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An tÚdarás Rialála Táirgí Sláinte
Health Products Regulatory Authority

Domperidone-containing Medicines:
Risk of Cardiac Adverse Reactions - Restricted Indication, New Contraindications, and Reduced Dose and Duration of Use

A recent Europe-wide review has recommended updates to the treatment advice for domperidone containing medicines following an evaluation of the benefits and risks of domperidone. This review was triggered following continued receipt of reports of cardiac adverse reactions, with a small increase in the risk of serious cardiac effects confirmed. A higher risk was observed in patients older than 60 years, in adults taking daily oral doses of more than 30mg, and those taking QT-prolonging medicines or CYP3A4 inhibitors concomitantly.

The review concluded that domperidone is associated with a small increased risk of serious cardiac adverse reactions. Its use is now restricted to the relief of symptoms of nausea and vomiting and the dosage and duration of use have been reduced. Domperidone is now contraindicated in those with underlying cardiac conditions and other risk factors.

These recommendations are based on an evaluation of the available evidence of safety and efficacy of domperidone from various sources. This comprised of non clinical and clinical data, both published and unpublished, including a Thorough QT (TQT) study, a cumulative review of case reports of cardiac disorders and vascular investigations from the safety databases for domperidone containing products and pharmacoepidemiological studies. Overall there was sufficient evidence to support the use of oral domperidone 10mg up to three times a day in the relief of nausea and vomiting in adults. There were limited data to support paediatric use in this indication, and although the mechanism of action is not expected to differ between adults and children, studies to provide further data to support efficacy in the paediatric population have been requested. Data in support of other indications were extremely limited. In particular, there was little evidence in support of the long-term efficacy of domperidone in dyspepsia and gastro-oesophageal reflux disorder. The benefits in these indications were therefore not considered to outweigh the risk.

Although the results of the TQT study with domperidone indicate that it does not significantly prolong the QTc interval when administered to healthy subjects at 10mg and 20mg four times daily, there are limitations in the study that restrict the conclusions that can be drawn. Epidemiological studies mostly suggest that domperidone exposure was associated with an increase in risk for sudden cardiac death or ventricular arrhythmia. Some of these studies also supported a greater risk in patients over 60 years of age or who were taking high doses (over 30mg/day).

Advice for Healthcare Professionals

Restricted indication

- The use of domperidone is now restricted to the relief of symptoms of nausea and vomiting. The available evidence of efficacy was not sufficient to support its use for other indications.

New contraindications

Domperidone is now contraindicated in people with:

- conditions where cardiac conduction is, or could be, impaired,
- in those with underlying cardiac diseases such as congestive heart failure,
- in those receiving other medications known to prolong QT interval or potent CYP3A4 inhibitors, and
- in people with severe hepatic impairment.

Restrictions on dose

The dosage and duration of use have been reduced to mitigate the risk of cardiac adverse reactions as follows:

Oral formulations

- For adults and adolescents over 12 years of age and weighing 35kg or more, the recommended maximum dose in 24 hours is 30mg (dose interval: 10mg up to three times a day)
- In children under 12 years of age and weighing less than 35kg, the recommended maximum dose in 24 hours is 0.75mg/kg body weight (dose interval: 0.25mg/kg body weight up to three times a day).
- In order to accurately measure doses to paediatric patients, oral suspensions should be given using an adapted graduated oral syringe.

Suppository formulation

- Suppositories should only be used in adults and adolescents weighing 35kg or more, the recommended maximum daily dose in 24 hours is 60mg (dose interval: 30mg twice a day).

Duration of treatment

- Domperidone should be used at the lowest effective dose for the shortest possible duration.
- The maximum treatment duration should not usually exceed one week.
- Patients currently receiving long-term treatment with domperidone should be reassessed at a routine appointment to advise on treatment continuation, dose change, or cessation.

Key messages

- Domperidone is associated with a small increased risk of serious cardiac adverse reactions effects. Use of domperidone is now restricted to the relief of symptoms of nausea and vomiting. It should no longer be used for the relief of bloating and heartburn.
- The dosage and duration of use have been reduced. It should be used at the lowest effective dose for the shortest duration possible. The maximum treatment period should not usually exceed one week.
- Domperidone is now contraindicated in those with underlying cardiac conditions and other risk factors.

**Products currently authorised in Ireland include Motilium and Domerid. Further details are available at www.imb.ie*

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