European Medicines Agency

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QUESTIONS AND ANSWERS ON THE RECOMMENDATION TO WITHDRAW THE MARKETING AUTHORISATION OF VERALIPRIDE

The European Medicines Agency (EMEA) has completed a review of the safety and effectiveness of veralipride. The Agency's Committee for Medicinal Products for Human Use (CHMP) has concluded that veralipride's benefits do not outweigh its risks, and that all marketing authorisations for medicines containing veralipride should be withdrawn throughout Europe. The review was carried out under an 'Article 31' referral[1].

What is veralipride?
Veralipride is a medicine used to treat hot flushes associated with the menopause in women. It was first made available in 1979 and is still authorised in Belgium, France, Italy, Luxembourg and Portugal under the trade names Agreal and Agradil. It is only available with a prescription.

Veralipride is a neuroleptic. It works by blocking the activity of a neurotransmitter called dopamine. Neurotransmitters are chemicals in the nervous system that allow nerve cells to communicate with each other. The reasons why women have hot flushes is unclear, but since dopamine seems to be involved, veralipride can reduce these symptoms.

Why was veralipride reviewed?
Until June 2005, veralipride was also marketed in Spain. Following reports of serious side effects affecting the nervous system, the Spanish medicines regulatory authority reviewed the safety and effectiveness of the medicine and concluded that its benefits did not outweigh its risks. The Spanish authority therefore withdrew veralipride's marketing authorisation on 27 June 2005, meaning that the medicine could no longer be sold on the Spanish market. This was followed by a number of regulatory actions in other countries where veralipride is authorised, including making changes to veralipride's product information (the instructions on how a medicine should be used). These changes aimed to reduce the risk of patients developing side effects.

Consequently, the European Commission asked the CHMP to carry out a full assessment of the benefit-risk balance of veralipride and to issue an opinion on whether the marketing authorisations for products containing veralipride should be maintained, varied, suspended or withdrawn across the European Union.

Which data has the CHMP reviewed?
In this review, the CHMP has assessed all of the available information on the safety and effectiveness of veralipride. This included 11 studies involving a total of around 600 women, in which veralipride was compared with placebo (a dummy treatment), and two studies in a total of around 100 women where it was compared with conjugated oestrogens (a type of hormone replacement therapy [HRT], the standard treatment for the symptoms of the menopause). The CHMP also looked at other small studies and reports of side effects from women taking veralipride.

[1] Article 31 of Directive 2001/83/EC as amended, referral under Community interest.

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What are the conclusions of the CHMP?

Based on the information available, the CHMP has concluded that:

- Veralipride shows limited effectiveness in reducing the frequency and intensity of hot flushes.
- The use of veralipride can be associated with side effects, including depression, anxiety, sleep disorders, tremor (shaking) and tardive dyskinesia (an involuntary movement disorder which may be long-lasting or irreversible). Some of these side effects can occur not only during treatment, but also after it is stopped. It is also impossible to predict which women may be at risk.

The CHMP considered restricting the use of veralipride to a maximum of three months. However, it concluded that the risk of side effects would not be reduced sufficiently by this measure. In addition, hot flushes usually persist for up to two years.

Therefore, the CHMP concluded that the benefits of veralipride do not outweigh its risks. It recommended that the marketing authorisation of veralipride be withdrawn and that all veralipride-containing medicines be recalled from the European Union markets. It also recommended that the companies that market these medicines inform all healthcare professionals about the withdrawal directly.

What are the recommendations for patients and prescribers?

- Patients who are taking veralipride for the treatment of hot flushes should consult their doctors to discuss what other treatment they can use.
- Prescribers should not issue any new prescriptions for veralipride and should switch patients currently taking the medicine to an alternative treatment if necessary. Since abrupt discontinuation of veralipride may lead to symptoms such as anxiety, insomnia (difficulty sleeping) and depression, prescribers should consider gradually reducing the dose of veralipride over one to two weeks.
- Patients who have any questions should speak to their doctor or pharmacist.

A European Commission Decision on this opinion will be issued in due course.