Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
October 4, 2023

Location: All meeting participants were heard, viewed, captioned, and recorded for this advisory committee meeting via an online teleconferencing and/or video conferencing platform.

Topic: The Committee discussed new drug application (NDA) 215500, for eflornithine tablets, submitted by USWM, LLC (doing business as US WorldMeds). The proposed indication (use) for this product is to reduce the risk of relapse in pediatric patients with high-risk neuroblastoma (HRNB) who have completed multiagent, multimodality therapy.

These summary minutes for the October 4, 2023 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration were approved on November 9, 2023.

I certify that I attended the October 4, 2023 meeting of the Oncologic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	**/s/**
Joyce Frimpong, PharmD	Christopher H. Lieu, MD
Acting Designated Federal Officer, ODAC	Acting Chairperson, ODAC

Final Summary Minutes of the Oncologic Drugs Advisory Committee Meeting
October 4, 2023

The Oncologic Drugs Advisory Committee (ODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on October 4, 2023. The meeting presentations were heard, viewed, captioned, and recorded through an online video conferencing platform. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and US WorldMeds. The meeting was called to order by Christopher H. Lieu, MD (Acting Chairperson). The conflict of interest statement was read into the record by Joyce Frimpong, PharmD (Acting Designated Federal Officer). There were approximately 600 people in attendance. There were 9 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 Committee discussed new drug application (NDA) 215500, for eflornithine tablets, submitted by USWM, LLC (doing business as US WorldMeds). The proposed indication (use) for this product is to reduce the risk of relapse in pediatric patients with high-risk neuroblastoma (HRNB) who have completed multiagent, multimodality therapy.

Attendance:
Oncologic Drugs Advisory Committee Members Present (Voting): Mark R. Conaway, PhD; William J. Gradishar, MD; Christopher H. Lieu, MD (*Acting Chairperson*); David E. Mitchell (*Consumer Representative)*; Jorge J. Nieva, MD; Alberto S. Pappo, MD; Daniel Spratt, MD; Neil Vasan, MD, PhD

Oncologic Drugs Advisory Committee Members Not Present (Voting): Ranjana H. Advani, MD; Toni K. Choueiri, MD; Pamela L. Kunz, MD; Ravi A. Madan, MD (*Chairperson*); Ashley Rosko, MD

Oncologic Drugs Advisory Committee Member Present (Non-Voting): Johnathan D. Cheng, MD (*Industry Representative*)

Temporary Members (Voting): G. Caleb Alexander, MD, MS; Shahab Asgharzadeh, MD; Mary Ellen Cosenza, PhD, DABT; AeRang Kim, MD, PhD; Gianna McMillan, DBE, MFA (*Patient Representative*); Donald Williams (Will) Parsons, MD, PhD; Pamela Shaw, PhD, MS; Til Stürmer, MD, MPH, PhD; Clare J. Twist, MD; Yoram Unguru, MD, MS, MA, HEC-C; Brian Weiss, MD; Brigitte Widemann, MD

FDA Participants (Non-Voting): Richard Pazdur, MD; Paul Kluetz, MD; Martha Donoghue, MD; Nicole Drezner, MD; Diana Bradford, MD; Elizabeth S. Duke, MD; Arup Sinha, PhD; Emily Wearne, PhD

Acting Designated Federal Officer (Non-Voting): Joyce Frimpong, PharmD

Open Public Hearing Speakers: Melissa Block; Sarah Bartosz (Beat Childhood Cancer Foundation, Inc.); Patrick Lacey; Deanna Mitchell, MD; Jacqueline Kraveka, DO; Crystal Shaw (Team Parker 4 Life); Sarah Stephens; Rachel Sal Jansheski; Ashley Burnette

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The agenda was as follows:

