Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee Joint Meeting
June 7, 2016

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

Topic: The committees were asked to discuss new drug application (NDA) 207975, hydrocodone bitartrate extended-release tablets, submitted by Teva Branded Pharmaceutical Products R&D, Inc., with the proposed indication of management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The product is an extended-release formulation intended to have abuse-deterrent properties based on its physicochemical properties. The committees were asked to discuss whether the data submitted by the Applicant are sufficient to support labeling of the product with the properties expected to deter abuse.

These summary minutes for the June 7, 2016, joint meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee of the Food and Drug Administration were approved on July 18, 2016.

I certify that I attended the June 7, 2016, joint meeting of the Anesthetic and Analgesic Drug Products 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/	/s/
Stephanie L. Begansky, PharmD	Raeford Brown, MD
Designated Federal Officer, AADPAC	Acting Chairperson, AADPAC

Summary Minutes of the
Joint Meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee
June 7, 2016

The following is a final report of the joint meeting of the Anesthetic and Analgesic Drug Products Advisory Committee and the Drug Safety and Risk Management Advisory Committee, held on June 7, 2016. A verbatim transcript will be available in approximately six weeks, sent to the Division of Analgesia, Anesthesia and Addiction Products and the Office of Safety and Epidemiology and posted on the FDA website at: http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/AnestheticAndAnalgesicDrugProductsAdvisoryCommittee/ucm486848.htm and http://www.fda.gov/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/DrugSafetyandRiskManagementAdvisoryCommittee/ucm486856.htm

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

The Anesthetic and Analgesic Drug Products 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 June 7, 2016, at the FDA White Oak Campus, 10903 New Hampshire Avenue, Building 31 Conference Center, the Great Room (Rm. 1503), Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Teva Branded Pharmaceutical Products R&D, Inc. The meeting was called to order by Raeford Brown, MD, FAAP (Acting Chairperson). The conflict of interest statement was read into the record by Stephanie Begansky, PharmD (Designated Federal Officer). There were approximately 100 people in attendance. There were 2 Open Public Hearing (OPH) speaker presentations.

Issue: The committees were asked to discuss new drug application (NDA) 207975, hydrocodone bitartrate extended-release tablets, submitted by Teva Branded Pharmaceutical Products R&D, Inc., with the proposed indication of management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate. The product is an extended-release formulation intended to have abuse-deterrent properties based on its physicochemical properties. The committees were asked to discuss whether the data submitted by the Applicant are sufficient to support labeling of the product with the properties expected to deter abuse.

Attendance:

Anesthetic and Analgesic Drug Products Advisory Committee Members Present (Voting): Brian T. Bateman, MD, MSc; Raeford E. Brown, Jr., MD, FAAP (Acting Chairperson); Charles W. Emala Sr., MS, MD; Jennifer G. Higgins, PhD (Consumer Representative); Abigail B. Shoben, PhD

Anesthetic and Analgesic Drug Products Advisory Committee Members Not Present (Voting): David S. Craig, PharmD; Jeffrey L. Galinkin, MD, FAAP; Anita Gupta, DO, PharmD; Rafael V. Miguel, MD

Anesthetic and Analgesic Drug Products Advisory Committee Member Present (Non-Voting): W. Joseph Herring, MD, PhD (Industry Representative)

Drug Safety and Risk Management Advisory Committee Members Present (Voting): Kelly Besco, PharmD, FISMP, CPPS; Niteesh K. Choudhry, MD, PhD; Tobias Gerhard, PhD, RPh

Drug Safety and Risk Management Advisory Committee Members Not Present (Voting): Christopher H. Schmid, PhD; Andy S. Stergachis, PhD, RPh; Til Sturmer, MD, MPH, PhD; Linda Tyler, PharmD, FASHP; Almut G. Winterstein, RPh, PhD, FISPE

Drug Safety and Risk Management Advisory Committee Member Not Present (Non-Voting): Linda Scarazzini, MD (Industry Representative)

Temporary Members (Voting): Melinda Campopiano, MD; Alan D. Kaye, MD, PhD; Mary Ellen McCann, MD; Elaine Morrato, DrPH, MPH; Cynthia Chauhan (Patient Representative); Jeanmarie Perrone, MD, FACMT; Michael Sprintz, DO; Sharon Walsh, PhD; Ursula Wesselmann, MD, PhD

FDA Participants (Non-Voting): Sharon Hertz, MD; Ellen Fields, MD, MPH; Judy Staffa, PhD, RPh

Designated Federal Officer (Non-Voting): Stephanie Begansky, PharmD

Open Public Hearing Speakers: Bob Twillman, PhD, FAPM (American Academy of Pain Management); Edwin R. Thompson (Pharmaceutical Manufacturing Research Services, Inc.)

