

## **PUBLIC HEALTH LINK**

### **To: Directors of Public Health of PCTs to forward to:**

- All GENERAL PRACTITIONERS - please ensure this message is seen by all practice nurses and non-principals working in your practice and retain a copy in your 'locum information pack'.
- Deputising services
- Community Paediatricians
- Project manager/Nurse lead in Walk in Centres
- Lead nurses in PCTs to forward to school nurses and young people's health services
- Leads at nurse-led PMS Pilots
- PCT Pharmaceutical Advisers to forward to community pharmacists
- PCT Prescribing Advisers

### **To: Medical Directors of NHS Trusts to forward to:**

- Consultant psychiatrists
- Consultant paediatricians
- Nurse Executive Directors of NHS Trusts and Mental Health Trusts and NHS Trusts with Child and Adolescent Mental Health Services
- Trust Chief Pharmacists to forward to Medicines Information Pharmacists

### **Cc:**

- Regional Directors of Public Health
- Directors of Public Health of Strategic Health Authorities to forward to: SHA pharmaceutical advisers and SHA lead nurses
- UK CMOs
- Chairmen of Professional Executive Committee

**From:** Professor Gordon Duff, Chairman – Committee on Safety of Medicines

**Date:** 10th December 2003

**Reference:** CEM/CMO/2003/20, Gateway ref: 2369

**Category:** \*\*URGENT MESSAGE\*\*

**\*\*PLEASE ACTIVATE THE CASCADE \*\***

Dear Colleague

### **SELECTIVE SEROTONIN REUPTAKE INHIBITORS - USE IN CHILDREN AND ADOLESCENTS WITH MAJOR DEPRESSIVE DISORDER**

I wrote to you in June and September to inform you that paroxetine and the related antidepressant, venlafaxine should not be used to treat depressive illness in children and adolescents under the age of 18 years. Since then the Expert Working Group of the Committee on Safety of Medicines (CSM) has completed its review of the safety and efficacy of the SSRI class in the treatment of paediatric major depressive disorder.

On the basis of this review of the available clinical trial data, CSM has advised that the balance of risks and benefits for the treatment of major depressive disorder (MDD) in under 18s is judged to be unfavourable for sertraline, citalopram and escitalopram and unassessable for fluvoxamine. Only fluoxetine (Prozac) has been shown in clinical trials to have a favourable balance of risks and benefits for the treatment of MDD in the under 18s.

In adults, on the basis of evidence to date, the benefits of treatment are considered to outweigh the risks for all SSRIs.

Like paroxetine and venlafaxine, none of these drugs has ever been licensed for use in depressive illness in under 18s but we know they are used in this age group outside their licensed indications. Sertraline and fluvoxamine are licensed for treatment of obsessive compulsive disorder (OCD). This new advice does not relate to use in OCD.

### **Summary of advice**

#### **In patients under 18 years old:**

- \* Paroxetine, venlafaxine, sertraline, citalopram and escitalopram are now contraindicated in paediatric MDD in the under 18s.
- \* There are no data on the safety and efficacy of fluvoxamine in paediatric MDD. Safety and efficacy in adults cannot be extrapolated to those under 18 and therefore this product should not be used in this age group.
- \* The balance of risks and benefits of fluoxetine in the treatment of MDD in under 18s appears to be favourable.

#### **General prescribing advice for paroxetine, venlafaxine, sertraline, citalopram escitalopram and fluvoxamine:**

1. These products should not be prescribed as new therapy for patients under 18 years of age with depressive illness.
2. If your patient is being successfully treated with any of these products, then the normal completion of the planned treatment course should be considered as an option in the management of the illness.
3. If your patient is not doing well on any of these products, change of treatment should be considered.
4. A decision to prescribe any of these for paediatric MDD, for example if a patient is intolerant to fluoxetine, should only be made with specialist advice and after careful consideration of all available information.

**Fluoxetine** does not have a marketing authorisation for MDD in under 18 year olds. However the CSM has considered the clinical trial data and advised that the balance of risks and benefits is favourable. Again, a decision to prescribe fluoxetine for paediatric MDD in a patient under 18 should be made with specialist advice.

### **Stopping SSRIs**

No SSRI should be stopped abruptly. Gradual decrease in dose may be required, particularly for venlafaxine and paroxetine. Information on what to expect when stopping individual products is already present in product information.

### **Further information**

1. Attached is an overview of the regulatory status of these products and the advice of CSM. We fully appreciate the need for prescribers to have access to the data supporting the regulatory decisions and to this end we have published on the Medicines and Healthcare products Regulatory Agency (MHRA) website two further levels of detailed information. One contains a summary of the safety and efficacy data for each product in paediatric MDD and the other describes the individual trials reviewed by the CSM. This information is provided to enable

prescribers to make informed decisions on the management of their paediatric patients who may already be receiving treatment with SSRIs or who may need pharmacotherapy for MDD.

2. A leaflet for patients about SSRIs and depression is also attached.

3. Further information for prescribers and patients including questions and answers and the SSRI fact sheet issued together with Current Problems in Pharmacovigilance in September 2003 is available on the website of the MHRA ( <http://www.mhra.gov.uk> ).

Please report any suspected adverse reactions to SSRIs via the Yellow Card reporting scheme to the CSM/ MHRA.

Should you require any additional information, please telephone 020 7084 2000 at the MHRA.

