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PRAC List of questions

To be addressed by the marketing authorisation holder(s) for medicinal products containing lactose of bovine origin for IV/IM use in acute allergic reactions

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

Procedure number: EMEA/H/A-31/1449

Active substance: methylprednisolone

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

Question 1

Concerning your IV/IM methylprednisolone-containing medicinal product(s) formulated with lactose from bovine origin and authorised for treatment of acute allergic reactions, please provide in the annexed table for this indication:

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

b) Figures on sales and patient exposure by product, member state and age. Data on the use in clinical practice including information on dose and duration of treatment.

c) Information included in the summary of product characteristics (SmPC), labelling and/or package leaflet (PL) regarding the risk of allergic reactions. Please highlight the main differences between the product(s) information (PI) in the different EU member states.

Question 2

A cumulative review of all cases (serious and non-serious) where allergic reaction or lack of efficacy/effect were reported following the IV/IM administration of the methylprednisolone medicinal product(s) containing lactose of bovine origin used in acute allergic conditions.

For this purpose, all the MedDRA Preferred Terms (PTs) within the SMQ anaphylactic reaction (broad), angioedema (broad), asthma/bronchospasm (broad), lack of efficacy/effect (broad) or hypersensitivity (narrow) reported where IV/IM methylprednisolone-containing medicinal product(s) formulated with lactose of bovine origin was used in acute allergic conditions should be provided.

Causality assessment should be performed for the serious cases and possible risk factors should be discussed. Cases should be presented in a tabulated format and narratives should be provided. The tabulation should include, but not be limited to, the following: seriousness, patient age, sex, relevant medical history (including any data about patient's allergies and data on the severity of cow's milk allergy and asthma), dose administered, time to onset, outcome and indication for the use, concomitant medications and illnesses, or any other factors. Also, if available, please provide information on re-challenge and whether the non-resolution of initial allergic reaction upon first administration led to repeated administration of the medicinal product.

Question 3

Please provide data about prevalence of cow's milk allergy in patients treated for acute allergic conditions/anaphylactic shock, stratified per age groups as relevant. Please comment on risk factors in these patient populations for developing allergic reaction and their impact on the severity/seriousness/outcome of the allergic reaction.

Question 4

Lactose contained in the concerned medicinal product complies with the European Pharmacopoeia (Ph. Eur.) monograph for lactose monohydrate which does not exclude traces of cow's milk proteins (limit test). Please discuss influence of qualitative and quantitative composition of milk proteins in your

medicinal product(s) concerned by this review on the risk for leading to allergic reaction in patients allergic to cow's milk proteins, using data from literature and/or internal data if applicable (highly sensitive assays).

Question 5

Provide a full benefit/risk assessment of IV/IM methylprednisolone-containing medicinal product(s) formulated with lactose of bovine origin in the treatment of acute allergic conditions/anaphylactic shock in the EU. This should include a discussion of the benefit and effectiveness of the product in the treatment of acute allergic conditions/anaphylactic shock as well as the clinical importance of the risk (i.e. seriousness, frequency, predictability, preventability, reversibility and impact on patients) and an assessment of the impact of its occurrence on the benefit/risk balance. Important differences in the benefit-risk balance among patient populations within the indication should also be discussed.

Question 6

Please provide details of any specific measures that may have already been taken in order to minimise the risk(s) of hypersensitivity in patients treated for allergic reaction with IV/IM medicinal products containing lactose from bovine origin and comment on the effectiveness of such measures.

Question 7

Please provide proposals and justifications for any further risk minimisation measures (including changes to the SmPC/labelling/PL) which may improve the benefit/risk balance of IV/IM medicinal products containing lactose from bovine origin for use in allergic reactions and how their effectiveness should be monitored. In addition, please comment on the possibility of manufacturing these products without traces of cow's milk proteins.

Annex

Question 1

a)

INN	Product name	Type of marketing authorisation	Marketing and legal status	Indications	Pharmaceutical forms and strengths	Sales figures	Estimated patient exposure[1]	Doses (in clinical practice)	Treatment duration (in clinical practice)

[1] Expressed in patient years and stratified by Member State, by indication and by age (<12, 12-18 and >18). Reasonable efforts should be made to obtain this information; potential sources in addition to sales data include registries and healthcare databases. If no precise data is available an estimate can be provided.

b)

PI	SmPC	PL	Main differences in SmPCs/PLs between the different EU Member States
Contraindications			
Warnings and precautions			
Undesirable effects			