OFFICE OF CLINICAL PHARMACOLOGY (OCP) ADDENDUM

NDA: 021945/ SD # 51 Submission Date(s): 07/12/2010, 02/03/2011
Brand Name Makena®
Generic Name 17-a Hydroxyprogesterone Caproate
Reviewer Sandhya Apparaju, Ph.D.
Team Leader Myong Jin Kim, Pharm.D.
OCP Division Division of Clinical Pharmacology 3
OND Division Division of Reproductive and Urologic Products
Sponsor Hologic Inc.
Submission Type Resubmission/Class 2
Formulation; Strength(s) Injection for intramuscular use; 250 mg/mL
Indication Prevention of Preterm Birth

Recommendation: NDA 021945 is acceptable from a Clinical Pharmacology perspective.

Post-Marketing Commitments (PMCs): The following Clinical Pharmacology PMCs will be communicated to the sponsor in the NDA action letter:

- To submit an academic publication of pharmacokinetic data on hydroxyprogesterone caproate and metabolites in plasma and urine of pregnant women throughout different stages of gestation:
  Final Report Submission December 2011

- If the publication described in the above PMC is not submitted by December 31, 2011, or if the results from the publication do not include all the relevant findings (e.g., urinary metabolites), you will conduct the following clinical trial:
  o A non-randomized clinical pharmacokinetic trial of hydroxyprogesterone caproate and its metabolites in pregnancy. This study will provide data characterizing the pharmacokinetics of hydroxyprogesterone caproate and its metabolites in plasma and urine throughout different stages of gestation.
    Final Protocol Submission June 2012
    Trial Completion Date June 2014
    Final Report Submission November 2014

- To conduct a nonclinical in vitro study using human hepatocytes to determine whether HPC induces or alters the metabolic activities of CYP1A2, CYP2A6, and CYP2B6:
  Final Protocol Submission June 2011
  Study Completion Date March 2012
  Final Report Submission July 2012

Labeling: The revised labeling for Makena as submitted on 02/03/2011 is acceptable from a Clinical Pharmacology perspective.
This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

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02/03/2011

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02/03/2011
Division Director Concurrence

Reference ID: 2900206