7 May 2015
EMA/PRAC/290016/2015

PRAC List of questions

To be addressed by the marketing authorisation holders for inhaled corticosteroids (ICS) containing medicinal products indicated in the treatment of chronic obstructive pulmonary disease (COPD)

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

Procedure number: EMEA/H/A-31/1415

BiResp Spiromax EMEA/H/A-31/1415/C/003890/0006
Budesonide Formoterol Teva EMEA/H/A-31/1415/C/003951/0002
DuoResp Spiromax EMEA/H/A-31/1415/C/002348/0008
Relvar Ellipta EMEA/H/A-31/1415/C/002673/0014
Revinty Ellipta EMEA/H/A-31/1415/C/002745/0010
Vylaer Spiromax EMEA/H/A-31/1415/C/003952/0003

INNs: beclomethasone, budesonide, flunisolide, fluticasone propionate, fluticasone furoate

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1. Background

The review of inhaled corticosteroid (ICS)-containing medicines has been requested by the European Commission to evaluate the risk of pneumonia in patients with chronic obstructive pulmonary disease (COPD). The risk of pneumonia with these medicines was reviewed by the EMA Pharmacovigilance Working Party in 2010 but as new studies of individual inhaled corticosteroids and meta-analyses on the class of inhaled corticosteroids have provided further data on this risk, it was considered necessary that a thorough review be performed to further characterise this risk and that the PRAC gives a recommendation as to whether any regulatory action should be taken.

2. Questions

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

Question 1

Concerning your inhaled corticosteroid containing product indicated for the treatment of COPD, please provide:

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

b) Figures on sales and patient exposure by product, member state, indication.

c) Data on the use in clinical practice in the treatment of COPD including information on dose, duration of treatment and concomitant treatment.

d) Information included in the summary of product characteristics (SmPC) and package leaflet (PL) on posology for the treatment of COPD, and regarding the risk of pneumonia, on contraindications, warnings and precautions, undesirable effects and pharmacodynamic properties. Please highlight the main differences between the product(s) information (PI) in the different EU member states.

   The above requested information (Questions 1a to 1d) should be provided in the annexed table.

e) Details of the risk of pneumonia as captured in Module SVII of the risk management plan, if available, and information on any additional risk minimisation measures which are in place to address this risk in COPD patients; the impact of such measures should be commented upon.

f) Details of completed or ongoing pharmacovigilance activities in place to further characterise the risk of pneumonia in the COPD indication and captured in the risk management plan, if available.

Question 2

In relation to the risk of pneumonia in the COPD indication, please provide the following safety data and a critical analysis of each:

a) Data from all completed or ongoing interventional studies in the clinical development programme for your product (including the definition of pneumonia used and the tests performed to confirm a diagnosis of pneumonia);

b) Data from all epidemiological studies with your product;

c) Data from all meta-analyses and systematic reviews which refer to your product;

d) Data from any other relevant published literature concerning your product;

Question 3

a) Discuss the potential mechanisms that may underlie the development of pneumonia in patients with COPD and the influence of the ICS dose and of the co-administration with a long-acting beta agonist on this risk.

b) Please provide an overall discussion of the risk of pneumonia with your ICS product in the COPD indication taking into account the effect of dose and duration of treatment. Please comment on the possible effects of concomitant treatments (especially LABAs) and on any risks factors.

Question 4

Provide an assessment of the impact of occurrence of pneumonia on the benefit/risk balance of your product in the COPD indication and consider how the benefit/risk balance may differ according to age, dose, concomitant treatment or other identified factor.

Question 5

Based on the response provided to the above questions and if appropriate, please provide proposals and justifications for any risk minimisation measures (including changes to the SmPC/PL) which may improve the benefit/risk balance of you inhaled corticosteroids–containing medicinal product(s) indicated in the treatment of COPD and how their effectiveness should be monitored. If no risk minimisation measure is deemed necessary, justification should be provided.

Annex

Question 1

a-b-c)

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

[1]. Expressed in patient years and stratified by Member State, for the COPD indication. 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.

d)

PI	SmPC	PL	Main differences in SmPCs/PLs between the different EU Member States
Posology (incl. max. daily dose)			
Contraindications			
Warnings and precautions			
Undesirable effects			
Pharmacodynamic properties			