Proprietary medicinal products based on metoclopramide, intestinal motility stimulant: PRIMPERAN, ANAUSIN METOCLOPRAMIDE, PROKINYL and their generic equivalents

Use in adults and children to be restricted to situations where prescription of an antiemetic appears indispensable

Main points

- Metoclopramide, a neuroleptic dopamine antagonist, is indicated in adults for the prevention and/or treatment of nausea and vomiting, including that associated with chemotherapy, radiation therapy, surgery and migraine, depending on the proprietary medicinal product concerned.

- In children above 1 year old, it is restricted to the second-line treatment of post-operative nausea and vomiting (IV administration only) and the prevention of delayed chemotherapy-induced nausea and vomiting (oral and IV administration only).

- PRIMPERAN may be prescribed to adults and/or children, depending on the proprietary medicinal product concerned. ANAUSIN METOCLOPRAMIDE and PROKINYL are restricted to adults.

- In adults, as in children, its efficacy is poorly established in the indications and at the dosage in the current Marketing Authorisation. Its use must not be considered unless the prescription of an antiemetic appears indispensable and it is in strict accordance with its Marketing Authorisation.

- Metoclopramide can trigger serious adverse effects, mainly of a neurological nature: sometimes irreversible peripheral extrapyramidal symptoms and tardive dyskinesia, particularly in elderly individuals. Serious cardiac adverse effects (ventricular arrhythmia, sudden cardiac death) have also been observed, but the excess risk attributable to metoclopramide cannot be quantified. The probable risk factors that have been identified are the concomitant use of other medicines that also prolong the QTc interval, advanced age and hypokalemia.

Therapeutic use

- The treatment of nausea and vomiting is etiological.

- In view of the risk of serious cardiac adverse effects (ventricular arrhythmia, sudden cardiac death, neurological disorders observed under domperidone and metoclopramide), the prescription of an antiemetic (domperidone, metoclopramide, metopimazine) in situations that are not normally serious must not be considered except in patients with symptoms (particularly vomiting) that could rapidly lead to serious or very disturbing complications.

- **Role of the medicinal products in the therapeutic strategy**

  In adults, the therapeutic value of metoclopramide has not been documented by clinical data from studies with a good level of evidence at the recommended dosage. Its use must not be considered unless the prescription of an antiemetic appears indispensable and it is in strict accordance with its Marketing Authorisation, making use, in particular, of the lowest dosage possible (< 30 mg/day or 0.5 mg/kg/day), the shortest possible period of treatment (< 5 days) and in observing the contraindications (the patient's co-morbidities, drug interactions). Metoclopramide must be avoided in elderly patients, because of the risk of tardive dyskinesia, and in patients with cardiac conduction disorders (including prolongation of the QT interval), uncorrected electrolyte imbalance, bradycardia, and in those taking other medicines know to prolong the QT interval. The medicinal product increases the risk of severe cardiovascular effects, especially
if it is administered intravenously. Metoclopramide no longer has a role in chronic gastrointestinal disorders (such as dyspepsia, gastroparesis, gastro-oesophageal reflux).

In children, metoclopramide is now restricted to second-line treatment of post-operative nausea and vomiting, by intravenous administration only (maximum duration of treatment: 2 days) and the prevention of delayed nausea and vomiting induced by chemotherapy, by oral or intravenous administration (maximum duration of treatment: 5 days).

Clinical data

- There are few clinical data of good methodological quality for assessing the size of the effect of metoclopramide in its current indications in adults and children.
- In adults, in the treatment and prevention of delayed nausea and vomiting induced by anticancer drugs, the prevention nausea and vomiting induced by radiation therapy or surgery, the data indicate that metoclopramide is effective at a dosage of 10 mg x 3/day. Overall, metoclopramide is less effective than setrons and the size of the effect appears at best moderate in comparison with placebo. It has not been evaluated as a second-line treatment in these situations. In the symptomatic treatment of non-serious nausea and vomiting associated with migraine attacks and the size of the effect of metoclopramide cannot be evaluated.
- In children, apart from in the treatment of post-operative nausea and vomiting, the data for the evaluation of the therapeutic value metoclopramide are very limited. In the treatment of delayed chemotherapy-induced nausea and vomiting, this indication is retained despite the absence of convincing data, but taking into consideration the data relating to the efficacy in adults, as the number of alternatives for children is limited.
- Metoclopramide can trigger sometimes irreversible, peripheral extrapyramidal symptoms and tardive dyskinesias. The risks are increased when high doses are used or during a prolonged period of treatment. Particularly in the case of the extrapyramidal symptoms, the risk is higher in children than in adults.
- Cardiac adverse effects have also been observed under metoclopramide: serious ventricular arrhythmia and sudden cardiac death due to prolongation of the QTc in the ECG. The size of the excess risk cannot be quantified.

Benefit of the medicinal product

- The actual benefit* of the proprietary medicinal products based on metoclopramide is moderate in adults (METOCLOPRAMIDE ANAUSIN, PRIMPERAN, PROKINYL) and in children (PRIMPERAN).
- Recommends continued inclusion on the list of reimbursable products for supply be pharmacists and for hospital use.

---

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.