Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Joint Meeting of the Psychopharmacologic Drugs Advisory Committee (PDAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM) October 8, 2020

Location: Please note that due to the impact of the COVID-19 pandemic, all meeting participants joined this advisory committee meeting via an online teleconferencing platform.

Topic: The committees discussed new drug application (NDA) 211179, for amphetamine sulfate immediate-release oral capsules, submitted by Arbor Pharmaceuticals, LLC, for the proposed indication of Attention Deficit Hyperactivity Disorder. This product has been formulated with properties intended to deter non-oral abuse, and the applicant has submitted data to support these abuse-deterrent properties for this product. The committees were asked to discuss the overall risk-benefit profile of the product, including the potential public health impact, and whether the Applicant has demonstrated abuse-deterrent properties for their product that would support labeling.

These summary minutes for the October 8, 2020 joint meeting of the Psychopharmacologic Drugs Advisory Committee (PDAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM) of the Food and Drug Administration were approved on November 24, 2020.

I certify that I attended the October 8, 2020 joint meeting of the PDAC and DSaRM of the Food and Drug Administration and these minutes accurately reflect what transpired.

/s/
LaToya Bonner, PharmD
Acting Designated Federal Officer, PDAC

/s/
Rajesh Narendran, MD
Chairperson, PDAC

Final Summary Minutes of the Joint Meeting of the Psychopharmacologic Drugs Advisory Committee (PDAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM) October 8, 2020

The Psychopharmacologic Drugs Advisory Committee (PDAC) and the Drug Safety and Risk Management Advisory Committee (DSaRM) of the Food and Drug Administration, Center for Drug Evaluation and Research met on October 8, 2020. The meeting presentations were heard, viewed, captioned, and recorded through an online teleconferencing platform. Prior to the meeting, the members and temporary voting members were provided the briefing materials and pre-recorded presentations from the FDA and Arbor Pharmaceuticals, LLC. The meeting was called to order by Rajesh Narendran, MD (Chairperson). The conflict of interest statement was read into the record by LaToya Bonner, PharmD (Acting Designated Federal Officer). There were approximately 300 people online. There were a total of eleven Open Public Hearing (OPH) speaker presentations.

A verbatim transcript will be available, in most instances, at approximately ten to twelve weeks following the meeting date.

Agenda: The committees discussed new drug application (NDA) 211179, for amphetamine sulfate immediate-release oral capsules, submitted by Arbor Pharmaceuticals, LLC, for the proposed indication of treatment of Attention Deficit Hyperactivity Disorder. This product has been formulated with properties intended to deter non-oral abuse, and the applicant has submitted data to support these abuse-deterrent properties for this product. The committees were asked to discuss the overall risk-benefit profile of the product, including the potential public health impact, and whether the Applicant has demonstrated abuse-deterrent properties for their product that would support labeling.

Attendance:

PDAC Members Present (Voting): Walter S. Dunn, MD, PhD; Jess G. Fiedorowicz, MD, PhD; Satish Iyengar, PhD; Felipe A. Jain, MD; Jessica J. Jeffrey, MD, MPH, MBA; Sonia L. Krishna, MD, FAPA, DFAACAP; Rajesh Narendran, MD (Chairperson); Patrick S. Thomas, Jr., MD, PhD; Kim O. Witczak (Consumer Representative)

PDAC Members Not Present (Voting): None

PDAC Member Present (Non-Voting): Robert W. Baker, MD (Industry Representative)

DSaRM Members Present (Voting): Denise M. Boudreau, PhD, RPh; Karim Anton Calis, PharmD, MPH, FASHP, FCCP; Marie R. Griffin, MD, MPH; Laurel A. Habel, MPH, PhD; Sonia Hernandez-Diaz, MD, MPH, DrPH; Martin Kulldorff, PhD; Steven B. Meisel, PharmD, CPPS; Lewis S. Nelson, MD

DSaRM Members Not Present (Voting): Collin A. Hovinga, PharmD, MS, FCCP; Soko Setoguchi, MD, DrPH

DSaRM Member (Non-Voting): Reema J. Mehta, PharmD, MPH (Industry Representative)

Temporary Members (Voting): Traci C. Green, PhD, MSc; Brandon D.L. Marshall, PhD; Christopher R. McCurdy, BSPh, PhD, FAAPS; James J. McGough, MD, MS; Philip Posner, PhD (Patient Representative); Jon E. Zibbell, PhD

FDA Participants (Non-Voting): Billy Dunn, MD; Eric Bastings, MD; Tiffany R. Farchione, MD; Bernard Fischer, MD; Judy Staffa, PhD, RPh; Tamra Meyer, PhD, MPH; Dominic Chiapperino, PhD

Acting Designated Federal Officer (Non-voting): LaToya Bonner, PharmD

Open Public Hearing Speakers: Robert Cattoi (Children and Adults with Attention Deficit/Hyperactivity Disorder); Kristin Seymour; Linda B. Cottler; Lucas Borgschulte; Ann Childress, MD; Julie Buckner; Doris M. Greenburg; Sidney Wolfe, MD (Public Citizen's Health Research Group); Kevin Martin Antshel, MD; Andrew Ewald; Meg Seymour, MD (National Center for Health Research)

The agenda was as follows:

Call to Order	**Rajesh Narendran, MD** Chairperson, PDAC
Introduction of Committee and Conflict of Interest Statement	**LaToya Bonner, PharmD** Acting Designated Federal Officer, PDAC
FDA Opening Remarks	**Tiffany R. Farchione, MD** Director (Acting) Division of Psychiatry (DP) Office of Neuroscience (ON) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATION	**Arbor Pharmaceuticals**
Summary Presentation – AR19 (amphetamine sulfate) Manipulation-Resistant, Immediate-Release Capsules for the Treatment of ADHD	**Evan Scullin, MD** Vice President, Medical Affairs Arbor Pharmaceuticals **Stephen Faraone, PhD** Vice Chair for Research, Department of Psychiatry Distinguished Professor of Psychiatry Distinguished Professor of Neuroscience & Physiology SUNY Upstate Medical University

APPLICANT PRESENTATION (CONT.)

