Recommendations on restricting use of domperidone confirmed by CMDh

29.04.2014 | Circular Number P08/2014

The European Medicines Agency's Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) has endorsed recommendations to restrict the use of domperidone-containing medicines. The CMDh, a medicines regulatory body with members representing each of the EU Member States, agreed that these medicines should only be used to relieve symptoms of nausea and vomiting, that doses and length of treatment should be restricted and that they should be adjusted carefully by the patient's weight where available for use in children.

The recommendations were originally made by the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) at its meeting of 3-6 March, after a careful evaluation of the available evidence on the benefits and risks of such medicines (see Medicines Authority Circular P06/2014) As the CMDh position was adopted by majority vote, the CMDh position will now be sent to the European Commission, which will take a final EU-wide legally binding decision.

In Malta

The Medicines Authority has participated fully in these EU fora and is in full agreement with the new advice and restrictions in use.

The products in the Table below are authorised to be sold in Malta. For these licensed products the product information including the package leaflet will be changed to reflect the new recommendations by the companies involved.

In Malta no domepridone containing products will be removed from the market since the formulations affected by the new advice do not have a license to be placed on the Maltese market.

ATC code	Active Ingredient	Product Name	Pharmaceutical form	Authorisation number	Licence Holder Name
A03FA03	Domperidone Maleate 10mg	Domperidone 10mg Film-Coated Tablets	COATED TABLET	AA154/05801	Wockhardt UK Ltd.

Medicines Authority
203 Level 3, Rue D'Argens, Gzira, GZR 1368 – Malta.
Tel. (+356) 23439000 Fax. (+356) 23439161 www.medicinesauthority.gov.mt

A03FA03	Domperidone Maleate 10mg	Domperidone 10mg Tablets	TABLET	AA729/03301	Cherubino Ltd.
A03FA03	Domperidone 10mg (as maleate)	Domperidone 10mg Tablets	TABLET	AA244/37201	P & D Pharmaceuticals Limited
A03FA03	Domperidone 10mg	Domerid 10mg Tablets	TABLET	AA521/06101	Medicem Limited
A03FA03	Domperidone 10mg	Cinet 10mg tablets	TABLET	AA531/00201	Laboratorio Medinfar - Produtos Farmaceuticos SA
A03FA03	Domperidone 10mg	Motilium	FILM-COATED TABLET	MA018/01605	Janssen-Cilag International NV
A03FA03	Domperidone 10mg	Costi	TABLET	MA032/02601	Medochemie Limited
A03FA03	Domperidone 10mg	Domperidon Actavis 10mg tablets	TABLET	MA651/00301	Actavis Group h.f.
A03FA03	Domperidone 10mg	Motilium	TABLET	PI515/02101A	AlphaFarma Ltd.
A03FA03	Domperidone 10mg	Motilium	FILM-COATED TABLET	PI521/02001A	Medicem Limited
A03FA03	Domperidone 10mg	Motilium	FILM-COATED TABLET	PI908/04801A	NeoFarma Pharmaceuticals Ltd.
A03FA03	Domperidone 1mg/ml	CINET 1 mg/ml oral suspension	ORAL SUSPENSION	AA531/00202	Laboratorio Medinfar - Produtos Farmaceuticos SA
A03FA03	Domperidone 1mg/ml	Motilium	ORAL SUSPENSION	MA018/01604	Janssen-Cilag International NV
A03FA03	Domperidone 1mg/ml	Motilium	ORAL SUSPENSION	PI521/02002A	Medicem Limited
A03FA03	Domperidone 30mg	Motilium	SUPPOSITORIES	MA018/01602	Janssen-Cilag International NV
A03FA03	Domperidone 30mg	Motilium	SUPPOSITORIES	PI521/02003A	Medicem Limited

New Recommendations for Healthcare Professionalsprescribing domepridone.

- The new recommended dose in adults (and adolescents ≥ 35 kg where licensed) is 10 mg orally up to three times daily (maximum dose of 30 mg daily). Adults may also be given 30 mg twice daily rectally as suppositories.
- Where suitable domperidone products are available for children, the recommended dose is 0.25 mg/kg bodyweight up to three times daily by mouth. In order to accurately measure doses to paediatric patients, oral suspensions should be given using an adapted graduated oral syringe.
- Domperidone products are contraindicated in patients with severe hepatic impairment, conditions where cardiac conduction is, or could be, impaired or where there is underlying cardiac disease such as congestive heart failure, and when co-administered with QT-prolonging medicines or potent CYP3A4 inhibitors.
- Formulations not consistent with the new dosage recommendations will be withdrawn from the market, as will combinations of domperidone with cinnarizine. However this does not apply for Malta. The product information for domperidone-containing products

Medicines Authority
203 Level 3, Rue D'Argens, Gzira, GZR 1368 – Malta.
Tel. (+356) 23439000 Fax. (+356) 23439161 www.medicinesauthority.gov.mt

will be updated, and a letter will be sent to healthcare professionals explaining the new recommendations.

A review of the evidence confirms a small increased risk of serious cardiac adverse drug reactions related to the use of domperidone, including QTc prolongation, torsade de pointes, serious ventricular arrhythmia and sudden cardiac death. A higher risk was observed in patients older than 60 years, adults taking daily oral doses of more than 30 mg, and those taking QT-prolonging medicines or CYP3A4 inhibitors concomitantly. These recommendations are based on careful consideration of data on the safety and efficacy of domperidone from various sources. This comprised non-clinical and clinical data, both published and unpublished, including a thorough QT study, cumulative review of case reports of cardiac disorders and vascular investigations from the safety databases for domperidone products, pharmacoepidemiological studies, and published and unpublished efficacy studies.

Information to Patients

- Domperidone is a prescription-only medicine that has been used for various stomach and digestive problems. There have been concerns that it might increase the risk of side effects on the heart, including dangerously irregular heartbeats in some patients.
- Because a review has shown that the risks of domperidone are greatest at high doses or when it is used for a longer period, the medicine should only be approved for use in low doses to treat symptoms of nausea and vomiting (feeling or being sick). Treatment should generally only be given for up to one week.
- The recommended dose in adults is 10 mg by mouth up to three times a day, or 30 mg as a suppository twice a day. Where suitable products are available for children, doses should be calculated depending on bodyweight and given with a device that allows accurate measuring. Some products will be withdrawn from EU markets because their strength does not match the new doses but this does not apply for Malta.
- There is no good evidence to support the use of domperidone for other conditions such as bloating and heartburn, and so it will no longer be authorised to treat these conditions.
- Patients with certain existing heart problems, or who are taking certain other medicines that enhance the effects of domperidone or reduce its breakdown in the body, should not take domperidone.

Medicines Authority
203 Level 3, Rue D'Argens, Gzira, GZR 1368 – Malta.
Tel. (+356) 23439000 Fax. (+356) 23439161 www.medicinesauthority.gov.mt

Patients or carers who have any concerns should speak to a healthcare professional. Those who are taking domperidone long-term or in higher doses, or for conditions other than nausea and vomiting, should consult their doctor at their next scheduled appointment or speak to their pharmacist to discuss their treatment. For more information please visit **www.ema.europa.eu**

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on domperidone containing medicinal products. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form or online at **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Prof John J Borg PhD (Bristol)
Post-licensing Director

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Medicines Authority
203 Level 3, Rue D'Argens, Gzira, GZR 1368 – Malta.
Tel. (+356) 23439000 Fax. (+356) 23439161 www.medicinesauthority.gov.mt

JJB