The agenda was as follows:

Call to Order and Introduction of Committee	**Raeford E. Brown, Jr., MD, FAAP** Acting Chairperson, AADPAC
Conflict of Interest Statement	**Stephanie L. Begansky, PharmD** Designated Federal Officer, AADPAC
FDA Introductory Remarks	**Ellen Fields, MD, MPH** Deputy Director Division of Anesthesia, Analgesia, and Addiction Products (DAAAP) Office of Drug Evaluation II (ODE-II) Office of New Drugs (OND), CDER, FDA

APPLICANT PRESENTATIONS	**Teva Branded Pharmaceutical Products R&D, Inc.**
Introduction	**Douglas C. Harnish, PhD** Senior Director, Pain and Migraine Regulatory Affairs Teva Pharmaceuticals
Chronic Pain and Opioid Abuse	**Charles Argoff, MD** Professor of Neurology Director, Comprehensive Pain Center Albany Medical Center, New York
Clinical Efficacy and Safety	**Richard Malamut, MD** Senior Vice President, Global Clinical Development Teva Pharmaceuticals
Abuse Deterrence Studies (Category 1)	**Derek Moe, PhD** Vice President, Drug Delivery Technology Teva Pharmaceuticals
Abuse Deterrence Studies (Category 2 and 3)	**Lynn Webster, MD** Vice President, Scientific Affairs PRA Health Sciences Salt Lake City, Utah
Summary & Benefit-Risk	**Richard Malamut, MD**
Clarifying Questions	
BREAK	
FDA PRESENTATIONS	
Drug Utilization Patterns for Hydrocodone ER and Other ER/LA Opioid Analgesics 2011-2015	**Joann H. Lee, PharmD** Drug Utilization Data Analyst Division of Epidemiology II (DEPI-II) Office of Pharmacovigilance and Epidemiology Office of Surveillance and Epidemiology (OSE) CDER, FDA
Vantrela ER (hydrocodone bitartrate) Extended-Release Tablets Labeling Section 9: Drug Abuse	**Robert A. Levin, MD** Medical Officer DAAAP, ODE-II, OND, CDER, FDA
Clarifying Questions	
LUNCH	
Open Public Hearing	

Charge to the Committee — **Sharon Hertz, MD**
Director
DAAAP, ODE-II, OND, CDER, FDA

Questions to the Committee/Committee Discussion

BREAK

Questions to the Committee/Committee Discussion (cont.)

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Please discuss whether there are sufficient data to support a finding that Vantrela ER (hydrocodone bitartrate extended-release tablets) has properties that can be expected to deter abuse, commenting on support for abuse-deterrent effects for each of the three possible routes of abuse:

    a. Oral
    b. Nasal
    c. Intravenous

    Committee Discussion: *It was the general consensus of the committee that Vantrela ER has sufficient data to support a finding of abuse-deterrent characteristics for the oral, nasal and intravenous routes of administration. The committee stated that data presented for all three routes of administration show at least a moderate amount of reduction in the possibility of abuse. It was also noted that although the reduction is incremental, the committee found the data to be compelling at the present time. Please see the transcript for details of the committee discussion.*

2. **VOTE:** Should Vantrela ER be approved for the proposed indication, management of pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate?

    Vote Result: Yes: 14 No: 3 Abstain: 0

    Committee Discussion: *The majority of the committee voted "Yes," agreeing that Vantrela ER should be approved for the proposed indication. Those members who voted "Yes" stated that the clinical development program met the standard for demonstrating efficacy.. Those members who voted "No" stated that they were concerned with how opioid products are regulated and approved, as well as the potential effect this process has on the opioid epidemic. Please see the transcript for details of the committee discussion.*

3. **VOTE:** If approved, should Vantrela ER be labeled as an abuse-deterrent product by the oral route of abuse?

Vote Result: Yes: 14 No: 3 Abstain: 0

Committee Discussion: *The majority of the committee voted "Yes," agreeing that Vantrela ER should be labeled as an abuse-deterrent product by the oral route of abuse. Those members who voted "Yes" stated that there were sufficient data provided to label the drug as abuse deterrent. Those members who voted "No" stated that they were unconvinced as the data was not compelling and felt the abuse- deterrent properties of Vantrela ER would not be significant in clinical practice. Please see the transcript for details of the committee discussion.*

4. **VOTE:** If approved, should Vantrela ER be labeled as an abuse-deterrent product by the nasal route of abuse?

Vote Result: Yes: 14 No: 3 Abstain: 0

Committee Discussion: *The majority of the committee voted "Yes," stating that Vantrela ER should be labeled as an abuse-deterrent product by the nasal route of abuse. Those members who voted "Yes" agreed that the data provided moderately convincing evidence that Vantrela ER was formulated with abuse-deterrent properties and was a step forward in making opioids safer for patients. Those members who voted "No" stated that they were unimpressed with the small margin of change. Please see the transcript for details of the committee discussion.*

5. **VOTE:** If approved, should Vantrela ER be labeled as an abuse-deterrent product by the intravenous route of abuse?

Vote Result: Yes: 16 No: 1 Abstain: 0

Committee Discussion: *The majority of the committee voted "Yes," stating that Vantrela ER should be labeled as an abuse-deterrent product by the intravenous route of abuse because the studies show that Vantrela ER has a high viscosity and low syringability. The member who voted "No" stated that there was no evidence that Vantrela ER was safer than other products that still get injected and abused despite their high viscosity. Please see the transcript for details of the committee discussion.*

The meeting was adjourned at approximately 3:03 p.m. on June 7, 2016.