

**Food and Drug Administration  
Center for Drug Evaluation and Research**

Summary Minutes of the  
Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and  
Risk Management Advisory Committee  
November 1, 2017

Location: FDA White Oak Campus, Building 31 Conference Center, The Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland

Topic: The committees discussed new drug application (NDA) 210136, buprenorphine subcutaneous injection, submitted by Braeburn Pharmaceuticals, Inc., for treatment of opioid dependence.

These summary minutes for the November 1, 2017 joint meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee Meeting of the Food and Drug Administration were approved on December 4, 2017.

I certify that I attended the November 1, 2017 Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/S/

\_\_\_\_\_  
Kalyani Bhatt,  
*Designated Federal Officer, PDAC*

/S/

\_\_\_\_\_  
Rajesh Narendran, MD,  
*Chairperson, PDAC*

November 1, 2017

Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee Meeting

***Summary Minutes***

***Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee Meeting***

**November 1, 2017**

The following is a final report of the joint meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee held on November 1, 2017. A verbatim transcript will be available in approximately six weeks, sent to the Division of Anesthesia, Analgesic, and Addiction Products and the Office of Safety and Epidemiology and posted on the FDA website at:

<https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PsychopharmacologicDrugsAdvisoryCommittee/ucm535446.htm> and

<https://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm536632.htm>.

All external requests for the meeting transcript should be submitted to the CDER Freedom of Information Office.

The meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research, met jointly on November 1, 2017, at the FDA White Oak Campus, Building 31, The Great Room (Rm. 1503), White Oak Conference Center, Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the background materials from the FDA, and from Braeburn Pharmaceuticals, Inc. The meeting was called to order by Rajesh Narendran, MD (Chairperson). The conflict of interest statement was read into the record by Kalyani Bhatt, BS, MS (Designated Federal Officer). There were approximately 210 people in attendance for the meeting. There were 13 Open Public Hearing speakers.

**Issue:** The committees discussed new drug application (NDA) 210136, buprenorphine subcutaneous injection, submitted by Braeburn Pharmaceuticals, Inc., for treatment of opioid dependence.

**Attendance:**

**Psychopharmacologic Drugs Advisory Committee Members Present (Voting):** Satish Iyengar, PhD; Rajesh Narendran, MD (Chairperson); David Pickar, MD; Erick H. Turner, MD; Kim O. Witzczak (Consumer Representative)

**Psychopharmacologic Drugs Advisory Committee Members Not Present (Voting):** Walter S. Dunn, MD, PhD; Jess G. Fiedorowicz, MD, PhD; Felipe A. Jain, MD; Jessica J. Jeffrey, MD, MPH, MBA

**Psychopharmacologic Drugs Advisory Committee Members Present (Non- Voting):** Robert Russell Conley, MD (Industry Representative)

November 1, 2017

Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee Meeting

**Drug Safety and Risk Management Advisory Committee Members Present (Voting):**

Denise M. Boudreau, PhD, RPh; Laurel A. Habel, MPH, PhD; Steven B. Meisel, PharmD; Suzanne B. Robotti (Consumer Representative); Anne-Michelle Ruha, MD, FACMT; Almut Winterstein, RPh, PhD, FISPE

**Drug Safety and Risk Management Advisory Committee Members Not Present (Voting):**

Kelly Besco, PharmD, FISMP, CPPS; Niteesh K. Choudhry, MD, PhD; Christopher H. Schmid, PhD; Soko Setoguchi, MD, DrPh; Terri L. Warholak, PhD, RPh, CPHQ, FAPhA

**Drug Safety and Risk Management Advisory Committee Members Not Present (Non-Voting):**

Linda Scarazzini, MD, RPh (Industry Representative)

**Temporary Members (Voting):**

G. Caleb Alexander, MD, PhD; Kathleen T. Brady, MD, PhD; Chester Buckenmaier, II, MD; Melinda Campopiano, MD; Kathleen M. Carroll, PhD; Daniel Ciccione, MD, MPH; Adam J. Gordon, MD, MPH, FACP, FASAM; Daniel L. Krinsky, MS, RPh; Sabrina Numann (Patient Representative)

**FDA Participants (Non-Voting):** Sharon Hertz, MD; Rigoberto Roca, MD; Celia Winchell, MD; Judy Staffa, PhD, RPh; Cynthia LaCivita, PharmD; Dominic Chiapperino, PhD

