31 May 2018
EMA/CHMP/274832/2018

CHMP List of questions

To be addressed by the marketing authorisation holder(s) for metamizole-containing medicinal products

Referral under Article 31 of Directive 2001/83/EC

Procedure number: EMEA/H/A-31/1469

INN: metamizole

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1. Background

Metamizole is an analgesic authorised in several member states in European Union (EU). It is indicated for severe acute and chronic pain and also for fever which is not responding to other treatments. Discrepancies were noted in the maximum daily dose and in the contraindications concerning pregnancy and breastfeeding in the products authorised in different European member states. In the view of this, the Polish Competent Authority (URPL) initiated a referral under Article 31 of Directive 2001/83/EC based on interests of the Union, and requested the CHMP to give its opinion as to whether the marketing authorisations of medicinal products containing metamizole should be varied. The scope of this procedure concerns all metamizole containing products authorised in EU, taking into consideration all pharmaceutical forms and posology.

2. Questions

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

Question 1

Concerning the metamizole -containing medicinal products the MAHs are requested to provide in the annexed table:

- Figures on sales and patient exposure by product, member state, indication and age.
- Information on the use in clinical practice including information on dose, duration of treatment and use during pregnancy and lactation.

Question 2

Information included in the summary of product characteristics (SmPC) and package leaflet (PL) on single dose and maximum daily dose depending on weight or age, on contraindications concerning pregnancy and lactation, and use in pregnancy and lactation. Please highlight the main differences between the product(s) information (PI) in the different EU member states (using the Annexed table).

Question 3

The MAHs are requested to provide all relevant available data regarding the single dose and maximum daily dose depending on weight or age for all metamizole -containing medicinal products.

Question 4

The MAHs are requested to provide all data available (including data from clinical trials, spontaneous reports, epidemiological studies, published literature, clinical guidelines and any other relevant data) regarding the use in pregnancy and lactation for metamizole -containing medicinal products.

Question 5

Based on the responses to previous questions, the MAHs should propose potential changes to the summary of product characteristics and package leaflet, with the aim to provide balanced information on single dose and maximum daily dose and minimise any potential risk to pregnant or lactating women and other possible safety issues in this population.

Please also comment on how the impact of such measures should be monitored and assessed.

Annex

Question 1

INN	Product name	Pharmaceutical forms and strengths	Sales figures	Estimated patient exposure[1]	Doses (as approved and used in clinical practice)	Treatment duration (as approved and used in clinical practice)	Use in pregnancy and breastfeeding (as per clinical practice)

[1]. Expressed in patient years and stratified by Member State, by indication and by age (e.g. <12, 12-18 and adults). 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.

Question 2

PI	SmPC	PL	Main differences in SmPCs/PLs between the different EU Member States (if relevant)
Single dose and maximum daily dose depending on weight or age			
Contraindications			
Pregnancy and lactation			