13 December 2018
EMA/CHMP/848509/2018

CHMP List of questions

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

Referral under Article 31 of Directive 2001/83/EC

Procedure number: EMEA/H/A-31/1476

INN/active substance(s): Fosfomycin Calcium
Fosfomycin Disodium
Fosfomycin Sodium
Fosfomycin Trometamol

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1. Background

This referral under Article 31 of Directive 2001/83/EC, concerning all fosfomycin medicinal products for systemic use, was triggered in order to revaluate the benefit-risk ratio of the approved indications considering the current scientific knowledge. Furthermore, the appropriate dose and duration of administration for both oral and intravenous formulations need to be discussed as well as the adequacy of safety relevant information and information about pharmacological properties.

2. Questions

The marketing authorisation holders MAH(s) are requested to address the following questions:

Question 1

Concerning your fosofmycin-containing medicinal product(s) please provide in the annexed table:

a) Information on type of marketing authorisation and, marketing and legal status.

b) Figures on patient exposure by product.

c) An overview of the approved indication(s) of fosfomycin-containing medicinal products outside the EU

Question 2

Information on all currently approved indications, posology and method of administration, special warnings and precautions, undesirable effects, pharmacodynamic properties and pharmacokinetic properties according to the SmPC in different EU Member States should be provided in the tabular format below. Furthermore, differences between EU Member States should be described in detail.

INN	Product name	Section 4.1 Indications	Section 4.2 Posology and method of administration	Section 4.4 Special warnings and precautions	Section 4.8 Undesirable effects	Section 5.1 Pharmaco-dynamic properties	Section 5.2 Pharmaco-kinetic properties

Question 3

A justification of the current positive B/R balance in the approved indications based on current scientific knowledge and available data from clinical studies, literature and recommendations in national and European treatment guidelines. The discussion should include a risk assessment on the probability of development of resistance during treatment.

Question 4

A discussion of the adequacy of the recommended dosage and duration of treatment for the approved indications for any population including a detailed description of the underlying pharmacokinetic

analyses including determination of the pharmacodynamic index (PDI), target attainment analyses and PK/PD analyses for efficacy according to the Guideline on the use of pharmacokinetics and pharmacodynamics in the development of antimicrobial medicinal products (EMA/CHMP/594085/2015).

Question 5

The MAHs should provide a scientifically sound rationale for safety relevant information in sections 4.3 to 4.9 of the SmPC. In addition, the frequencies of the adverse drug reactions listed in section 4.8 of the SmPC should be justified based on data from clinical and epidemiological studies.

Question 6

The MAHs should provide a discussion on the adequacy and currentness of data regarding sections 5 of the SmPC.

Question 7

Proposals for updates of relevant sections of the product information in line with current scientific data and in accordance with the guideline on summaries of product characteristics and available QRD referral templates http://www.ema.europa.eu/htms/human/qrd/qrdtemplate.htm

Annex

Question 1

a) & b)

INN	Product name	Type of marketing authorisation	Marketing and legal status	Estimated patient exposure