EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

31 October 2012
EMA/PRAC/696495/2012

PRAC List of questions

To be addressed by the marketing authorisation holder(s) for diclofenac containing medicinal products (systemic formulations)

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

Procedure number: EMEA/H/A-31/1344

INN/active substance: diclofenac

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

Question No. 1

How is diclofenac used?

Please provide:

- Information on the currently authorised diclofenac containing products in the different Member States and their current marketing status including information on approved indications(s), doses, treatment duration, contraindications, warnings and precautions included in the summary of product characteristics;

- Information on sales figures and estimated patient exposure for diclofenac. This should include a yearly breakdown of sales and exposure over the last 10 years for each Member State;

- Data on the way diclofenac is used in clinical practice including information on daily dose and duration of treatment.

Question No. 2

What is the evidence for the risk of thrombotic events associated with diclofenac?

The October CHMP scientific opinion on the cardiovascular risks of non-selective NSAIDs has concluded that diclofenac appears to be associated with thrombotic risks similar to those of selective COX-2 inhibitors.

Please provide your detailed analysis of these risks, and in particular for myocardial infarction and ischaemic stroke associated with diclofenac from:

- Clinical trials;
- Pharmacoepidemiological studies;

Please also provide a comprehensive comparison of the thrombotic risks associated with diclofenac with those of other non-selective NSAIDs and COX-2 inhibitors, and provide an estimate of the absolute risk (i.e. additional serious cardiovascular events per 1000 patient years exposure, relative to no treatment or selective COX-2 inhibitors). As far as possible, please comment on the level of risk at different licensed doses of diclofenac.

Question No.3

Please also discuss the potential mechanisms underlying the thrombotic risks associated with diclofenac. In addition, please discuss any differences with the known mechanism of other non-selective NSAIDs and COX-2 inhibitors.

Question No.4

What is your analysis of the balance of risks and benefits of diclofenac?

A benefit/risk assessment of diclofenac in its licensed indication(s), and whether this is modified by the thrombotic risk in any indications or populations.

Question No. 5

Please provide proposals and justification with supportive evidence for any measures including changes to the SPC/PIL which may improve the benefit/risk of diclofenac and how their effectiveness should be monitored.