28 June 2018
EMA/CHMP/346196/2018

CHMP List of questions

To be addressed by the marketing authorisation holders for bacterial lysates-containing medicinal products for respiratory conditions

Referral under Article 31 of Directive 2001/83/EC

Procedure number: EMEA/H/A-31/1465

Active substances:

Haemophilus influenzae / klebsiella pneumoniae / moraxella catarrhalis / staphylococcus aureus / streptococcus mitis / streptococcus pneumoniae / streptococcus pyogenes,

Haemophilus influenzae / klebsiella pneumoniae / moraxella catarrhalis / staphylococcus aureus / streptococcus pneumoniae / streptococcus pyogenes,

Streptococcus pneumoniae / streptococcus agalactiae / staphylococcus aureus / haemophilus influenzae,

Haemophilus influenzae / klebsiella ozaenae / klebsiella pneumoniae / moraxella catarrhalis / staphylococcus aureus / streptococcus pneumoniae / streptococcus pyogenes / streptococcus viridans,

Haemophilus influenzae / membrane fraction of klebsiella pneumoniae / ribosomal fractions of klebsiella pneumoniae / streptococcus pneumoniae / streptococcus pyogenes,

Escherichia Coli/ Klebsiella Pneumoniae / Staphylococcus Aureus / Staphylococcus Epidermidis / Streptococcus Salivarius / Streptococcus Pneumoniae/ Streptococcus Pyogenes / Haemophilus Influenzae / Corynebacterium Pseudodiphtheriticum / Moraxella Catarrhalis

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Questions

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

Question 1. Concerning your bacterial lysate-containing medicinal product(s) for respiratory diseases please provide in the annexed tables:

a) Information on type of marketing authorisation, marketing and legal status, figures on sales and patient exposure by product, member state, indication and age. Data on the use in clinical practice including information on dose, duration of treatment and concomitant treatment (characterisation of users, prescriptions).

b) The complete product information (summary of product characteristics (SmPC) and package leaflet (PL)). Please tabulate the differences between the SmPC in the different EU member states regarding 1. Name of the medicinal product, 2. Qualitative and quantitative composition, 3. Pharmaceutical form, 4.1 therapeutic indications, 4.2 posology and method of administration, 4.3 contraindications, 4.4 special warnings and precautions for use, 4.5 interaction with other medicinal products and other forms of interaction, 4.6 fertility, pregnancy and lactation 4.8 undesirable effects, 5.1 pharmacodynamic properties and 5.2 pharmacokinetic properties.

c) An overview of the approved indication(s) of bacterial lysate-containing medicinal product(s) outside the EU.

Question 2. Please provide and discuss all available evidence of the therapeutic benefit of the bacterial lysate based medicinal product indicated in respiratory diseases for each of the currently approved therapeutic indications in the EU. In this analysis, please consider all available data from any clinical trial, clinical study and published literature with each specific product. Where indications encompasses several heterogeneous disorders (e.g. upper respiratory tract infections); the MAHs should provide the above requested evidence and rationale for each specific respiratory condition included in the trials. When applicable, this information should be stratified by age, dose and concomitant treatment. Age class should be indicated as follow, if available: ≤ 6 months of age, > 6 months and ≤ 1 years of age, >1 and ≤ 6 years of age, >6 and ≤ 12 years of age, > 12 and ≤ 18 years of age, > 18 and ≤ 65 years of age and > 65 years of age.

Question 3. Please provide a tabulated system-organ-class (SOC) overview of all suspected ADR reports stratified by source (clinical trials, non-interventional studies, spontaneous reports) and seriousness, observed with each bacterial lysate-containing medicinal product for which you hold a marketing authorisation (including an analysis of adverse drug reactions (ADRs) classified by age and other relevant subgroups as appropriate) and a critical summary of reported ADRs with particular focus on immunological adverse reactions and making specific reference to (a) key safety concerns and (b) ADRs listed in the summary of product characteristics. These data should be presented by respiratory indication.

Question 4. Please also provide an analysis of all available data (e.g. from clinical trials and post-marketing) on possible therapeutic failure or disease exacerbation according to relevant criteria such as age, gender, severity of underlying disease, duration of treatment, concomitant treatment (with a

specific focus on vaccines, antibiotics, corticosteroids and bronchodilators) and concomitant/previous illness. These data should be presented by indication.

Question 5. Taking into consideration your responses to the above questions, please provide a complete and detailed benefit-risk balance assessment for each currently authorised respiratory indication(s) for your bacterial lysate-containing medicinal product(s). The impact of specific factors such as age (below 18 year of age and adults), severity of underlying disease, duration of treatment, concomitant/previous illness and concomitant treatment should also be discussed. In light of this assessment, provide any revised documentation (e.g. product information), as appropriate.

Annex

Question 1

a)

INN	Product name	Type of marketing authorisation	Marketing and legal status	Sales figures	Estimated patient exposure[1]

[1]. Expressed in patient years and stratified by Member State, by indication and by age class (see above). 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)

SmPC section	SmPC wording	List of EU Member States where authorised and main differences in SmPCs between these MS
1. Name of the medicinal product		
2. Qualitative and quantitative composition		
3. Pharmaceutical form		
4.1 therapeutic indications		
4.2 posology and method of administration		
4.3 contraindications		
4.5 special warnings and precautions for use		
4.5 interaction with other medicinal products and other forms of interaction		
4.6 fertility, pregnancy and lactation		
4.8 undesirable effects		

SmPC section	SmPC wording	List of EU Member States where authorised and main differences in SmPCs between these MS
5.1 pharmacodynamic properties		
5.2 pharmacokinetic properties		