Guidelines for antidepressant use in the RESPOND trial

A Background

The Department of Health/HTA funded RESPOND trial will compare antidepressant drug therapy versus Health Visitor delivered non-directive counselling for the treatment of postnatal depression (affecting 8-15% of postpartum women) in primary care.

B Diagnosis

Women in the RESPOND trial attending their GP for prescription of an antidepressant will have a confirmed diagnosis of postnatal depression – an EPDS ≥12 and a score on the standardised psychiatric interview (CIS-R) denoting symptoms severe enough to consider treatment with an antidepressant.

C General issues in prescribing

1. Patients should be advised not to suddenly stop medication without discussing it with their GP.
2. Usual criteria for referral to secondary care psychiatric services should be applied (significant suicide risk or risk to baby; consideration in more severe depression, treatment non-response and complex cases).
3. Patients expressing suicidal ideation but not intent are still eligible for the study but require careful monitoring (see E below).
4. St John's Wort should not be taken at the same time as an SSRI.

D Choice of antidepressant

1. Patient preference and particular patient characteristics, as well as past experience of treatment, should inform the choice of drug, taking into account special issues relevant to postnatal depression such as breastfeeding, sedation, suicidal ideation etc.
2. We suggest an SSRI will usually be the drug of choice as they are as effective as TCAs and are less likely to be discontinued due to side effects and are less toxic in overdose.
3. See C1 above. We are not generally advising or prohibiting any particular SSRI, but the following should be taken into account:
   i) If the woman is breastfeeding we <u>do not</u> advise fluoxetine due to its long half-life and higher levels in breast milk, although harmful effects on breastfed babies have not been detected in case reports.
   ii) If the woman is breastfeeding, the preferred drugs are sertraline, paroxetine and citalopram with no harmful effects on the baby observed in case series.
   iii) For second-line drugs (see G below), there is less experience and information about safety in breastfeeding, so extra caution is required.

E Monitoring/duration of treatment

1. Careful monitoring of symptoms, side-effects, suicide risk and risk to baby should be routinely undertaken, especially early in treatment when they may worsen or appear for the first time.
2. For patients expressing suicidal ideation but not intent, consideration should be given to the appropriate length of each prescription and support in administration of the medication.
3. We believe it is best practice to have an early follow up after the initial prescription and then to see women for each repeat prescription. We would like women to be seen at 2 weeks, 4 weeks, 8 weeks, 12 weeks, 16 weeks, 20 weeks, 24 weeks and 28 weeks.

4. It should be explained to the women that once remission has been achieved it is recommended that the medication will need to be continued at the same dose for at least 4 to 6 months to reduce the likelihood of relapse.
5. If the woman has a history of recurrent depression she may need to continue treatment for a longer period.
6. It should be explained that if a satisfactory response is not occurring by 6 to 8 weeks, it is possible that either dose will be increased or a medication from a different class will be tried (see below). In practice if there has been NO response by 4 weeks a dose increase or change of medication at this point is reasonable as subsequent response is unlikely.
7. It is important to monitor for relapse and discontinuation symptoms when reducing or stopping medication.
8. The dose would normally be reduced over 4 weeks unless fluoxetine is used as it has a long half-life and can be stopped abruptly.
9. If discontinuation symptoms are mild, practitioners should reassure the patient and arrange for monitoring. If severe symptoms are experienced, consider re-starting the original drug (or for SSRIs start fluoxetine) and reduce gradually while monitoring symptoms.
10. Patients should be advised to seek help from their GP for severe discontinuation symptoms.

F Explanation to be offered with first prescription

1. The tablets are to help treat your postnatal depression
2. They do not work immediately – it will be 10-14 days before you begin to notice any improvement.
3. I would like to see you again in 2 weeks.
4. You might notice a few side effects which tend to be worse early on, e.g. dry mouth, feeling sick. These are likely to be transient. You will find full details in the Patient Information Leaflet.
5. Occasionally people can get much worse and even begin to feel like harming themselves or others. In this situation contact me or another GP or your health visitor straight away.
6. If the side effects are difficult to bear, please make an appointment to see me or another GP.

G Drugs to consider

1st line drug

Drug	Starting dose	Review for side effects	1st review efficacy	If no improvement at 4 weeks or only slightly better at 6/8 wks
Fluoxetine (not if breastfeeding)	20mg	2 wks	4 wks	Increase to 40mg or change drug
Sertraline	50mg	2 wks	4 wks	Increase to 100mg or change drug
Paroxetine	20mg	2 wks	4 wks	Change drug*
Citalopram	20mg	2 wks	4 wks	Increase to 40mg or change drug
Escitalopram**	10mg	2 wks	4 wks	Increase to 20mg or change drug

2nd line drug

Drug	Starting dose	Review for side effects	1st review efficacy	If not/only slightly better at 6/8 wks
Lofepramine	70mg bd	2 wks	4 wks	Increase to 210mg/day
Reboxetine**	4mg	2 wks	4 wks	Increase to 8mg

* recent MCA guidance not to increase paroxetine dose above 20mg for depression
** lack of data re breastfeeding