

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- α 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:
 - 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.

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/s/

SANDHYA K APPARAJU
02/03/2011

MYONG JIN KIM
02/03/2011

EDWARD D BASHAW
02/03/2011
Division Director Concurrence