

**FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)**

Bone, Reproductive and Urologic Drugs Advisory Committee (BRUDAC) Meeting
FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
October 29, 2019

AGENDA

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

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AGENDA (cont.)

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)
Utilization 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

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AGENDA (cont.)

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**