

*From the Chief Medical Officer*  
Dr Henrietta Campbell CB



Department of  
**Health, Social Services  
and Public Safety**

An Roinn

**Sláinte, Seirbhísí Sóisialta  
agus Sábháilteachta Poiblí**

[www.dhsspsni.gov.uk](http://www.dhsspsni.gov.uk)

**HSS(MD)36-2005**

**URGENT COMMUNICATION**

To:

All GPs including Locums and Out-of-Hours Centres  
GP Advisers, Health & Social Services Boards  
Prescribing Advisers, Health & Social Services Boards  
Chief Executives, Health & Social Services Boards/Trusts  
Directors of Public Health, Health & Social Services Boards  
(for onward dissemination to GPs including Locums and Out-  
of Hours Centres, and Doctors working in Family Planning  
Clinics where appropriate)

Medical Directors, Health & Social Services Trusts (*for  
onward dissemination to Consultant Psychiatrists, Consultant  
Obstetricians and Gynaecologists, Consultant Paediatricians,  
and Doctors working in Family Planning Clinics*)

Directors of Nursing, Health & Social Services Boards  
Directors of Nursing, Health & Social Services Trusts (*for  
onward dissemination to nurses working in mental health  
services, midwives and paediatrics nurses*)

Directors of Pharmaceutical Services, HSS Boards

Directors of Pharmaceutical Services, HSS Trusts

Directors of Pharmaceutical Services, CSA

All Community Pharmacists

Castle Buildings

Stormont Estate

Belfast BT4 3SQ

Tel: 028 9052 0563

Fax: 028 9052 0574

Email: [Henrietta.Campbell@dhsspsni.gov.uk](mailto:Henrietta.Campbell@dhsspsni.gov.uk)

Your Ref:

Our Ref: HSS(MD)36-2005

Date: 7<sup>th</sup> December 2005

Dear Colleague

**PAROXETINE (SEROXAT) – SAFETY IN PREGNANCY**

The Commission on Human Medicines (CHM), chaired by Professor Gordon Duff, has highlighted new evidence relating to a possible increased risk of congenital malformations following maternal use of Paroxetine in the first trimester.

Attached to this letter is the advice from Professor Duff, including a summary of the findings from the recent relevant studies. The CHM and the Medicine Healthcare products Regulatory Agency (MHRA) are continuing to monitor the safety of Paroxetine and all suspected adverse reactions should be reported to them via the Yellow Card Reporting Scheme.

Yours sincerely

**Dr Henrietta Campbell**  
Chief Medical Officer

**Dr Norman Morrow**  
Chief Pharmaceutical Officer

**Mr Martin Bradley**  
Chief Nursing Officer



MESSAGE FROM PROFESSOR G DUFF, CHAIRMAN, COMMISSION ON HUMAN MEDICINES.

6<sup>th</sup> December 2005

CEM/CMO/2005/11

Dear Colleague,

**Paroxetine (Seroxat) – Safety in pregnancy**

I am writing to you about the safety in pregnancy of paroxetine, an SSRI antidepressant used in the treatment of major depressive disorders, anxiety disorders and obsessive-compulsive disorders. This is in light of recent discussions in the scientific and lay media about whether the use of paroxetine in pregnancy, particularly during the first trimester, may be associated with an increased risk of congenital malformations in newborns – [a summary of the findings from the recent studies is attached](#).

New data from Denmark, Sweden and the US represent a potential signal of an increased risk of congenital malformations following maternal use of paroxetine in the first trimester. However, other epidemiological studies have not supported such an increased risk. All available data are being actively investigated by the Commission on Human Medicines (CHM) and the Medicines and Healthcare products Regulatory Agency (MHRA) and, following our further investigations and discussions within Europe, if necessary new guidance will be issued.

The new studies suggest that in women taking paroxetine in the first trimester the risk of birth defects in the newborn may increase from 3% to around 4% for all congenital malformations and from 1% to around 2% for congenital heart malformations. Therefore, if real, any increased risk is small and needs to be considered in the context of the potentially greater risk to the foetus that may result from the mother's depression remaining untreated.

It is also important to be aware of the risk of serotonergic effects in neonates if maternal use of paroxetine continues into the later stages of pregnancy, particularly the third trimester. Withdrawal signs in the neonate include respiratory distress, cyanosis, apnoea, hyperreflexia, tremor, jitteriness, irritability, lethargy, constant crying and sleeping problems. In the majority of cases the complications begin immediately or soon (<24 hours) after delivery.

