Annex II

Scientific conclusions and grounds for positive opinion

Scientific conclusions

Overall summary of the scientific evaluation of Tibocina and associated names (see Annex I)

Tibolone is a synthetic steroid hormone drug which acts as an agonist, mainly on oestrogen receptors. Two applications under the decentralised procedure were submitted for the generic products Tibolona Aristo and Tibocina, both 2.5 mg tablets with the indication “treatment of oestrogen deficiency symptoms in women, more than one year after the menopause”. A single bioequivalence study was conducted to support both applications. During the assessment of the application dossiers, a Good Clinical Practice (GCP) inspection of the clinical site identified a lack of evidence documenting the transfer date and time and the identification of pharmacokinetic samples from the dry ice box used for flash freezing to the freezer used at this site until the samples were transferred to the bioanalytical site. These findings were classified as critical and one of the concerned member states therefore considered it impossible to conclude on the reliability of the bioequivalence study. A referral under Article 29(4) of Directive 2001/83/EC was triggered and the CHMP was requested to give its opinion on whether the proposed products Tibolona Aristo and Tibocina can be considered bioequivalent to the reference product.

The CHMP acknowledged that the findings are considered as a critical deficiency, however it did not consider that GCP inspection findings classified as critical should automatically invalidate the results of a bioequivalence study. Such decisions should instead be taken on a case by case basis, following an evaluation of the findings and their potential impact. The CHMP therefore reviewed the additional clinical evidence available, including the assessment carried out during the CMDh procedure and the evidence submitted by the Applicant.

Having reviewed the available data, the CHMP considered that there was sufficient additional evidence indicating that the study samples were not put at risks during the study and that these were maintained under adequate temperature conditions. In addition, the bioequivalence study conducted demonstrated bioequivalence, with observed drug concentrations being comparable or superior to those reported in the literature and the CHMP considered that these results suggest that no significant degree of drug degradation occurred.

The CHMP therefore concluded that while deviations from GCP requirements were identified, the totality of the available evidence confirms that the results of the bioequivalence study are reliable and demonstrates the bioequivalence of the proposed products and the reference product.

Grounds for positive opinion

Whereas

- the CHMP reviewed the available data, including the Rapporteurs’ assessment reports and the explanations submitted by the Applicant during the CMDh procedure
- the CHMP considered that the available data confirms that the results of the bioequivalence study are reliable and demonstrate the bioequivalence of the proposed products and the reference product

the CHMP has recommended the granting of the marketing authorisations for which the summary of product characteristics, labelling and package leaflet remain as per the final versions achieved during the Coordination group procedure as mentioned in Annex III for Tibocina and associated names (see Annex I).