Beatrice Setnik, PhD
Chief Scientific Officer
Altasciences

Eric Kinzler, PhD
President and Founder
Pellucid Advantage, LLC
Study Director
DRUGSCAN

John Dillberger, DVM, PhD
President
J. Dillberger, LLC
Fellow, International Academy of Toxicologic Pathology

Anthony Rostain, MD, MA
Chair of Psychiatry and Behavioral Health
Cooper University Healthcare

Clarifying Questions to Applicant

Clarifying Questions to FDA

LUNCH

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion

BREAK

Questions to the Committee/Committee Discussion (cont.)

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Considering the patterns of prescription stimulant nonmedical use in the United States, please discuss the potential public health impact of prescription stimulants formulated to be abuse-deterrent.

   Committee Discussion: *Collectively, the Committee shared the awareness that nonmedical use of prescription stimulants is a public health problem. However, the Committee generally agreed that prescription stimulants formulated to be abuse-deterrent will have little public health impact since many other formulations without abuse deterrent properties remain on the market. Some Committee members expressed safety concerns regarding the oral products being manipulated into an intravenous or intranasal substance, despite the abuse deterrent properties. Another concern noted is that the added excipients to deter abuse could lead to adverse effects if people are able to defeat the abuse deterrent properties, which could result in additional harms from these excipients if snorted or injected. For these reasons, the Committee generally agreed that this formulation likely provides limited benefit from a public health perspective and may possibly result in more harm than good. Please see the transcript for details of the Committees' discussion.*

2. **VOTE:** Based on the information provided, including the intranasal study comparing this product to amphetamine sulfate, has the Applicant provided adequate evidence that the immediate-release oral formulation of amphetamine sulfate (AR19) would deter intranasal use?

   Vote Result: **Yes: 4** **No: 19** **Abstain: 0**

   Committee Discussion: *Majority of the committee members agreed that the Applicant did not provide adequate evidence that the immediate-release oral formulation of amphetamine sulfate (AR19) would deter intranasal use. Those that voted, "No", expressed their concerns that manipulation could be done in multiple ways with little effort. Some members noted that the study failed to meet the endpoint set by the Applicant. For those who voted "Yes", they were convinced that the Applicant provided adequate evidence that the formulation would deter intranasal use and that the Applicant achieved its goal by providing a formulation that would be more difficult to manipulate and less rewarding than its marketed stimulant counterparts. Please see the transcript for details of the Committees' discussion.*

3. **VOTE:** Based on the information provided, including the syringeability study, has the Applicant provided adequate evidence that AR19 would deter intravenous use?

   Vote Result: **Yes: 8** **No: 15** **Abstain: 0**

   Committee Discussion*: Majority of the committee members agreed that the Applicant failed to provide adequate evidence that AR19 would deter intravenous use. However, some members who voted, "No", agreed that the Applicant presented data that would make the*

product at least more difficult to prepare for syringeability, but not sufficient to deter its abuse.

Some panel members voted, "Yes", stating that the AR19's formulation is substantially harder manipulate to extract and inject than its marketed counterparts and would be a deterrent, especially to casual or first-time users. Please see the transcript for details of the Committees' discussion.

4. **VOTE:** Based on the information provided, has the Applicant adequately characterized the safety of AR19?

   Vote Result: **Yes: 2** **No: 19** **Abstain: 2**

   Committee Discussion*: Majority of the committee members agreed that the Applicant did not adequately characterize the safety of AR19. Those that voted, "No", conveyed that the Applicant failed to show safety parameters when the product is manipulated into unintended routes of administration (i.e., intravenous and intranasal). In addition, a few members raised further concerns of intravenous use, suggesting that the gel-like formulation is not a deterrent, but a health hazard, putting the population at risk of infection (larger syringe) and other unintended toxicities caused by inert substances (i.e., talc and polyethene oxide (PEO)) in the formulation. The committee members who voted, "Yes", agreed that, as an oral medication, the Applicant presented adequate information supporting the safety profile of AR19 when used as directed. Please see the transcript for details of the Committees' discussion.*

5. **VOTE:** Do the benefits of AR19 outweigh the risks for the proposed indication?

   Vote Result: **Yes: 0** **No: 23** **Abstain: 0**

   Committee Discussion*: The committee members unanimously voted, "No", stating that the benefits of AR19 do not outweigh the risks for the proposed indication. The committee members agreed that there are too many significant toxicities. Some members went into more detail and expressed concerns about the risks of the excipients (talc and PEO) in the formulation, which to them, outweighed the questionable potential benefit of the product. Please see the transcript for details of the Committees' discussion.*

6. **DISCUSSION:** What, if any, additional data are needed to address outstanding issues of AR19?

   Committee Discussion*: The committee members made several comments to address the outstanding issues of AR19. Some members expressed the need for the Agency to provide clear definitions and thresholds for defining and evaluating abuse deterrent properties. Some panel members recommended to see more evaluations based on computerized models and more advanced scientific evaluations, for example, measuring dopamine release in the brain as opposed to just self-reported "drug-wanting or liking". One panel member noted that the age range was large and recommended narrowing to an age group where prevalence of*

nonmedical use is much higher. In addition, it was recommended that, if approved, post-marketing surveillance should be done to ensure any unintended consequences are detected. Please see the transcript for details of the Committees' discussion.

The meeting was adjourned at approximately 4:38 p.m.