16 January 2015

Metoclopramide: updated indications and posology to minimize the risk of (mainly neurological) adverse effects

Dear Healthcare Professional,

Amdipharm Limited, the European Medicines Agency and the Health Products Regulatory Agency (HPRA) of Ireland would like to inform you of the following important updated advice following a European review of the benefits and risks of metoclopramide:

Summary of new advice

Limited dose and durations of use

- Metoclopramide should only be prescribed for short-term use at the recommended doses and dose-intervals. This is in order to minimise the risks of neurological and other adverse reactions.
- Intravenous doses should be administered as a slow bolus (at least over 3 minutes) to minimise the risk of occurrence of adverse reactions, including cardiovascular events.

Restricted Indications for use:

Adult patients

- Metoclopramide is indicated for short-term use in the prevention and treatment of nausea and vomiting, including that associated with chemotherapy, radiotherapy, surgery (IV formulation only) and migraine. For detailed indications, please refer to the full list of indications in the product information (Annex 1).
- The maximum dose in 24 hours is 30mg (or 0.5mg/kg body weight), by the oral, rectal, intravenous or intramuscular route.
- The maximum recommended treatment duration is 5 days.

Paediatric patients (aged 1-18 years)

- Metoclopramide should be restricted to use as a second line option in children in the following indications:
  - treatment of established post-operative nausea and vomiting (intravenous route only)
  - prevention of delayed chemotherapy-induced nausea and vomiting (oral or intravenous routes only).
- The recommended dose is 0.1 to 0.15mg/kg body weight, repeated up to three times daily. The maximum dose in 24 hours is 0.5mg/kg body weight.
- Oral solutions should be administered using the adapted graduated oral syringe to ensure accuracy.

The following dosing table gives the recommended doses for metoclopramide across the various age groups and weights.

Dosing table

Age	Body Weight	Dose	Frequency
1-3 years	10-14 kg	1 mg	Up to 3 times daily
3-5 years	15-19 kg	2 mg	Up to 3 times daily
5-9 years	20-29 kg	2.5 mg	Up to 3 times daily
9-18 years	30-60 kg	5 mg	Up to 3 times daily
15-18 years	Over 60kg	10 mg	Up to 3 times daily

The maximum treatment duration is 5 days for prevention of delayed chemotherapy induced nausea and vomiting (CINV).

AMCo's Maxolon 10 mg Tablets are not suitable for use in children weighing less than 60 kg.

*******Please note that there is currently no suspension formulation of metoclopramide licensed in Ireland. *******

Paediatric patients (aged 0-1 year)

- Metoclopramide is contraindicated in children less than 1 year of age, and should not be used in any circumstances because of the risk of neurological reactions and methaemoglobinaemia

For more information please see the Summary of Product Characteristics (SmPC) and Patient Information Leaflet (PL) attached (Annexes 1 and 2).

Further information

In December 2011, a European review of the balance of benefits versus risks of metoclopramide, including a consideration of different age groups was initiated by the European Medicines Agency. This was triggered by the French national authority, because of reports related to possible neurological and cardiovascular toxicity.

The review has confirmed the well-established safety profile of metoclopramide alongside the risks of neurological adverse effects (e.g., acute extrapyramidal symptoms and irreversible tardive dyskinesia). The risk of these adverse effects is increased in high dose or long term treatment. The risk is also higher in children than in adults.

In chronic conditions the risks of neurological adverse reactions outweigh the benefits. Therefore metoclopramide should not be used in chronic indications such as e.g., gastroparesis, dyspepsia, gastro-oesophageal reflux disease.

In children, metoclopramide should be restricted to second line treatment of established post-operative nausea and vomiting (IV formulation only) and prevention of delayed chemotherapy induced nausea and vomiting. In all other indications, the risks of neurological adverse reactions outweigh the benefits.

Particular care should be taken in relation to doses and dose-intervals when prescribing and administering metoclopramide to children. A paediatric dosing table has been added in the SmPC. Full prescribing information can be found in the SmPC (Annex 1).

Given very rare reports of serious cardiovascular events (e.g., circulatory collapse, severe bradycardia, cardiac arrest and QT prolongation) associated with metoclopramide, particularly via the intravenous route, special care should be taken with at-risk populations including: the elderly, patients with cardiac conduction disturbances (including QT prolongation), those taking other drugs known to prolong QT interval,uncorrected electrolyte imbalance and bradycardia.

Please share this information with relevant colleagues and health care personnel.

Note:

Please note that the updated Summary of Product Characteristics (SmPC) and Patient Information Leaflet (PIL), with the new safety information will be available on the HPRA website. The revised PILs will be inserted in the packs in due course.

Call for reporting

Any suspected adverse events should be reported to the National. Spontaneous Reporting System according to the National Regulation.

Please report suspected adverse reactions with any medicine or vaccine to the HPRA through at HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517.
Website: www.hpra.ie; E-mail:medsafety@hpra.ie.

When reporting please provide as much information as possible, including information about medical history, any concomitant medication, onset and treatment dates.

Company contact point

The suspected adverse reactions may also be reported to the Medical Information department at AMCo on:

Tel: +353 1890 25 24 73

Email: medicalinformation@amcolimited.com

Fax: + 44 (0) 20 8686 0807

Medical Enquiries:

Please contact AMCo Medical Information department using the details above if you have any enquires.

Yours faithfully,

Dr Bharat Karbal

Chief Medical Officer

Annexes

1. Summary of Product Characteristics
2. Patient Information Leaflet