**Professor Gordon Duff**

Chairman – Committee on Safety of Medicines

**Level 1 – Overview of regulatory status and CSM advice relating to major depressive disorder in children and adolescents**

	<b>Fluoxetine</b>	<b>Sertraline</b>	<b>Citalopram</b>	<b>Escitalopram</b>	<b>Fluvoxamine</b>	<b>Paroxetine</b>	<b>Venlafaxine</b>
<b>Drug class</b>	SSRI	SSRI	SSRI	SSRI (active constituent of citalopram)	SSRI	SSRI	Serotonin and noradrenaline reuptake inhibitor (SNRI)
<b>Licensed indications children and adolescents</b>	None	Obsessive compulsive disorder	None	None	Obsessive compulsive disorder	None	None
<b>Efficacy in major depressive disorder (MDD) in children and adolescents</b>	Demonstrated in controlled clinical trials	Not demonstrated in controlled clinical trials	Not consistently demonstrated in controlled clinical trials	No data from clinical trials	No data from clinical trials	Not demonstrated in controlled clinical trials	Not demonstrated in controlled clinical trials
<b>Safety profile in MDD trials in children and adolescents</b>	Mania and hypomania more frequently reported than in adults, perhaps as a result of differing inclusion criteria in clinical trials. No increased rate of self-harm and suicidal thoughts compared with placebo.	Rate of events including agitation, anorexia, insomnia and suicidal thoughts and self harm increased compared with placebo.	Increased rate of self-harm compared with placebo in 1 of 2 trials.	No data from clinical trials	No data from clinical trials	Increased rate of self-harm and suicidal thoughts compared with placebo.	Increased rate of self-harm and suicidal thoughts compared with placebo.
<b>CSM advice in relation to MDD in children and adolescents</b>	<b>Risk/benefit balance is favourable.</b>	<b>Risk/benefit balance is unfavourable.</b>	<b>Risk/benefit balance is unfavourable.</b>	<b>Risk/benefit balance is presumed unfavourable. (Extrapolation from citalopram.)</b>	<b>Risk/benefit balance is not assessable – safety and efficacy in adults cannot be extrapolated to under 18 year olds.</b>	<b>Risk/benefit balance is unfavourable.</b>	<b>Risk/benefit balance is unfavourable.</b>

## **SELECTIVE SEROTONIN REUPTAKE INHIBITORS**

### **USE IN CHILDREN AND TEENAGERS WITH DEPRESSION**

Doctors have been told that some medicines used to treat depression in adults (SSRIs) are not suitable for use in children and teenagers under the age of 18 years to treat depression. This note is to explain what it's all about.

#### **What are SSRIs?**

SSRIs are medicines that are mostly used to treat depression. Some of them have other uses as well, for example to treat obsessive compulsive disorder. This note is just about the treatment of depression. It is nothing to do with obsessive compulsive disorder.

The following medicines are SSRIs:

- Sertraline (commonest brand Lustral)
- Citalopram (commonest brand Cipramil)
- Escitalopram (commonest brand CipraleX)
- Paroxetine (commonest brand Seroxat)
- Fluoxetine (commonest brand Prozac)
- Fluvoxamine (commonest brand Faverin)

Also there is a similar medicine called

- Venlafaxine (commonest brand Efexor ER)

#### **So what's new?**

For any medicine, a balance has to be made between any harmful effects of taking a medicine and whether it will make you better. This is known as the balance of the improvements against the side effects (or in other words, the good against the harm).

A group of experts, called the Committee on Safety of Medicines, advises the Government on the safe and effective use of medicines. It has looked at the results of research on these medicines in children and teenagers with depression. For sertraline, citalopram and escitalopram, the experts have decided that these medicines may do more harm than good in the treatment of depression in under 18s. (Previously the experts have also decided that paroxetine and venlafaxine may do more harm than good as well.) For fluvoxamine the experts could not make a decision as there is no proper research in children and teenagers with depression. Only one medicine, fluoxetine, seems to do more good than harm for the treatment of depression in the under 18s.

### **What does this mean?**

Doctors have been told that, for children and teenagers with depression,

\* Seroxat (paroxetine), Efexor (venlafaxine), Lustral (sertraline), Cipramil (citalopram) and Cipralex (escitalopram)

- should not be used in children and teenagers.

\* Faverin (fluvoxamine)

- should not be used because there has been no proper research in this age group.

\* Prozac (fluoxetine)

- Can be used in children and teenagers.

### **What does this mean for me?**

\* If you are being treated with any of these medicines at the moment and you are doing well on the medicine then you can finish the tablets you've got, if you and your doctor think that this is a good idea.

\* If you are being given any of these medicines at the moment and you are not doing well on the medicine, then you should talk to your doctor about a change of treatment.

\* If you have recently become depressed and you need a medicine your doctor should avoid giving you Seroxat, Efexor, Lustral, Cipralam, Cipralex or Faverin, if he/she possibly can.

\* If your doctor thinks that he needs to give you one of the medicines listed above, say if you don't feel well taking fluoxetine, he or she will only do this if they are a specialist or if a specialist has said it's OK.

### **Why is Prozac OK?**

The group of experts has looked at the research with Prozac and decided that on balance it does more good than harm in most of the under 18s.

If you are depressed and under 18 your doctor will ask a specialist before he or she gives you Prozac and will only give it if the specialist has said that it's OK.

### **Stopping SSRI medicines**

You should not suddenly stop taking these medicines. The dose needs to be lowered slowly especially if you are taking the ones called Efexor or Seroxat.

### **Further information**

Further information on your medicine can be found in the patient information leaflet which accompanies the medicine.

Further explanations of the new advice can be found on the website of the MHRA at <http://www.mhra.gov.uk/>