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EMA/PRAC/261900/2014

PRAC List of questions

To be addressed by the marketing authorisation holders for hydroxyzine containing medicinal products

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

Procedure number: EMEA/H/A-31/1400

INN/active substance: hydroxyzine

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

Question 1

The MAH(s) should provide the following:

a) information on the currently authorised hydroxyzine containing medicinal 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 in the EEA Member States and estimated patient exposure from the recent six years (2008 to 2014). This should include a yearly breakdown of sales and exposure over the last six years for each Member State. The patient exposure should be provided in “patient-days”; method of calculation should be explained by the MAHs.

c) exposure data for their hydroxyzine-containing medicinal products over the last six years: speciality of the prescribers, indications, daily dose, duration of treatment, age groups (< 18 years and over 18 years), formulations, sorted by year and countries.

Question 2

The MAHs should provide all QT-interval prolongation safety information available for their hydroxyzine-containing medicinal product. This should include the most relevant non-clinical (include both MAH-sponsored and non-sponsored studies), clinical data (include both MAH-sponsored and non-sponsored studies) as well as epidemiological studies and a review of the literature, including drug interactions. A cumulative review of all post-marketing case reports should also be provided, sorted by seriousness.

For this purpose, all the MedDRA Preferred Terms (PTs) within the SMQ “Torsade de pointes/QT prolongation” (broad) reported for the selected suspected or concomitant-hydroxyzine products should be provided and causality assessment should be performed. The review should include analyses on age, indication of use, dose, duration of treatment, time-to-onset, outcome, concomitant medication, relevant medical history.

Question 3

Taking into account the available efficacy data of hydroxyzine-containing medicinal products (prospective studies, retrospective studies, pooled analysis or meta-analysis), the MAHs should provide evidence of the therapeutic benefit of hydroxyzine and discuss the benefit-risk balance of hydroxyzine in all populations (adults and children separately) and in each individual approved indication(s) (i.e. indications of anxiety and pruritus, premedication before surgery, all approved indications in children and others) in the EU, and whether this is modified by the QT-interval prolongation risk in any indication or population. Any proposal for limitation of maximum daily dose should be justified.

Question 4

The MAHs should provide proposals and justification with supportive evidence for any risk minimisation measures which could be taken in order to improve the benefit-risk balance of these medicinal products, including changes to the summary of product characteristics, labelling and package leaflet.

Methods/actions for monitoring their effectiveness should be proposed.

TABULATION

Question 1

a)

INN	Product name	Marketing status	Legal Status	Indications	Strength	Pharmaceutical form

Maximum daily dose (SmPC)	Treatment duration (SmPC)	Contra-indications (SmPC)	Warnings and precautions (SmPC)	Undesirable effects (SmPC)	Contra-indications (PL)	Warnings and precautions (PL)	Undesirable effects (PL)	Main differences between the SmPC/PIL in the different EU Member States

b)

Year	Product name	Country	Indication	Formulation	Daily dose	Estimated patient exposure (in patient-days)

c)

Year	Product name	Country	Duration of treatment	Indication	Speciality of prescribers	Daily dose	Estimated patient exposure (in patient-days)	Estimated target population (0-6 years old, 6-12 years old, 12-17 years old, 18 years of age and older)