeding and the detrimental effects of psychiatric illness on the development of the infant and other children in the home.<sup>6</sup>

**Note:** Medicines are more likely to accumulate in premature infants because clearance is impaired. Breastfeeding immediately prior to a dose may help to minimise infant exposure, but considering newborn babies feed every 2-4 hours it is almost impossible to time the dose so the baby receives the lowest exposure.<sup>18</sup>

Table 2. Medicines in pregnancy classifications<sup>6</sup>

Category A	Medicines that have been taken by a large number of pregnant women without harmful effects on the foetus.
Category B	Medicines that have been taken by only a limited number of pregnant women without harmful effects on the foetus. Studies in animals may have shown an increase of foetal damage, the significance of which is uncertain in humans.
Category C	These medicines have caused, or may be suspected of causing harmful effects on the foetus or neonate without causing malformations. These should be given only if the potential benefit justifies the potential risk to the foetus. Either studies in animals have revealed adverse effects on the foetus and there are no controlled studies in women or studies in women and animals are not available.
Category D	There is positive evidence of human foetal risk, but the benefits from use in pregnant women may be acceptable despite the risk (eg if the medicine is needed in a life-threatening situation, or for a serious disease for which safer options cannot be used or are ineffective).
Category X	The risk of the medicine in pregnant women clearly outweighs any possible benefit. It is contraindicated in women who are or may become pregnant.

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