**Open Public Hearing Speakers:** Michelle Rapoza (Stanley Street Treatment and Resources); Kelly Corredor (American Society of Addiction Medicine); James G Sullivan, MD (Parkway Medical Center); General Barrye L. Price, U.S. Army, Retired, PhD (Community Anti-Drug Coalitions of America (CADCA)); Katie Donovan; Raj Shiwach, MD (InSite Clinical Research, LLC); Kyle Kampman, MD (Department of Psychiatry, Perelman School of Medicine University of Pennsylvania, Center for Studies of Addiction); Megan Polanin, PhD (National Center for Health Research (NCHR)); Jamie Boyer; Joshua Kanas; Dr. Andrea Barthwell (Female Opioid Research and Clinical Experts (FORCE)); Larysa Martin Reifinger; Ayeisha A. Cox (Center for Lawful Access and Abuse Deterrence (CLAAD)); statement read by Dr. Andrea Barthwell)

***The agenda was as follows:***

Call to Order and Introduction of Committee

**Raj Narendran, MD**  
Chairperson, PDAC

Conflict of Interest Statement

**Kalyani Bhatt, MS**  
Designated Federal Officer, PDAC

FDA Opening Remarks

**Celia Winchell, MD**  
Clinical Team Leader  
Division of Anesthesia, Analgesia, and Addiction Products (DAAAP)  
Office of Drug Evaluation II (ODE II)  
Office of New Drugs (OND), CDER, FDA

November 1, 2017

Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee Meeting

**APPLICANT PRESENTATIONS**

**Braeburn, Pharmaceuticals, Inc.**

Introduction

**Susan Franks, MS**  
SVP and Head of Regulatory Affairs  
Braeburn Pharmaceuticals, Inc.

Unmet Need

**Michelle Lofwall, MD, DFASAM**  
Associate Professor, Behavioral Science and  
Psychiatry, Center for Drug and Alcohol Research,  
University of Kentucky

Clinical Pharmacokinetics

**Fredrik Tiberg, PhD**  
President and CEO Head of Research and  
Development, Camurus AB

Efficacy: Opioid Challenge Study

**Sharon Walsh, PhD**  
Director, Center of Drug and Alcohol Research  
University of Kentucky

Efficacy and Safety: Phase 3 Studies

**Sonnie Kim, PharmD**  
Chief Scientific Officer  
Braeburn Pharmaceuticals, Inc.

Clinical Perspective

**Michael Frost, MD, FACP, FASAM**  
President/Medical Director  
The Frost Medical Group, LLC

Clarifying Questions

**BREAK**

**FDA PRESENTATIONS**

Clinical Overview

**Gioia Guerrieri, DO**  
Clinical Reviewer  
DAAAP, ODE II, OND, CDER, FDA

Blockade Study: Analyses and Issues

**Qianyu Dang, PhD**  
Lead Statistician  
Division of Biostatistics VI, Office of Biostatistics  
(OB) Office of Translational Sciences (OTS)  
CDER, FDA

November 1, 2017

Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee Meeting

Blockade Study: Pharmacokinetic-  
Pharmacodynamic Analyses of Drug  
Liking

**Michael Bewernitz, PhD**  
Pharmacometrics Reviewer  
Division of Pharmacometrics  
Office of Clinical Pharmacology  
OTS, CDER, FDA

Clinical and Statistical Review

**James Travis, PhD**  
Statistics Reviewer  
Division of Biostatistics II, OB, OTS, CDER, FDA

**Gioia Guerrieri, DO**

Proposed Risk Evaluation and  
Mitigation Strategies (REMS) for RBP-  
6000

**Somya Dunn, MD**  
Commander, United States Public Health Service  
RISK Management Analyst  
Division of Risk Management  
Office of Surveillance and Epidemiology  
CDER, FDA

Clarifying Questions

**LUNCH**

**OPEN PUBLIC HEARING**

Charge to the Committee

**Sharon Hertz, MD**  
Director  
DAAAP, ODEII, OND, CDER, FDA

Questions to the Committee/Committee Discussion

**BREAK**

Questions to the Committee/Committee Discussion (cont.)

**ADJOURNMENT**

*Questions to the Committee:*

- 1. DISCUSSION:** Discuss whether the provided safety data sufficiently support the use of all of the proposed doses and formulations of CAM2038, given that the steady-state plasma exposures associated with some doses/formulations exceed those associated with the highest labeled dose of the reference product, Subutex? If not, describe which doses have adequate safety data.