Call to Order	**Christopher H. Lieu, MD** Acting Chairperson, ODAC
Introduction of Committee/ Conflict of Interest Statement	**Joyce Frimpong, PharmD** Acting Designated Federal Officer, ODAC
FDA Opening Remarks	**Diana Bradford, MD** Cross Disciplinary Team Leader Division of Oncology 2 (DO2) Office of Oncologic Drugs (OOD) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**US WorldMeds**
Introduction	**Kristen Gullo** Vice President of Development and Regulatory Affairs US WorldMeds
High-risk Neuroblastoma (HRNB) Unmet Need and DFMO Development History	**Giselle Sholler, MD** Division Chief Pediatric Hematology, Oncology and Bone Marrow Transplant Penn State Health Children's Hospital
DFMO Efficacy	**Thomas Clinch** Senior Director Biometrics and Clinical Development US WorldMeds
Clinical Perspective	**Susan L. Cohn, MD** Professor and Director of Clinical Sciences Department of Pediatrics University of Chicago Medicine
Conclusion	**Kristen Gullo**

FDA PRESENTATIONS

Eflornithine (DFMO) for patients with high-risk neuroblastoma who have completed multiagent, multimodality therapy	**Elizabeth S. Duke, MD** Clinical Reviewer DO2, OOD, OND, CDER, FDA **Arup Sinha, PhD** Statistics Reviewer Division of Biometrics V Office of Biostatistics (OB), CDER, FDA **Emily Wearne, PhD** Nonclinical Reviewer Division of Hematology Oncology Toxicology (DHOT) OOD, OND, CDER, FDA
Clarifying Questions	

LUNCH

Charge to the Committee	**Nicole Drezner, MD** Deputy Division Director DO2, OOD, OND, CDER, FDA

OPEN PUBLIC HEARING

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **DISCUSSION:** Discuss the strengths and limitations of the externally controlled trial results to support the use of DFMO in pediatric patients with high-risk neuroblastoma.

   Committee Discussion: *Committee members appreciated the thorough analyses that had been performed by FDA and the Applicant to assess the impact of potential biases on the results of the externally controlled trial. However, there was not a unanimous consensus regarding the certainty or reliability of the results of the externally controlled trial. Many committee members had concerns about setting precedent regarding utilization of an external control. Several committee members questioned whether a randomized controlled trial could be performed in this setting, while others stated that such a trial would be infeasible. Some committee members were concerned about the impact of such an approval on other trials in pediatric oncology. Please see the transcript for details of the Committee's discussion.*

2. **DISCUSSION:** Discuss the strengths and limitations of the additional nonclinical and clinical data to support the use of DFMO in pediatric patients with high-risk neuroblastoma.

   Committee Discussion: *Some committee members noted that the nonclinical data appeared to use a relevant model and provided supportive evidence of the effect of DFMO in this setting. However, as for limitations, some committee members commented that nonclinical data does not always translate into an effect in clinical studies. Please see the transcript for details of the Committee's discussion.*

3. **VOTE:** Has the Applicant provided sufficient evidence to conclude that DFMO improves event-free survival in patients with high-risk neuroblastoma?

   Vote Result: Yes: 14 No: 6 Abstain: 0

   Committee Discussion: *The majority of the committee members agreed that the Applicant provided sufficient evidence to conclude that DFMO improves event-free survival in patients with high-risk neuroblastoma; however, there were questions for clarity around if this was intended to mean substantial evidence and deferred to FDA on that aspect. Committee members who voted "Yes", noted the totality of data appeared to support the assertion that DFMO improves event- free survival given the robustness and uniqueness of the external control. There was also trust in the nonclinical data. Those who voted "No", questioned whether this type design could be used to demonstrate efficacy given the concerns regarding confounding and bias that are inherent with use of external control arms. There were some differences of opinions among Committee members as to whether a randomized controlled trial of this drug in the proposed indication could be feasible, and, if so, whether such a trial could be completed in a timely fashion. Please see the transcript for details of the Committee's discussion.*

The meeting was adjourned at approximately 3:35 p.m.