23 July 2015
EMA/CHMP/492625/2015

CHMP List of questions

To be addressed by the marketing authorisation holder for InductOs

Article 20 of Regulation (EC) No 726/2004

InductOs EMEA/H/A-20/1422/C/0408/0082

Marketing authorisation holder: Medtronic BioPharma B.V.

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1. Background

InductOs, is a kit for implant, which consists of a powder containing the active substance, dibotermin alfa, a solvent and a matrix (absorbable collagen sponge, ACS). ACS has been classified as an excipient of InductOs. As such it is consequently inspected against EU-GMP guidelines.

The manufacturer of ACS, Integra LifeSciences Corporation (ILS), located in the third country (i.e. US), was inspected last in April 2015 by the Netherlands and Spain and found to be not compliant with the legal requirements and/or the principles and guidelines of GMP as provided for by Union law. The main concern identified was potential for particulate contamination. There is little information available regarding the nature of the contaminating particulate matter.

Consequently, the GMP certificate is withdrawn for this manufacturer which is the only one existent at present. The final statement of non-compliance was issued on 23 July 2015.

2. Questions

Questions relating to the benefit – risk

Question 1

The MAH should discuss the potential impact of the findings of the inspection of Integra LifeSciences Corporation facilities on the benefit-risk balance of InductOs. As part of this discussion the MAH should provide a detailed assessment of any safety reports or complaints that may have been collected and related to the contaminating particulate matter. Also the MAH should specifically comment on whether there is any patient population(s) for whom there is no other treatment option available.

Questions relating to the product supply and manufacturer

Question 2

The MAH is requested to provide details including timelines of the steps that have been taken or intended to undertake to ensure that the manufacturing of the ACS will be GMP compliant again. The MAH should specify corrective measures being already implemented by the current manufacturer.

Question 3

A list of batches currently available on the EU market should be presented and identify to which EU national markets these batches are distributed. The MAH should also indicate the usage per each EU member state.

Question 4

In case a shortage is foreseen, the MAH should provide the information on the following:

- anticipated shortage dates, duration and communication action plan;
- number of patients involved per EU member state;
- any on-going clinical trials that would be affected by the shortage;
- specific or vulnerable sub-populations that should be treated with the product,

which should receive priority treatment;
- forecasted demand rates and estimated stock out dates should be provided;

The MAH should discuss the need and feasibility of stock rotation between member states and any other measure needed.