The European Agency for the Evaluation of Medicinal Products
Post-authorisation evaluation of Medicines for Human Use

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Questions and answers on paroxetine

Revised version following the CHMP meeting of 8 December 2004

1. What is paroxetine?

Paroxetine is a selective Serotonin Re-uptake Inhibitor (an SSRI) medicine. It affects the transmission of chemical messages in the brain and nervous system. And is used to treat conditions such as depression, obsessive compulsive disorder, panic disorder with or without agoraphobia, social anxiety disorder (social phobia), generalised anxiety disorder and post-traumatic stress disorder.

2. Why did the EMEA/CHMP review paroxetine?

The EMEA and CHMP have conducted a review of the benefits and risks of paroxetine containing medicines through a formal referral procedure. The referral was made by UK due to safety concerns in relation to the use of these medicines.

3. What were these safety concerns?

Due to emerging data from clinical trials there were concerns about an increased risk of suicidal behaviour and hostility in children and adolescents treated with paroxetine. Concerns were also raised about the risk of withdrawal reactions upon stopping paroxetine treatment in adults and children and whether or not there was the possibility of an increased risk of suicidal behaviour in the adult population.

4. What evidence has CHMP reviewed?

In line with their legal obligations, companies (Marketing Authorisation Holders) provided CHMP with all scientific data relevant to the safety and efficacy of paroxetine treatment including data from clinical trials, spontaneous adverse reaction reports, epidemiological studies and published literature.
General background data on the medical conditions involved and treatment options were also reviewed.The committee consulted with relevant experts including child psychiatrists.

This enabled CHMP to evaluate the benefits of treatment with paroxetine and to balance these against the risks of side effects.

5. Is the paroxetine review now finalised?

The EMEA's scientific committee, the CHMP, gave a formal Opinion and recommendations on 22 April 2004. New data arising from observational studies have since become available. Therefore, at the request of the European Commission, the CHMP re-examined its previous opinion of 22 April 2004 in the light of the additional information. At its meeting of 8 December 2004, the CHMP confirmed its initial conclusions and recommendations.
In line with EU legislation the next step will be for the European Commission to give its Decision.

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6. What are the recommendations of the CHMP?

The CHMP concluded that the benefit-risk remains positive for paroxetine containing medicines in the treatment of adults but recommends changes to the product information for paroxetine on a EU-wide basis. These 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 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.

7. Is EMEA/CHMP banning the use of paroxetine in children and adolescents?

Paroxetine is not authorised to be used in these age groups. Should a child or adolescent however be receiving paroxetine, the treating doctor is advised to exercise caution. Child psychiatrists can also consider the use of alternative treatments such as cognitive behavioural therapy for childhood depression.

8. What are the withdrawal reactions occurring with paroxetine?

These symptoms may occur upon stopping treatment with paroxetine. Typically they can include dizziness, altered sensation (eg. numbness, “pins and needles”, “electric shock sensations”), sleep problems including intense dreams, anxiety and headache. Less common symptoms include agitation, nausea, tremor (shaking of parts of the body, eg. hands), confusion, sweating, diarrhoea, palpitations, emotional instability, irritability or problems with vision (eyesight).

In some patients withdrawal symptoms may be severe in nature or prolonged. Usually, however they are mild to moderate and self-limiting and should resolve within 2 weeks of stopping paroxetine. Patients treated with high doses, those treated for longer duration and patients whose treatment is abruptly stopped may be at an increased risk of withdrawal symptoms.

9. What can be done for withdrawal symptoms?

When a doctor decides to stop paroxetine the best approach is to gradually reduce the dose over several weeks or months. The treating physician or psychiatrist is best placed to determine how paroxetine is tapered and withdrawn according to the needs of the individual patient. Paroxetine must not be stopped suddenly, except on medical advice.

10. My child is already taking paroxetine. What should I do?

If you are concerned or if your child has experienced suicidal thoughts, it is vital that you discuss this with your doctor who is familiar with your child’s medical condition and the options for treatment. You should ensure that your child does not suddenly stop taking paroxetine as withdrawal symptoms can occur and may be severe in some patients. You should contact your doctor, who is best placed to advise on further management of your child.

11. What are the concerns regarding paroxetine and suicidal thoughts or behaviour?

Part of the /EMEA/CHMP review of paroxetine concerned the risk of suicidal thoughts and behaviour. This is a complex issue as some conditions, that paroxetine is used to treat (e.g. depression) are known to be associated with a risk of suicide. In addition, as with other antidepressants, paroxetine may only start to work effectively after some weeks of starting treatment. This means that pre-disposed patients could be particularly vulnerable to suicidal thoughts and behaviour in the early part of treatment.

Based on its review of available scientific data CHMP recommends close monitoring of patients at high risk. These include patients with a known history of suicidal behaviour or suicidal thoughts prior to starting treatment and possibly young adults.

Should suicidal thoughts or behaviour arise during paroxetine treatment, medical advice should be sought immediately.

12. Is the EMEA/CHMP also reviewing other SSRIs regarding safety?

Following a request from the European Commission, the CHMP has also been reviewing the data available to national competent authorities for other SSRI and SNRI medicinal products particularly as regards their use in the paediatric population.