Date: 7th September 2014

Domperidone, Prokinin® 10mg Film Coated Tablets, Prokinin® 5mg/ 5ml Oral Suspension: new recommendations to minimise the cardiac risks

Dear Healthcare Professional,

This letter is to inform you on the recent recommendations to minimise the cardiac risks of domperidone after the recent review on the benefits and risks of the product.

Summary

- The benefit/risk balance of domperidone remains positive in the relief of the symptoms of nausea and vomiting in adults, *adolescents and children.*
- This review confirms an increased risk of serious cardiac adverse drug reactions related to the use of domperidone. A higher risk was observed in patients older than 60 years, those taking daily doses of more than 30 mg, and those taking QT-prolonging drugs or CYP3A4 inhibitors concomitantly.
- Domperidone should only be used for nausea and vomiting.
- Domperidone should be used at the lowest effective dose for the shortest possible duration. The maximum treatment duration should not normally exceed one week.
- The new recommended doses are:
  - For adults and adolescents ≥ 35 kg:
    10 mg up to three times daily with a maximum dose of 30 mg per day orally or 30 mg twice daily as suppositories
  - For children and adolescents < 35 kg:
    0.25 mg/kg body weight per intake up to three times daily with a maximum dose of 0.75 mg/kg body weight per day
- Domperidone products are now contraindicated in patients with severe hepatic impairment, in certain heart conditions (including heart failure, previous heart attack, angina, and heart arrhythmia disorders) and, when co-administered with QT-prolonging drugs or potent CYP3A4 inhibitors.

Further information

The cardiac risks of medicinal products containing domperidone have been monitored for several years. The product information of domperidone containing products has been updated in recent years to reflect the associated risk of QTc prolongation and serious ventricular arrhythmia.

Since then, new cases of serious cardiac adverse reactions related to domperidone use have continued to be reported. Therefore, the SFDA reviewed the overall risk/benefit balance of domperidone products.
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. Epidemiological studies showed that domperidone was associated with an increased risk of serious ventricular arrhythmias or sudden cardiac death. A higher risk was observed in patients older than 60 years, those taking daily doses

of more than 30 mg, and in those taking other QT-prolonging drugs or CYP3A4 inhibitors concomitantly.

Based on available data, it is considered that the efficacy of domperidone is established in the relief of nausea and vomiting symptoms, and not established in other indications.

Overall, the benefit/risk balance of domperidone remains positive only for oral formulations (oral solid formulations dosed at 10 or 5 mg and oral solution) and adult suppositories (30 mg).

Finally, it was concluded that risk minimisation measures are necessary in order to improve the benefit/risk balance including restricted indications, use of lower doses, shorter treatment duration, addition of contraindications, warning and precautions.
In addition, in order to accurately measure and administer the doses to paediatric patients, oral suspensions should be given using an adapted graduated oral syringe.

The Product Information of all domperidone containing products will be updated to reflect these data.

The information in this letter has been agreed with the Saudi Food and Drug Authority (SFDA).

Call for reporting

Any suspected adverse events should be reported to the national spontaneous reporting system according to the national regulation.

- SFDA (National Pharmacovigilance and Drug Safety Center)
- E-mail to: npc.drug@sfda.sa.
- Fax: +966 -11- 2057662.
- online: http://ade.sfda.gov.sa/

Or

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