Ref: P02/2014/JJB

26 Feb 2014

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

Dear HEALTHCARE PROFESSIONAL,

Accord Healthcare Limited, Hameln Pharmaceuticals Limited; Medochemie Limited; Mercury Pharma International Limited; Metropolis Healthcare Limited; Remedica Limited, the European Medicines Agency and Malta Medicines Authority would like to inform you of the following updated advice following a European review of the benefits and risk of metoclopramide:

Summary of new advice

Limited dose and duration of use

- Metoclopramide should only be prescribed for short-term use at 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 reactions.
- Because of the risk of adverse reactions with high doses, the following high-strength formulations will be withdrawn:
    - Suppositories dosed at 20mg
    - Oral liquid formulations with concentration higher than 1mg/ml
    - Injectable formulations with concentration higher than 5mg/ml.

Indications for use are restricted as follows:

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 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.

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)
http://old.medicinesauthority.gov.mt/DHPC/DHPC_metoclopramide_A03FA01_MA_26022014.pdf

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 efficacy concerns and safety concerns related to neurological and cardiovascular toxicity.

The review has confirmed well-established the safety profile of metoclopramide, including the risks of neurological adverse effects (eg, 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 these chronic indications (eg, gastroparesis, dyspepsia, gastro-oesophageal reflux disease).

In children, metoclopramide should be restricted to second line treatment of established post-operative nausea and vomiting 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 reactions associated with metoclopramide, particularly via the intravenous route, special care should be taken to at-risk populations including: the elderly population, patients with cardiac conduction disturbances (including QT prolongation), uncorrected electrolyte imbalance, bradycardia, and those taking other drugs known to prolong QT interval.

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

Call for reporting

Any suspected adverse reactions and medication errors can be reported via the national Adverse Drug Reactions (ADRs) reporting system. Report forms can be downloaded from www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing Directorate, 203, Level 3, Rue D'Argens, Gżira GŻR 1368, MALTA, or sent by email to postlicensing.medicinesauthority@gov.mt

Company contact point
Contact point details for further information are given in the product information of the medicine (SmPC and Package Leaflet).

Post Licensing Directorate
Medicines Authority

Disclaimer
This Direct Healthcare Professional Communication has been submitted to you on behalf of Accord Healthcare Limited, Hameln Pharmaceuticals Limited; Medochemie Limited; Mercury Pharma International Limited; Metropolis Healthcare Limited; Remedica Limited.

Annexes

1. Summary of Product Characteristics
   http://old.medicinesauthority.gov.mt/DHPC/DHPC_metoclopramide_A03FA01_MA_26022014.pdf
2. Patient Information Leaflet
   http://old.medicinesauthority.gov.mt/DHPC/DHPC_metoclopramide_A03FA01_MA_26022014.pdf