Ref: 02/2019/MZ
07.03.2019

Direct Healthcare Professional Communication

Domperidone-containing products: removal of the paediatric posology and reminder of indication and contraindications related to serious cardiac side-effects

Dear Healthcare professional,

Janssen-Cilag International NV, Laboratorio Medinfar - Produtos Farmaceuticos SA, Medicem Limited, Neofarma Pharmaceuticals Ltd, Remedica Ltd, Wockhardt UK Limited in agreement with the European Medicines Agency and the Malta Medicines Authority, would like to inform you of the following:

Summary

- **The only registered indication for domperidone is the relief of symptoms of nausea and vomiting in adults and adolescents 12 years of age and older and weighing 35 kg or more**
  - **The indication in younger children has been deleted**
  - **The oral solution will no longer contain a pipette for dosing in children**

- **Domperidone products are contraindicated:**
  - **In patients with moderate to severe hepatic impairment**
  - **In patients who have known existing prolongation of cardiac conduction intervals (particularly QTc) and in patients with significant electrolyte disturbances or underlying cardiac diseases such as congestive heart failure**
  - **During co-administration with QT-prolonging drugs**
  - **During co-administration with potent CYP3A4 inhibitors (regardless of their QT-prolonging effects)**

- **Information on side-effects predominantly in very young children was deleted because it was no longer relevant to the approved indication**

- **The benefits remain to outweigh the risks in this indication.**

Further information

The safety of domperidone-containing products was reviewed in 2014 by the EMA's Pharmacovigilance Risk Assessment Committee (PRAC). This review confirmed the risk of serious cardiac adverse drug reactions related to domperidone use including QTc prolongation, torsade de pointes, serious ventricular arrhythmia and sudden cardiac death. It was concluded that risk minimisation measures are necessary in order to improve the benefit/risk balance including:

- Restricting the registered indication to the relief of symptoms of nausea and vomiting
- Use of lower doses: 10 mg up to 3 times daily with a maximum dose of 30 mg per day for adults and adolescents 12 years of age and older and weighing ≥35 kg
- Shorter treatment duration: use for the shortest possible duration. The maximum treatment duration should not usually exceed 1 week
- Addition of the following contraindications: in patients with moderate to severe hepatic impairment; conditions where the cardiac conduction intervals, particularly QTc, are impaired or could be affected and underlying cardiac diseases as congestive heart failure; in patients with significant electrolyte disturbances; and/or when co-administered with QT-prolonging drugs or potent CYP3A4 inhibitors
    - Domperidone is contraindicated with QT-prolonging drugs including apomorphine, unless the benefit of co-administration with apomorphine outweighs the risks, and only if the recommended precautions for co-administration mentioned in the apomorphine SmPC are strictly fulfilled
- Addition of warnings and precautions regarding cardiovascular effects of domperidone

In addition, PRAC requested 2 follow-up studies: an efficacy study conducted at the new lower dosage in paediatrics and an efficacy study testing the dissemination of the DHPC.

A placebo-controlled study in children below the age of 12 with acute nausea and vomiting using the new lower dosage as an add-on to oral rehydration did not show any difference in efficacy and safety compared with placebo. Based on these study results, the posology of domperidone products was restricted to adults and adolescents above the age of 12 and weighing ≥35 kg.

Recent studies conducted in several European countries have shown that a proportion of physicians are not aware of domperidone's restricted indication and its contraindications. All healthcare professionals are thus reminded of the safe use of domperidone-containing products in accordance with the product information.

Call for reporting

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are reminded to continue to report suspected adverse reactions associated with Domperidone-containing products in accordance with the national spontaneous reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Post-licensing directorate, Medicines Authority, Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000, Malta or sent by email to postlicensing.medicinesauthority@gov.mt.

Company contact point

Should you have any questions or require additional information, please call Medical Information at:

Company	Product name	Email	Phone
Janssen-Cilag International NV	Motilium 1mg/ml oral suspension	C.Kitromilidou@phadisco.com.cy	+357 22715043
	Motilium 10mg film-coated tablet		
Laboratorio Medinfar - Produtos Farmaceuticos SA	Cinet 10mg tablets	phv@medinfar.pt	+351 214997465
	Cinet 1mg/ml oral suspension		
Medicem Limited	Motilium 10mg film-coated tablet	crouchermartin@gmail.com alansammut@gmail.com	+356 99471241 +356 99422232
	Motilium 1mg/1ml oral suspension		
Neofarma Pharmaceuticals Ltd	Motilium 10mg film-coated tablets Motilium oral suspension 1mg/ml Motilium Fastmelts Orodispersible tablet 10mg	Info@neofarma.com.mt	+356 20109494 +356 99109494
Remedica Ltd	Peptomet 10mg film-coated tablets	a.vasiliou@remedica.com.cy DrugSafety@remedica.com.cy	+357 25553251 +357 25553000
Wockhardt UK Limited	Domperidone 10mg film-coated tablets	Drug.safety@wockhardt.co.uk	+44 (0)1978669272

Yours faithfully,

Post-Licensing Directorate

Medicines Authority

Disclaimer

This Direct Healthcare Professional Communication has been submitted to you on behalf of Janssen-Cilag International NV, Laboratorio Medinfar - Produtos Farmaceuticos SA, Medicem Limited, Neofarma Pharmaceuticals Ltd, Remedica Ltd, Wockhardt UK Limited.