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PRAC List of questions

To be addressed by the marketing authorisation holder(s) for bromocriptine-containing medicinal products indicated in the "*prevention or suppression of physiological lactation in the immediate post-partum period and in the late post-partum period*"

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

Procedure number: EMEA/H/A-31/1379

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Marketing authorisation holders (MAHs) are requested to provide the following:

Question 1

Concerning your bromocriptine-containing product(s) indicated in the prevention or suppression of physiological lactation post-partum, MAHs are requested to provide the following information:

a) The current marketing status in the European Union including information about the indication(s) related to post-partum or post-abortum inhibition of lactation. In addition, MAHs should clearly indicate for which country a specifically dedicated presentation has been granted for this indication (e.g. specific presentation in France for the inhibition of lactation).

b) The posology, treatment duration, contraindications, warnings and precautions and undesirable effects included in the summary of products characteristics (SmPC) and the package leaflet regarding the risk of cardiovascular, neurological and psychiatric adverse events. Main differences between SmPCs/PLs in the different EU Member States should be tabulated as indicated in the annexed tables.

c) The estimated patient exposure in the different EU Member States for the indication prevention or suppression of physiological lactation post-partum (in number of treatments per year) by country in 2012 (method used for estimation should be explained and detailed) should be tabulated as indicated in the annexed tables.
The estimated target population (women between 15 and 49 years, in the post-partum) by country should also be provided. Finally, information on treatment dose and treatment duration used should be provided, if available.

d) An overview of the current national/European/international guidelines/recommendations on inhibition of lactation.

e) Worldwide, the countries where the indication was withdrawn for safety reasons, and the rationale for such a decision.

Question 2

The MAHs should provide an analysis of all available safety data relevant for the indication in inhibition or suppression of lactation for each safety concern: cardiovascular adverse events, neurological adverse events and psychiatric adverse events with a specific discussion on all fatal outcomes.

These analyses should include comprehensive cumulative reviews of data from clinical trials (including both MAH sponsored and non-sponsored studies), pharmacoepidemiological studies, published literature and spontaneous reporting (including discussion on causality). They should also properly consider how the occurrence of these ADRs is influenced by treatment dose, treatment duration and/or respect of dose titration.

An evaluation of compliance with SmPC recommendations (4.2) and the proportion of all cases of cardiovascular, neurological and psychiatric adverse events reported in patients with an identified listed contraindication or precaution/risk factor (as listed in sections 4.3 and 4.4 of the SmPC) should be submitted.

CIOMS forms for all cases reported during the postmarketing period in the indication prevention or suppression of physiological lactation post-partum should be provided and the number of adverse drug reactions should also be presented in a summary tabulation. The coding of adverse events should be based on the Medical Dictionary for Regulatory Activities (MedDRA) and presented by Preferred Term (PT) sorted by System Organ Class (SOC).

Question 3

All available data on the efficacy of bromocriptine in the prevention or suppression of physiological lactation post-partum from clinical studies and all other available data sources (including post-marketing data) should be provided.

Question 4

In light of the responses to question 2 (safety concerns) and 3 (efficacy), the MAHs should discuss the benefit/risk balance of their product(s) in the indication prevention or suppression of physiological lactation in the post-partum period.

Question 5

a) The MAHs should provide details of any specific measures that have already been taken in order to minimise the risk of cardiovascular, neurological and psychiatric adverse events in users of their medicinal product(s) and comment on the impact of such measures.

b) In addition, the MAHs should consider additional proposals for any complementary measures to further minimise the risks of bromocriptine-containing medicinal products authorised in the prevention or suppression of physiological lactation post-partum, including changes to the SmPC and package leaflet.

TABULATION

Question 1

a)

INNs	Product name	Indication(s)	Type of marketing authorisation	Strength	Pharmaceutical form	Route of administration	Marketing status

Contra-indications (SmPC)	Warnings and precautions (SmPC)	Undesirable effects (SmPC)	Contra-indications (PIL)	Warnings and precautions (PIL)	Undesirable effects (PIL)	Main differences between the SmPC/PIL in the different EU Member States

b)

INNs	Product name	Country	Sales figures	Estimated patient exposure (in number of treatment per year)	Estimated target population (women between 15 and 49 years, in the post-partum)