10 September 2015
EMA/PRAC/550969/2015

PRAC List of questions

To be addressed by the marketing authorisation holders for fusafungine containing medicinal products for oromucosal and nasal use

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

Procedure number: EMEA/H/A-31/1420

INN/active substance: fusafungine

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1. Background

Fusafungine containing medicinal products (nasal/oromucosal spray solution) have been authorised in Europe as a local antibacterial and anti-inflammatory treatment of diseases of the upper respiratory airways.

Safety concerns were identified following the reporting of allergic reactions (including anaphylactic reactions) in paediatric and adult populations. In addition recent Cochrane review *(Reveiz, et al, 2015)* concluded that the benefit of the use of antibiotics in the treatment of acute laryngitis in adults may not outweigh the risk of adverse effects.

In that respect the marketing authorisation holders (MAHs) are requested to address the following questions.

2. Questions

Question 1

Concerning your fusafungine containing medicinal products, please provide in the annexed table:

a) Information on type of marketing authorisation, marketing and legal status (i.e. prescription vs. non-prescription) .

b) Information included in the summary of product characteristics (SmPC) on indication(s), posology (incl. maximum daily dose and treatment duration), contraindications, warnings and precautions. Please highlight the main differences between the product information (PI) in the different EU member states.

c) An overview on sales figures for fusafungine containing products. The information on exposure should be stratified:

   i) by age: populations 30 months to 12 years, 12 to 18 years, above 18 years of age

   ii) by Member State: exposure data should also include a yearly breakdown of sales and exposure over the last 10 years for each Member State.

Question 2

Please provide all available safety information regarding hypersensitivity (i.e anaphylactic reactions including laryngospasm, angioedema) with fusafungine since the launch of medicinal product. This should include non-clinical, clinical data as well as pharmaco-epidemiological studies, published literature and CIOMS line listing. A cumulative review of all case reports (serious and non-serious) should also be provided. For this purpose, all the MedDRA Preferred Terms (PTs) within the SMQ Hypersensitivity (broad), reported for the selected suspected or interacting fusafungine-containing products should be provided. Causality assessment should be performed for serious cases and stratification by age: populations 30 months to 12 years, 12 to 18 years, above 18 years of age, when available, should be made. Possible risk factors should be discussed. Results should include analyses on age and sex of patient, indication of use, duration and dose, time to onset, outcome, seriousness, concomitant medications and illnesses, relevant medical history or any other factors.

Cases with fatal outcome should be discussed separately (cf. question 3).

Question 3

Please provide the detailed analysis of the all fatal cases for fusafungine together with causality assessment and stratification by age: populations 30 months to 12 years, 12 to 18 years, above 18 years of age.

Question 4

Please discuss the potential role of all excipients of the finished product in the development of allergic reactions.

Question 5

Please provide evidence of the therapeutic benefit and available non-clinical and clinical efficacy data of fusafungine for each approved therapeutic indication in the EU. This information should be stratified by age (populations 30 months to 12 years, 12 to 18 years, above 18 years of age).

In particular all available data on the evidence of efficacy of fusafungine when used for infections sustained by Streptococcus pyogenes or Streptococcus viridans that are present in oropharynx and may be responsible of serious complications, should be provided.

Question 6

Please discuss the potential and mechanism of fusafungine resistance.

Question 7

Please provide a benefit-risk balance evaluation of fusafungine-containing medicinal products, in each of their licensed indications. Based on the responses to the above questions, this should consider how the benefit risk-balance may differ according to age, separating the populations of 30 months to 12 years old, 12 to 18 years old, and above 18 years of age.

Please discuss the place of fusafungine-containing medicinal products among the currently available therapeutic armamentarium for patients (paediatric and adult populations) with the indicated diseases of the upper respiratory airways.

Question 8

Please provide proposals and justifications with supportive evidence for any risk minimisation measures (including changes to the SmPC/PL) which may improve the benefit/risk balance of fusafungine-containing products and how their effectiveness should be monitored.

Annex

Question 1

Member State	Product name	Pharmaceutical forms and strengths	Type of marketing authorisation	Legal status	Indications	Posology (incl. max. daily dose and treatment duration)	Contraindications	Warnings and precautions