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Neonatal & Paediatric Pharmacists Group

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2<sup>nd</sup> May 2014

## REVISED DOSING FOR DOMPERIDONE USE IN BABIES and CHILDREN

### Advice for Paediatric and Neonatal Pharmacists

Dear all;

On April 25<sup>th</sup> 2014 the MHRA revised the licensed indications and dosages for domperidone following an EMEA review of safety data. The Pharmacovigilance Risk Assessment Committee (PRAC) found that domperidone was associated with a small increased risk of potentially life-threatening effects on the heart, especially in people:

- aged over 60,
- taking large doses and
- taking concomitant CYP-3A4 inhibitors.

This review was carried out at the request of the Belgian medicines regulator after concerns were raised in adult patients.

Domperidone is prescribed for gastric transit enhancement in the treatment of neonatal and infant gastric reflux despite limited evidence to support its use in this disease. Unfortunately there are very few alternative prokinetic agents:

- Cisapride was withdrawn in 2000 following similar concerns about arrhythmia.
- Metoclopramide is not recommended in children because of its neurological side effects (although the evidence for use is greater than that of domperidone).
- Erythromycin is also associated with cardiac side effects and arrhythmias and as an antibiotic there is no understanding of the effects more widespread use would have on antibiotic resistance in the community as a result.

Cardiac arrhythmias in children are rare. The evidence reviewed by the PRAC was in adults who were already predisposed to arrhythmias as a result of underlying acquired cardiac disease. In children arrhythmias are more commonly genetic or secondary to congenital heart defects.

The Neonatal and Paediatric Pharmacists Group takes a pragmatic view to this MHRA decision. We recommend to our members the following actions to ensure patient safety and continued access to effective treatment:

#### **Children with congenital heart disease**

Consider stopping domperidone therapy or discuss with parents/carers and ensure that cardiac monitoring is regularly performed. Consider offering an alternative treatment where appropriate.

#### **Other children with established reflux or nausea and vomiting**

Take no immediate action in patients already established on domperidone. Consider reducing the dose (where appropriate) to 250microgram/kg three times a day at the next convenient review. Consider routine cardiac monitoring where there are concerns (e.g. cardiovascular instability, concomitant CYP3A4 inhibitors prescribed).

#### **Children with newly diagnosed reflux or at risk of nausea and vomiting**

In the majority of cases reflux is self-limiting, not serious and resolves before the child's second birthday once the child is weaned onto solid food. Simple measures should be introduced first - feeding the infant upright and keeping them upright after feeds, and the use of feed thickeners should be considered first-line where the child is on liquid feeds. These measures should be given a proper trial before considering pharmacological intervention – at least two weeks. In more serious cases, and after the introduction of thickeners then consider the benefits and risks of medical anti-reflux/anti-acid secretion treatment. If domperidone is to be used, give an initial maximum of 250micrograms/kg three times a day. Where reflux or nausea is refractory to this then give increased doses to a maximum of 400micrograms/kg (max 20mg) three times a day and recommend regular cardiac monitoring.

#### **Use in nursing mothers to promote lactation**

This is an unlicensed use and prescribers should consider the benefits and risks for the individual patient; using the lowest effective dose (maximum 10mg three times a day) for the shortest period of time necessary. Advice in this patient group will be reviewed in line with advice from the UKMI Pregnancy and Lactation that is expected imminently.

#### **Advice to Parents and Carers**

Reassure parents that the increased risk of developing cardiac problems is small and has to date only been seen in adults who already have cardiac disease. Patients, parents and carers should be directed to the Medicines for Children Patient Information Leaflet entitled "Domperidone for gastro-oesophageal reflux" available from [www.medicinesforchildren.org.uk](http://www.medicinesforchildren.org.uk)

#### **Advice to Prescribers**

The usual considerations when prescribing medicines off-label should be taken given that domperidone has only ever been licensed in children for the relief of the symptoms of nausea and vomiting and use in GORD has always been an off label indication.

We hope that this position statement allows you to present prescribers and carers with a pragmatic temporary response to this difficult situation until such a time that the Joint Medicines Committee can come to a final determination of the position of both the RCPCH and the NPPG on the use of domperidone in children.

Yours sincerely

Penny North-Lewis  
NPPG Chair

Steve Tomlin  
NPPG Professional Secretary