European Medicines Agency
*Press office*

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# Press release

# CHMP meeting on Paroxetine and other SSRIs

The European Medicines Agency scientific committee, the Committee for Medicinal Products for Human Use (CHMP), held an extraordinary meeting in London on 8 December 2004 and took two actions relating to paroxetine and to other SSRIs.

Firstly, the CHMP, at the request of the European Commission, re-examined its 22 April 2004 opinion on **paroxetine** in the light of additional information arising from newly available observational studies.

The CHMP, following the assessment of this additional information, confirmed its initial conclusion that the benefit/risk balance of paroxetine remains positive in the treatment of adults. The Committee also reaffirmed its previous conclusion that changes to the product information should be introduced, especially with regard to warnings of suicide-related behaviour in children and adolescents (see annex I for further details).

Secondly, following a request from the European Commission, the CHMP has also been reviewing the data available to national competent authorities for other **SSRI[1] and SNRI[2] products** particularly as regards their use in the paediatric population. The CHMP considers that on the basis of the available evidence there is a signal of an increase in suicidal behaviour, including suicide attempts and suicidal ideation and/or related behaviour like self-harm, hostility and mood lability in children and adolescents treated with SSRIs and SNRIs. However, there were no deaths due to suicide in children or adolescents reported in the clinical trials (see annex II for further details).

The Committee will now inform the European Commission that there are public health concerns in relation to the safe use of these medicinal products in children and adolescents with depression, anxiety and related conditions, irrespective of the therapeutic indication. The CHMP will recommend to the European Commission that these concerns are further investigated at Community level.

Whilst further investigations at Community level are being conducted, **the Committee already wishes to inform prescribers, patients and parents as follows:**

- SSRIs/SNRIs are not authorised Europe-wide for the treatment of depression and anxiety disorders in children or adolescents.
- These compounds should generally not be used in this age group because clinical trials have shown an increased risk of suicidal behaviour (such as suicide attempts and suicidal thoughts).
- Nevertheless, a decision is sometimes taken, based on clinical need, to treat such patients. In these cases, the patient should be carefully monitored for the appearance of suicidal behaviour, self-harm and hostility. This is particularly important at the beginning of treatment.

[1] SSRI stands for 'Serotonin-Selective Reuptake Inhibitors'
[2] SNRI stands for 'Serotonin-Norepinephrine Reuptake Inhibitors'

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- The treatment should not be stopped by the patient or the parents without first seeking medical advice from the treating doctor because there is a risk of experiencing withdrawal symptoms, such as dizziness, sleep problems and anxiety if discontinuation is abrupt.
- When treatment is being stopped, it is recommended to gradually reduce the dose over several weeks or months.
- Patients or parents who have any concerns about the medication are advised to consult the treating doctor at the next available opportunity to discuss treatment.

The CHMP also discussed the rapid alert issued by the UK national competent authority relating to venlafaxine and concerns over cardiotoxicity and toxicity in overdose. The Committee recommends that this question as well as other safety issues concerning the use in adults of other SSRIs, including fluvoxamine, should be brought to the attention of its Pharmacovigilance Working Party for assessment.

--ENDS--

NOTES:

1. The EMEA press release from 22 April 2004 can be found [here], together with the question and answer document relating to Paroxetine [here].
2. This press release, together with other information on the work of the EMEA, can be found on the EMEA website at http://www.emea.eu.int

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**ANNEX I – CHMP recommendations on Paroxetine**

The CHMP reaffirmed its conclusion from April 2004 that the benefit/risk balance remains positive for paroxetine-containing medicines used in the treatment of adults and reconfirmed the previous recommended changes to the product information for paroxetine on an EU-wide basis. These changes include:

- A warning to reflect that paroxetine should not be used in children and adolescents. In the EU paroxetine is not authorised for use in this population. Data from clinical trials raised concerns regarding suicidal behaviour and hostility. In addition, data from clinical trials have not adequately demonstrated efficacy in these age groups.
- A warning to prescribers recommending close monitoring of patients at high risk of suicidal behaviour. These include patients with a known history of suicidal behaviour or suicidal thoughts prior to starting treatment and possibly also young adults.
- Prescribers and patients should be warned regarding the occurrence of withdrawal reactions upon stopping treatment. Generally these are mild to moderate and self-limiting. However, in some patients they may be severe and/or prolonged.

**ANNEX II – Use of SSRIs in children and adolescents**

Following the Article 31 referral on Paroxetine, the European Commission requested the EMEA Scientific Committee, the Committee for Medicinal Products for Human Use (CHMP) to advise whether there was any public health concern in relation to the safe use of SSRIs in children and adolescents.

The CHMP evaluation focussed on the following products: Atomoxetine, Citalopram, Duloxetine, Escitalopram, Fluoxetine, Fluvoxamine, Mianserine, Milnacipran, Mirtazapine, Paroxetine, Reboxetine, Sertraline and Venlafaxine.

The CHMP reviewed the data available to national competent authorities for these compounds in children and adolescents. This included:

- 28 short-term placebo controlled randomised clinical trials (RCTs) that were submitted to the EU competent authorities (15 in Major Depressive Disorder (MDD), 7 in anxiety disorders and 6 in Attention Deficit/Hyperactivity Disorder (ADHD)). In total more than 5000 patients were evaluated.
- 8 additional RCTs that were published in the medical literature.
- Several observational studies (based on the UK General Practice Research Database (GPRD) and ecological studies).
- Active control trials and uncontrolled extension data were not taken into account as they do not provide a comparison with placebo.

The CHMP also set up an ad-hoc expert group which included child psychiatrists in order to advise the Committee on this matter.

The studies that were examined indicate the following:

- There were no reports of deaths due to suicide in any of the clinical trials in children and adolescents.
- MDD studies showed consistent increase in the risk of suicidal related behaviour (such as suicide attempts and suicidal thoughts) in all antidepressants.
- The signal in anxiety disorders studies was less strong but still present.
- ADHD studies did not show increased suicidal behaviour.
- For each compound reviewed where sufficient data were available there was a signal of suicidal related behaviour, self-harm or hostility. These concerns cannot be excluded for those compounds where data on children and adolescents were limited.
- From the GPRD studies there were some apparent differences between products. However, the evidence from the randomised clinical trials did not show such a difference.

Therefore the CHMP considers that there is a need to warn physicians and parents that there is a signal of an increase in suicidal behaviour, including suicide attempts and suicidal ideation and/or related behaviour like self-harm, hostility and mood lability in children and adolescents treated with SSRIs and SNRIs. There were no reports of deaths due to suicide in the clinical trials reviewed in children and adolescents.