EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

11 July 2013
EMA/PRAC/418738/2013

PRAC List of questions

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

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

Procedure number: EMEA/H/A-31/1377

INN: zolpidem

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

1. Information in the SmPC of currently authorised zolpidem-containing medicinal products in the different member states, in particular on the indication(s), posology, formulation and the effects on the ability to drive and use machines.
2. The estimated patient exposure for the dosages of 5 mg and 10mg immediate release (IR) formulation.
3. Please provide:
    a) the reporting rate of the selected events (“impaired driving ability”, “road traffic accident”, “somnambulism”, “sleep driving”) for each authorised dosage;
    b) an analysis of all individual case reports of impaired driving ability, road traffic accident, somnambulism and sleep driving, stratified by 5mg and 10mg dosages;
    c) an analysis of pharmacodynamic interactions that may enhance impaired driving ability, road traffic accident, somnambulism and sleep driving caused by zolpidem-containing medicinal products;
    d) Information from all other data sources, including epidemiological studies, driving simulation and laboratory studies and publications on impaired driving ability, road traffic accident, somnambulism and sleep driving should be provided.
4. All available data on the efficacy of the 5 mg and 10 mg dosages from clinical studies and all other available data sources (including post-marketing data) should be provided. Of particular interest is data on the direct comparison between the efficacy of the 5 mg and the 10 mg dosage.
5. Please present any relevant evidence on the PK-PD relationship across dose levels (5mg and 10mg) including in subgroups. Please present an evaluation of any available evidence on the impact of age, weight, gender, liver impairment etc.
6. Having taken into consideration the concerns of impaired driving ability, road traffic accidents, somnambulism and sleep driving, please discuss the benefit-risk balance both for the 5mg and 10 mg dosages of zolpidem-containing medicinal products.
   Based on the MAH’s conclusions, risk minimisation measures (including SmPC amendments or further measures) should be proposed.