29 May 2019
EMA/CHMP/285881/2019

CHMP List of questions

To be addressed by the applicants /marketing authorisation holders for methocarbamol/paracetamol-containing medicinal products

Referral under Article 31 of Directive 2001/83/EC

Procedure number: EMEA/H/A-31/1484

INN/active substance: methocarbamol/paracetamol

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1. Background

On 27 May 2019, EMA received a notification from Germany (BfArM) requesting the initiation of an Article 31 procedure for the fixed dose combination methocarbamol/paracetamol, based on concerns on efficacy (due to the dose of methocarbamol and role of paracetamol in the combination) and potential interactions between its active ingredients leading to potential safety risks. In the EU/EEA the combination is only authorised in Spain (since 1968), for use in the short-term, symptomatic treatment of painful muscle spasms associated with acute musculoskeletal disorders. The above concerns arose during the assessment of generic marketing authorisation applications (MAAs) referencing the Spanish marketing authorisation that are currently under assessment in UK and Germany.

2. Questions

The applicant(s) and marketing authorisation holder(s) are requested to address the following questions:

Question 1

Concerning your methocarbamol/paracetamol–containing medicinal product(s) for oral use in painful muscle spasms associated with acute musculoskeletal disorders please provide in a table information on type of marketing authorisation, marketing and legal status and an overview of the approved indication(s). Please also provide figures on sales by product and by member state.

Question 2

Please provide scientific evidence related to the therapeutic efficacy of methocarbamol/paracetamol-containing medicinal products for oral use in painful muscle spasms associated with acute musculoskeletal disorders, in particular in the authorised dose (380 mg/300 mg). New scientific evidence deriving from a Cochrane Review[1] which raise concerns with regard to the efficacy of paracetamol in low back pain should be discussed, including its impact on efficacy of your combination medicinal product(s), as it is labelled.

Question 3

Please provide scientific evidence related to the safety of methocarbamol/paracetamol-containing medicinal products for oral use in painful muscle spasms associated with acute musculoskeletal disorders. The risk of interactions, especially an increase of the toxic metabolite of paracetamol N-Acetyl-p-benzoquinoneimine should be discussed taking into account that both substances are metabolized in the liver and conjugated to glucuronic and sulfuric acid.

Question 4

Provide a full benefit-risk assessment of methocarbamol/paracetamol-containing medicinal product(s) for oral use in short-term, symptomatic treatment of painful muscle spasms associated with acute musculoskeletal disorders. This should include an assessment of the impact of the results of the above mentioned published review on the benefit-risk balance in treatment of painful muscle spasms associated with acute musculoskeletal disorders.

[1] Saragiotto BT1, Machado GC, Ferreira ML, Pinheiro MB, Abdel Shaheed C, Maher CG. Paracetamol for low back pain. Cochrane Database Syst Rev. 2016 Jun 7;(6):CD012230.

Question 5 (to originator MAH only)

Please provide an English translation of the Product Information (Summary of Product Characteristics and Package Leaflet).