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

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

Bromocriptine-containing medicinal products for oral use indicated in post-partum inhibition of lactation

INN: bromocriptine

## Divergent statement

The undersigned members of the CMDh do not agree with the CMDh's position endorsing the PRAC recommendation on the variation to the Marketing Authorisation of oral bromocriptine-containing products authorised in the indication post-partum inhibition of lactation.

The reasons for this divergent position rely on a disagreement with the proposed regulatory actions, focused on the indication and the risk minimisation measures adopted and are as follows:

- physiological nature of post-partum lactation, which ceases in one to two weeks if the infant is not put to the breast;
- bromocriptine efficacy for lactation inhibition in the late post-partum period has not been demonstrated and bromocriptine use is not pharmacologically justified due to the physiological lactation process;
- the role of bromocriptine in serious and fatal cases of cardiovascular, cerebrovascular, neurologic and psychiatric disorders occurred during bromocriptine administration cannot be ruled out, as agreed also by the PRAC;
- a high number of reported cases of use failed to comply with the contraindications, warnings and posology of bromocriptine containing products;
- use for "medical reason only" is already mentioned in most of indication section of the EU SmPCs.
- risks of cardiovascular, cerebrovascular, neurologic and psychiatric disorders are already described in EU SmPCs;
- reinforcement of the SmPC in France in 1994 of the bromocriptine containing-products was insufficient to limit cardiovascular, cerebrovascular, neurologic and psychiatric disorders and misuse;
- the indication lactation inhibition was withdrawn by Canada in 1994 and by the FDA in 1995 for safety concerns (mainly cardiovascular and neuro-vascular events), and it was also withdrawn afterwards by Italy and some Arabic countries on the basis of similar concerns;
- alternative pharmacological treatments are authorised in Europe.

Taking all these aspects into account, the undersigned members of the CMDh considered that risk minimisation measures proposed by the PRAC and endorsed by the CMDh (e.g. amendments and harmonisation of the bromocriptine containing-products SmPCs through EU) are not sufficient to mitigate the risks of cardiovascular, cerebrovascular, neurologic and psychiatric disorders associated with the oral use of bromocriptine in post-partum inhibition of lactation and therefore considered that the benefit/risk ratio of bromocriptine in this indication is negative. Thus, they propose the withdrawal of all oral bromocriptine-containing products authorised in this indication.

**CMDh member expressing a divergent position:**

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| Virginie Bacquet (FR) | 20 August 2014 | Signature: ……..... |
| Sandra Petraglia (IT) | 20 August 2014 | Signature: ……..... |