HAUTE AUTORITÉ DE SANTÉ

CARDIOLOGY
Focus
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BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

Domperidone-based proprietary medicinal products, intestinal motility stimulant: MOTILIUM, PERIDYS, OROPERIDYS and their generics

In children, insufficient clinical benefit due to unproven efficacy
In adults, low actual benefit due to poorly established efficacy at the dosage now recommended to reduce the risk of serious cardiac adverse effects

Main points

- Domperidone, a dopamine antagonist neuroleptic, now has Marketing Authorisation only for the relief of symptoms of nausea and vomiting in adults and children.
- In adults, its efficacy has not been established in the indication and at the dosage in the revised Marketing Authorisation. Its use should not be considered unless prescribing an antiemetic appears indispensable and is in strict accordance with its Marketing Authorisation; in particular, the dosage should be as low as possible (< 30 mg/day), the length of treatment should be as short as possible (usually less than 1 week) and there should be no contraindications (patient's comorbidities, drug interactions).
- In children, its therapeutic benefit has not been documented. Domperidone should no longer be used.
- There is a risk of serious cardiac adverse effects in adults and children. The excess risk attributable to domperidone is difficult to quantify. The probable risk factors that have been identified are the concomitant use of other medicines that also prolong the QTc interval, advanced age and hypokalaemia.

Therapeutic use

- The treatment of nausea and vomiting is etiological.
- In view of the risk of serious cardiac adverse effects (ventricular arrhythmia, sudden death, neurological disorders observed on domperidone and metoclopramide), the prescription of an antiemetic (domperidone, metoclopramide, metopimazine) in situations that are not normally serious should not be considered except in patients with symptoms (particularly vomiting) that could lead in the short term to serious or very disruptive complications.
- **Role of the medicinal products in the therapeutic strategy**

  In adults, to relieve acute nausea and vomiting that requires short-term treatment, the therapeutic benefit of domperidone at the recommended dosage of 30 mg/day has not been documented by clinical data from studies with a good level of evidence. Its use must not be considered unless the prescription of an antiemetic appears indispensable and it is in strict accordance with its Marketing Authorisation. In older patients (> 60 years), pregnant women and breast-feeding women, prescribing domperidone must be avoided because of the increased risk of sudden death or serious ventricular arrhythmia.
  Domperidone must no longer be used in the following clinical situations: dyspepsia, gastroparesis, gastro-oesophageal reflux, nausea and vomiting induced by radiotherapy, chemotherapy or a dopamine agonist, and stimulation of milk production.

  In children, until there are clinical trial results that document its efficacy, domperidone no longer has a role.

Clinical data

- The only clinical data available come from placebo-controlled studies, in off-label clinical situations and with a non-recommended duration.
- In the indications and at the dosage recommended (30 mg/day for a short period < 7 days), the clinical efficacy of domperidone has not been established in children. In adults, at the dosage of 10 mg 3 x daily, the available data cannot be used to solidly establish efficacy, or in particular to measure the effect size versus placebo or another antiemetic.
- Domperidone exposes adult and child patients to the risk of serious ventricular arrhythmias and sudden death, by prolonging the QTc interval on ECG, and to rare neurological adverse effects. Based on the available data, it is difficult to quantify the size of the excess cardiac risk on domperidone in the general population and in high-risk subgroups (particularly older patients aged over 60 years). Epidemiological studies suggest that the excess cardiac risk is only present at a dosage of more than 30 mg/day. However, no studies are available to support the cardiac impact of a reduction in dosage, in either adults or children.

Benefit of the medicinal product

In adults:

- As long as the measures for minimising cardiovascular risks are taken, the actual benefit* of domperidone-based medicinal products (MOTILIUM, PERIDYS and OROPERIDYS) is low in the Marketing Authorisation indication and dosage.
- Recommends continued inclusion on the list of reimbursable products for supply by pharmacists and for hospital use under these conditions.

In children:

- The actual benefit* of domperidone-based medicinal products (MOTILIUM, PERIDYS and OROPERIDYS) is insufficient to justify reimbursement by National Health Insurance.
- Does not recommend continued inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

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This document was created on the basis of the Transparency Committee Opinion of 29 April 2015 and is available at **www.has-sante.fr**

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* 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.