**Committee Discussion:** *The majority of the committee members agreed that unsafe side effects were not observed with CAM2038. A few members commented that the clinical trial design mimics real world practice and is reflective of an effectiveness rather than efficacy trial, which should predict its success in treating opioid use disorders. However, other members disagreed and commented that the inherent design of the clinical trial, which did not allow for the collection of highly controlled data to predict the safety and efficacy of the CAM2038 doses investigated, was disappointing and a drawback. The members also were unclear about how seeing more data will change the risk vs. benefit ratio with respect to what we know already based on the experience with sublingual buprenorphine. Several members voiced concern that one cannot conclude the highest doses were safe. In addition, concerns about the lack of real time longitudinal data (beyond 3 months) were raised by some members. Please see the transcript for details of the committee discussion.*

2. **DISCUSSION:** Discuss whether the provided safety data sufficiently support the proposed indefinite use of both the weekly and monthly formulations.

**Committee Discussion:** *Most members of the committee agreed that the data is sufficient to support its use in a chronic disease. One member commented that the pragmatic trial design gives confidence that it can be administered in a chronic disease and that 6 months seems reasonable. However, some members disagreed, and stated that the lack of long term data especially for the highest doses to which very few individuals were exposed is a concern. Other noted that there are some concerns with respect to elevated liver function tests (LFTs) and there needs to be more frequent LFT monitoring at higher doses. In addition, several committee members thought there was a need for more information on the removal of the depot dose and the potential medical and surgical complications that may arise from it. Please see the transcript for details of the committee discussion.*

3. **VOTE: Do the provided safety data support:**

- A) all of the proposed doses
- B) some of the proposed doses
- C) none of the proposed doses

**A:1**

**B:17**

**C:2**

**Abstain: 0**

**Committee Discussion:** *The majority of the committee members agreed that safety data support some of the proposed doses for the above stated reasons (see answers to question #2). Please see the transcript for details of the committee discussion.*

4. **VOTE:** Do the data from the clinical trial, taken together with the results of the blockade study, provide substantial evidence of effectiveness of CAM2038 weekly and monthly

formulations for the treatment of opioid use disorder in patients who are newly initiating buprenorphine treatment for:

- A) all of the proposed doses
- B) some of the proposed doses
- C) none of the proposed doses

**A: 2**

**B: 17**

**C:1**

**Abstain: 0**

**Committee Discussion:** *The majority of the committee members voted that the data from the clinical trial, taken together with the blockade study, provide substantial evidence of effectiveness of CAM2038 weekly and monthly formulations for the treatment of opioid use disorder in patients who are newly initiating buprenorphine treatment for some of the doses (for stated reasons see answers to question #1). Please see the transcript for details of the committee discussion.*

**5. DISCUSSION:** Discuss the pros and cons of the restricted distribution under a Risk Evaluation and Mitigation Strategy (REMS) to mitigate the risks that might ensue from direct distribution of CAM2038 to patients.

- a. What barriers to access may arise from implementing a restricted distribution system?
- b. What systemic or institutional barriers might be anticipated for a restricted distribution system?
- c. What modifications might address barriers to access while mitigating risk?
- d. Is the proposed REMS sufficient, or are other measures needed?

**Committee Discussion:** *The majority of the committee members agreed and supported the need for the FDA's proposed addition to the REMS to include a one-time certification of health care settings that order and dispense CAM2038 to put systems in place from being dispensed directly to the patient. Some members commented that it may be too difficult to implement the REMS from a policy standpoint because of differences in State laws. The members also noted that the need for community pharmacists to be aware of patients use of CAM2038 via sharing of medication lists. Some members had reservations about the drug being dispensed to providers for administration to patients in a pre-filled syringe, questioning whether that presentation would increase the risk for abuse by intravenous injection. Please see the transcript for details of the committee discussion.*

November 1, 2017

Joint Meeting of the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee Meeting

**6. VOTE:** Do you recommend approval of this application?

- A) all of the proposed doses
- B) some of the proposed doses
- C) none of the proposed doses

**A: 0                      B: 17    C: 3                      Abstain: 0**

***Committee Discussion:*** *The majority of the committee members recommended approval for some of the proposed doses. The committee members voting “C” expressed concerns over the trial design being problematic, and limited clinical data. Please see the transcript for details of the committee discussion.*

*The meeting was adjourned at approximately 3:36 p.m.*