1 April 2016
EMA/CHMP/233295/2016

CHMP List of questions

To be addressed by the marketing authorisation holder for Symbioflor 2 (Escherichia coli bacteria (cells and autolysate)) and associated names

Article 31 of Directive 2001/83/EC

Procedure number: EMEA/H/A-31/1441

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Concerning Symbioflor 2 and associated names available on the EU market, the marketing authorisation holder (MAH) is requested to provide the following:

1. Please provide the complete product information (summary of product characteristics, labelling and package leaflet) in English. Please tabulate the differences between the product information in the different Member States as per the table in annex.

2. Information on marketing and legal status in the Member States as per the table in annex.

3. Figures on patient exposure by product and by Member State.

Efficacy

4. Please provide and discuss all available evidence of the therapeutic efficacy of Symbioflor 2 and associated names for each of the currently approved therapeutic indications in the EU. In this analysis, please consider all available data from any clinical trials and published literature with this product, in particular, all data available from randomised, controlled trials. With regards to the indication "functional gastrointestinal diseases", the current indication wording encompasses all functional gastrointestinal diseases which are heterogeneous, ranging from functional oesophageal, gastric, intestinal, biliary, pancreatic to functional anorectal disorders, with a wide range of different underlying pathophysiologies and symptomatic entities; the MAHs should provide above mentioned evidence in each of these diseases.

Safety

5. Please provide a tabulated system-organ-class (SOC) overview of all spontaneous reports observed with Symbioflor 2 and associated names (including an analysis of adverse drug reactions (ADRs) classified by age and other potentially relevant subgroups) and a critical summary of reported ADRs, making specific reference to (a) key safety concerns and (b) ADRs listed in the summary of product characteristics.

6. Please also provide an analysis of all available data (clinical trials, post-marketing data) of possible risk factors according to relevant criteria such as age, gender, potential cumulative dose, severity of underlying disease, duration of treatment, co-medications and concomitant/previous illness. These data should be presented by indication.

Benefit-risk balance

7. In light of the requested abovementioned data, please provide a justification and relevant supporting data/evidence for the maintenance of the approved therapeutic indication(s), and provide any revised documentation (e.g. product information), as appropriate.

Annex

Question 1

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			

Question 2

INN	Product name	Type of marketing authorisation	Marketing and legal status	Indications[1]	Pharmaceutical forms and strengths	Sales figures	Estimated patient exposure[2]	Doses (in clinical practice)	Treatment duration (in clinical practice)

[1]. MAH should clearly indicate for which country a specifically dedicated presentation has been granted for a particular indication
[2]. Expressed in patient years and stratified by Member State, by indication and by age (<12 and 12-18). 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.