



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

07 March 2013
EMA/PRAC/137417/2013

PRAC List of questions

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

Article 107i of Directive 2001/83/EC

Procedure number: EMEA/H/A-107i/1363

INN/active substance: flupirtine



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

Question 1

Please provide information on the current authorisations, marketing status and legal status of your flupirtine containing medicinal products in the different member states and non EU-countries, data on sales figures and estimates of patient exposure.

Question 2

Please provide information on the approved indications, doses, treatment duration, contra indications, warnings and precautions for use and undesirable effects included in the Summary of Products Characteristics (SmPCs) and Package Leaflet (PLs) of your flupirtine containing medicinal product(s). Please tabulate the main differences between the SmPCs of the different member states.

Question 3

Please provide an analysis of all individual cases you are aware of reporting liver failure or liver transplantation and of all cases with a fatal outcome from the SOC hepatic and biliary disorders for flupirtine containing medicinal products including a causality assessment based on the RUCAM score and on the WHO-UMC system.

Question 4

Please provide an aggregate analysis of all individual cases from the SOC hepatic and biliary disorders for flupirtine containing medicinal products not covered by the previous question.

Question 5

Please provide information on and analysis of all data that you are aware of that could be relevant to evaluate the risk of hepatotoxicity associated with flupirtine, including data from pre-clinical and clinical studies as well as from published literature.

Question 6

Please provide evidence of the therapeutic benefit of flupirtine containing medicinal products for each approved therapeutic indication in the EU. Data should be presented by type of pain (acute/chronic), intensity of pain and indication (cause of pain).

Question 7

In light of the responses provided to questions 3 to 6 above, please discuss the impact of the risk of hepatotoxicity in the benefit-risk of flupirtine containing medicinal products for both the acute and the chronic pain indications. Please provide proposals and justification with supportive evidence for any measures to further minimise the risks including changes to the SmPC and package leaflet which could improve the benefit-risk ratio of flupirtine.