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PRAC recommends restricting use of domperidone

Benefits still considered to outweigh risks when given short-term and in low doses to treat nausea or vomiting

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has completed a review of domperidone-containing medicines and has recommended changes to their use throughout the European Union (EU), including using these medicines only to relieve symptoms of nausea and vomiting, restricting the dose and adjusting doses carefully by weight where it is licensed in children. Reducing the recommended dose and duration of treatment was considered key to minimising its risks.

Domperidone-containing medicines have been authorised nationally in individual Member States of the EU for the treatment of nausea and vomiting of various causes (including in children in some Member States) but also for the management of symptoms such as bloating, discomfort and heartburn.

The review of domperidone was carried out at the request of the Belgian medicines authority over concerns about the medicine's effects on the heart. The injectable form of domperidone was withdrawn in 1985 because of such side effects. Serious effects on the heart, including QT prolongation (an alteration of the electrical activity of the heart) and arrhythmias (unstable heartbeats), have previously been evaluated by the EMA's former Pharmacovigilance Working Party (PhVWP). In 2011, the PhVWP recommended that the product information for domperidone-containing medicines be updated to reflect the risk of these adverse effects and to warn that domperidone should be used with caution in patients with certain heart conditions. However, cases of heart problems in patients using the medicine continued to be reported, and the PRAC was therefore asked to examine whether the benefits still outweighed the risks for these medicines in their approved uses, and whether their marketing authorisations should be maintained or changed across the EU.

The PRAC recommended that domperidone-containing medicines should remain available and may continue to be used in the EU for the management of the symptoms of nausea and vomiting, but that the recommended dose should be reduced to 10 mg up to three times daily by mouth for adults and adolescents weighing 35 kg or more. These patients may also be given the medicine as suppositories of 30 mg twice daily. Where the medicine is licensed in children and adolescents weighing less than 35 kg, it should be given by mouth at a dose of 0.25 mg per kg bodyweight up to three times daily. Measuring devices should be included with liquid formulations to allow accurate dosing by bodyweight. The medicine should not normally be used for longer than one week.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7129
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

Domperidone should no longer be authorised to treat other conditions such as bloating or heartburn. It must not be given to patients with moderate or severe impairment of liver function, or in those who have existing abnormalities of electrical activity in the heart or heart rhythm, or who are at increased risk of such effects. In addition, it must not be used with other medicines that have similar effects on the heart or reduce the breakdown of domperidone in the body (thus increasing the risk of side effects). The product information should be amended appropriately. Products supplying a dose of 20 mg by mouth, and suppositories of 10 or 60 mg are no longer recommended for use and should be withdrawn, as should combination products with cinnarizine (an antihistamine) where available.

The Committee's recommendations follow a careful assessment of all the available evidence on the effectiveness and safety of domperidone, including published studies and reviews, experimental data, reports of side effects, post-marketing studies and other external information and comment. Domperidone was clearly associated with a small increased risk of potentially life-threatening effects on the heart. This was seen particularly in patients older than 60 years, those taking daily doses of more than 30 mg and those taking other medicines that have similar effects on the heart or reduce the breakdown of domperidone in the body. PRAC considered that reducing the recommended dose and duration of treatment was a particular key to minimising the risks with domperidone.

The Committee noted that although use was long-established, data supporting the effectiveness of domperidone in children and data supporting the effectiveness of the suppositories were limited, and asked for further studies to be carried out.

The PRAC recommendation will now be sent to the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) for consideration at its meeting on 22-24 April 2014[1].

More about the medicine

Domperidone-containing medicines have been authorised in most EU Member States via national procedures since the 1970s and are widely available as over-the-counter or prescription-only medicines. They are available as tablets, oral suspension and suppositories under various trade names (such as Motilium), and in some Member States can be obtained without a prescription. A combination product with cinnarizine (an antihistamine) is available in some Member States for the treatment of motion sickness.

Domperidone works by blocking receptors for the neurotransmitter dopamine found in the gut and in the part of the brain linked to vomiting. This helps prevent nausea (feeling sick) and vomiting.

More about the procedure

The review of domperidone was initiated on 01 March 2013 at the request of the Belgian medicines authority, the Federal Agency for Medicines and Health Products (FAGG-AFMPS), under Article 31 of Directive 2001/83/EC.

The review has been carried out by the PRAC, the Committee responsible for the evaluation of safety issues for human medicines, which has made a set of recommendations. As domperidone-containing medicines are all authorised nationally, the PRAC recommendation will be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a final position. The CMDh is a regulatory body representing EU Member States, and is

[1] The companies that market domperidone have the right to ask for a re-examination of the PRAC recommendation within 15 days of receipt of the PRAC recommendation, which would delay the expected time of finalisation of this review.

responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.

If the CMDh position is agreed by consensus, the agreement will be directly implemented by the Member States where the medicines are authorised. Should the CMDh position be adopted by majority vote, the CMDh position will be sent to the European Commission, for the adoption of an EU-wide legally binding decision.

Contact our press officers

Monika Benstetter or Martin Harvey

Tel. +44 (0)20 7418 8427

E-mail: