07 March 2013
EMA/PRAC/124198/2013

PRAC List of questions

To be addressed by the marketing authorisation holder(s) for domperidone containing medicinal products

Article 31 of Directive 2001/83/EC resulting from pharmacovigilance data

Procedure number: EMEA/H/A-31/1365

INN/active substance: domperidone

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8668
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

The marketing authorisation holders MAH(s) for domperidone-containing medicinal products are requested to provide the following:

Question 1

How is domperidone used?

Please provide:

a) Information on the currently authorised domperidone-containing products in the different Member States and their current marketing and legal (i.e. prescription vs. non-prescription) status, including information on the approved indication(s), doses, contraindications, warnings and precautions, and undesirable effects included in the Summary of Product Characteristics (SmPC) and the Package Leaflet (PL). Please tabulate the main differences between the SmPCs/PLs in the different EU Member States.
The specific information about treatment duration and the maximum daily dose present in the SmPC should be specified.

b) Information on sales figures and estimated patient exposure for domperidone. This should include a yearly breakdown of sales and exposure over the last 5 years for each Member State. The patient exposure should be provided in “patient-days”; method of calculation should be explained by the MAHs.

c) The MAHs are requested to provide the following data for their domperidone-containing medicinal products over the last 5 years: speciality of the prescribers, daily dose, duration of treatment, age groups (< 18 years and over 18 years), sorted by year and countries.

d) Specific information on the off-label use of domperidone especially in the context of insufficient lactation, diabetic gastroparesis and gastro-oesophageal reflux should be provided. The MAHs should review whether off-label use of domperidone is included in any guidelines related to these indications and what are the dose and treatment duration recommended, if applicable.

Question 2

Risk of cardiac events

Please provide all cardiac safety information available for your domperidone-containing medicinal product. This should include the most relevant non-clinical, clinical data as well as epidemiological studies and a review of the literature, including drug interactions. A cumulative review of all serious case reports should also be provided.
For this purpose, all the MedDRA Preferred Terms (PTs) within the System Organ Class (SOC) Cardiac disorders, and the High Level Group Term (HLGT) Cardiac and vascular investigations (excl enzyme tests), reported for the selected suspected or interacting-domperidone products should be provided and causality assessment should be performed. The review should include analyses on age, indication of use (including off-label cited above), dose, duration of treatment, time-to-onset, outcome, concomitant medication, relevant medical history.

Question 3

Taking into account the available efficacy data of domperidone-containing medicinal products (prospective studies, retrospective studies, pooled analysis or meta-analysis), the MAHs should provide evidence of the therapeutic benefit of domperidone and discuss the benefit-risk balance of domperidone in all population and in each individual indication(s) approved or not in the EU (including insufficient lactation, diabetic gastroparesis and gastro-oesophageal reflux), and whether this is modified by the cardiac risk in any indications or populations.

Question 4

Please provide proposals and justification with supportive evidence for any measures including changes to the SmPC/PL which may improve the benefit-risk balance of domperidone and how their effectiveness should be monitored.