**Advice to prescribers:**

- Paroxetine should only be used in pregnancy when strictly indicated and only if the benefits for the mother are thought to outweigh the potential risk to the foetus.
- Until this issue is further investigated, consideration should be given as to whether paroxetine is the most suitable SSRI to be used in pregnant women or those planning to become pregnant
- If a decision is made to stop paroxetine treatment this should be done gradually over a period of several weeks. Abrupt cessation can cause withdrawal symptoms (most commonly dizziness, numbness and tingling, gastrointestinal disturbances, headache, sweating, anxiety and sleep disturbances), which can be severe in some patients.

**Advice to patients:**

- Women taking paroxetine who want to become pregnant are advised to discuss the balance of risks and benefits of continued treatment with their doctor.
- Pregnant women who are currently taking paroxetine should not stop their treatment but should discuss their treatment with their doctor or midwife at their next routine appointment.

Please report any suspected adverse reactions to paroxetine via the Yellow Card Reporting Scheme to the CHM/MHRA

For further information please call the Medicines and Healthcare products Regulatory Agency on 020 7084 2000 or visit the website ([www.mhra.gov.uk](http://www.mhra.gov.uk))

#### Appendix – Summary of new epidemiological study data which examine the use of paroxetine during pregnancy

Two recent studies have raised concerns about a possible increase in the risk of congenital malformations associated with the use of paroxetine in pregnancy. A brief overview of the findings of these studies and preliminary information from a new study examining data from the Swedish Medical Birth Registry is provided below.

The first, a Danish population based cohort study<sup>1</sup>, found an association between maternal use of SSRIs during the first trimester and an increased risk of both congenital malformations overall (odds ratio 1.4 (95% CI 1.1-1.9)) and congenital cardiac malformations (odds ratio 1.6 (95% CI 1.0-2.6)). The second, a retrospective study conducted by GlaxoSmithKline (GSK)<sup>2</sup>, suggests that compared with other antidepressants paroxetine use during the first trimester is associated with an increased risk of both congenital malformations overall (odds ratio 2.2 (95% CI 1.34-3.63)) and congenital cardiac malformations (odds ratio 2.08 (95% CI 1.0-4.23)). The type of abnormalities seen in this study reflected those seen in the general population, the most common of which were cardiovascular. Of those cardiovascular abnormalities, the most common were ventricular septal defects.

Most recently preliminary information about the results of a new study examining data from a Swedish Medical Birth Registry have been made available<sup>3</sup>. This study suggests that babies born to mothers who have taken paroxetine in the first trimester of pregnancy are at an approximately 2 fold higher risk of congenital cardiac malformations compared with the equivalent frequency in the population (odds ratio 2.22 (95% CI 1.39-3.55)). This study also suggests that the other SSRIs examined (citalopram, fluoxetine and sertraline) are not associated with an increased risk of congenital malformations.

The results of these studies suggest that in women taking paroxetine in the first trimester the risk of birth defects in the newborn may increase from 3% to around 4% for all congenital malformations and from 1% to around 2% for congenital cardiac malformations.

1. Wogelius P, Nørgaard M, Munk EM, Mortensen PB, Lipworth L, Sørensen HT. Maternal use of selective serotonin reuptake inhibitors and risk of adverse pregnancy outcome (Abstract) *Pharmacoepidem Drug Safety* 2005; 14: S72-S73. This abstract is available on the MHRA website ([www.mhra.gov.uk](http://www.mhra.gov.uk)).
2. GlaxoSmithKline Clinical Trial Register. [Epidemiology Study: Preliminary Report on Bupropion in Pregnancy and the Occurrence of Cardiovascular and Major Congenital Malformation](http://ctr.gsk.co.uk/Summary/paroxetine/studylist.asp) (<http://ctr.gsk.co.uk/Summary/paroxetine/studylist.asp>).
3. [www.janusinfo.org](http://www.janusinfo.org) Källén B, Otterblad Olausson P. Antidepressant drugs during pregnancy and infant congenital heart defect. (Letter). Submitted for publication. An English translation of this information is available on the MHRA website ([www.mhra.gov.uk](http://www.mhra.gov.uk))