The committee will discuss supplemental new drug application (sNDA 021945/S-023) for MAKENA (hydroxyprogesterone caproate injection, 250 milligrams per milliliter) manufactured by AMAG Pharmaceuticals. In 2011, MAKENA received approval under the accelerated approval pathway (21 CFR part 314, subpart H, and section 506(c) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 356(c)) for reducing the risk of preterm birth in women with a singleton pregnancy who have a history of singleton spontaneous preterm birth. MAKENA was shown in the preapproval clinical trial to reduce the proportion of women who delivered at less than 37 weeks gestation, a surrogate endpoint that FDA determined was reasonably likely to predict a clinical benefit of preterm birth prevention, such as improved neonatal mortality and morbidity. As required under 21 CFR 314.510, the Applicant conducted a postapproval confirmatory clinical trial to verify and describe clinical benefit. AMAG Pharmaceuticals has disclosed that this completed confirmatory trial did not demonstrate a statistically significant difference between the treatment and placebo arms for the co-primary endpoints of reducing the risk of recurrent preterm birth or improving neonatal mortality and morbidity. The committee will consider the trial’s findings and the sNDA in the context of AMAG Pharmaceuticals’ confirmatory study obligation.

8:15 a.m. Call to Order and Introduction of Committee
Vivian Lewis, MD
Chairperson, BRUDAC

8:25 a.m. Conflict of Interest Statement
Kalyani Bhatt, BS, MS
Designated Federal Officer, BRUDAC

8:30 a.m. FDA Opening Remarks
Christine Nguyen, MD
Deputy Director for Safety
Division of Bone, Reproductive and Urologic Products (DBRUP)
Office of Drug Evaluation III (ODE III)
Office of New Drugs (OND), CDER, FDA

8:45 a.m. APPLICANT PRESENTATIONS
AMAG Pharmaceuticals, Inc.

Introduction
Julie Krop, MD
Chief Medical Officer
Executive Vice President, Development & Regulatory Affairs
AMAG Pharmaceuticals, Inc.

Clinical Background and Unmet Need
Michelle Owens, MD
Professor and Medical Director
School of Medicine
Department of Obstetrics and Gynecology
The University of Mississippi Medical Center
APPLICANT PRESENTATIONS (CONT.)

Meis Study Design and Results
   Baha Sibai, MD
   Professor
   Department of Obstetrics, Gynecology, and Reproductive Sciences
   Investigator, MFMU
   University of Texas Health Science Center of Houston
   MFMU¹ Network

PROLONG: Efficacy and Safety
   Laura Williams, MD, MPH
   Sr. Vice President, Clinical Development & Biostatistics
   AMAG Pharmaceuticals, Inc.

Prevention of Preterm Birth:
   Clinical Perspective
   Sean Blackwell, MD
   Professor and Chair
   Department of Obstetrics, Gynecology, and Reproductive Sciences
   Principal Investigator, MFMU
   University of Texas Health Science Center of Houston
   MFMU¹ Network

Conclusion
   Julie Krop, MD

10:00 a.m.  Clarifying Questions to Applicant
10:25 a.m.  BREAK
10:35 a.m.  FDA PRESENTATIONS

Clinical Overview
   Barbara Wesley, MD, MPH
   Medical Officer
   DBRUP, ODEIII, OND, CDER, FDA

Efficacy in Confirmatory Trial 003
   Jia Guo, PhD
   Statistical Reviewer
   Division of Biometrics 3 (DB3)
   Office of Biostatistics (OB)
   Office of Translational Sciences (OTS), CDER, FDA

Hydroxyprogesterone Caproate (HPC)
   Utility in the United States
   Huei-Ting Tsai, PhD
   Epidemiologist
   Division of Epidemiology II (DEPI-II)
   Office of Pharmacovigilance and Epidemiology (OPE)
   Office of Surveillance and Epidemiology (OSE)
   CDER, FDA
FDA PRESENTATIONS (cont.)

Summary Remarks

Christina Chang, MD, MPH
Clinical Team Leader
DBRUP, ODEIII, OND, CDER, FDA

11:40 a.m. Clarifying Questions to FDA

12:00 p.m. LUNCH

1:00 p.m. OPEN PUBLIC HEARING

2:00 p.m. Clarifying Questions to Applicant or FDA

2:20 p.m. BREAK

2:30 p.m. Questions to the Committee/Committee Discussion and Voting

5:00 p.m. ADJOURNMENT