

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

**Final Summary Minutes of the Psychopharmacologic Drugs Advisory Committee Meeting  
July 18, 2025**

Location: FDA White Oak Campus, 10903 New Hampshire Ave., Bldg. 31 Conference Center, the Great Room (Rm. 1503), Silver Spring, Maryland. The public also had the option to participate via an online teleconferencing and/or video conferencing platform, and the meeting presentations were heard, viewed, captioned, and recorded through an online video conferencing platform.

Topic: The Committee discussed supplemental New Drug Application (sNDA) 205422/S-012, for REXULTI (brexpiprazole) tablets, submitted by Otsuka Pharmaceutical Company, Ltd., for the proposed indication of treatment of adults with post-traumatic stress disorder (PTSD), in combination with sertraline.

These summary minutes for the July 18, 2025 meeting of the Psychopharmacologic Drugs Advisory Committee (PDAC) of the Food and Drug Administration were approved on August 6, 2025.

I certify that I attended the July 18, 2025 meeting of the PDAC of the Food and Drug Administration and that these minutes accurately reflect what transpired.

\_\_\_\_\_  
/s/  
Joyce Frimpong, PharmD  
Designated Federal Officer, PDAC

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/s/  
Rajesh Narendran, MD  
Acting Chairperson, PDAC

## Summary Minutes of the Psychopharmacologic Drugs Advisory Committee Meeting July 18, 2025

The Psychopharmacologic Drugs Advisory Committee (PDAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on July 18, 2025, at the FDA White Oak Campus, 10903 New Hampshire Ave., Bldg. 31 Conference Center, the Great Room (Rm. 1503), Silver Spring, MD 20993-0002. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Otsuka Pharmaceutical Company, Ltd. The meeting was called to order by Dr. Rajesh Narendran (Acting Chairperson). The conflict of interest statement was read into the record by Joyce Frimpong (Designated Federal Officer). There were approximately 70 people in attendance in-person, and approximately 816 people online. There were 15 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 supplemental New Drug Application (sNDA) 205422/S-012, for REXULTI (brexpiprazole) tablets, submitted by Otsuka Pharmaceutical Company, Ltd., for the proposed indication of treatment of adults with post-traumatic stress disorder (PTSD), in combination with sertraline.

**Attendance:**

**Psychopharmacologic Drugs Advisory Committee Members Present (Voting):** Patrick S. Thomas, Jr., MD, PhD (*via video conferencing platform*)

**Psychopharmacologic Drugs Advisory Committee Member Present (Non-Voting):** Carla M. Canuso, MD (*Industry Representative*)

**Temporary Members (Voting):** Jacob S. Ballon, MD, MPH; Laura C. Block, PharmD (*Patient Representative*); Christopher S. Coffey, PhD, MS; Walter S. Dunn, MD, PhD; Jess G. Fiedorowicz, MD, PhD (*via video conferencing platform*); Rajesh Narendran, MD (*Acting Chairperson*); Murray Raskind, MD (*via video conferencing platform*); Pamela A. Shaw, PhD (*via video conferencing platform*); Brian R. Shiner, MD, MPH; Gregory Simon, MD, MPH

**FDA Participants (Non-Voting):** Teresa Buracchio, MD; Tiffany R. Farchione, MD; Bernard Fischer, MD; Valentina Mantua, MD, PhD; Roberta Rasetti, MD, PhD; Peiling Yang, PhD; Yiming Chen, PhD

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

**Open Public Hearing Speakers:** Todd Lynch; Jeff Winton (Rural Minds); Ron Blake; Michael Abrams, MPH, PhD (Public Citizen); Diana Zuckerman, PhD (National Center for Health Research); Kimberly Witczak (Woodymatters); Clark Sabo; Saundra Maass-Robinson, MD; Debbie Plotnick (Mental Health America); William Sauve, MD (Osmind); James Knutson, MD;

Vanessa Walker (Depression and Bipolar Support Alliance); Lloyd Briggery; Kathryn Santoro  
Policy Center for Maternal Mental Health.

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

9:00 a.m.	Call to Order and Introduction of Committee	<b>Rajesh Narendran, MD</b> Acting Chairperson, PDAC
9:05 a.m.	Conflict of Interest Statement	<b>Joyce Frimpong, PharmD</b> Designated Federal Officer, PDAC
9:15 a.m.	FDA Opening Remarks	<b>Tiffany R. Farchione, MD</b> Director Division of Psychiatry (DP) Office of Neuroscience (ON) Office of New Drugs (OND), CDER, FDA
9:25 a.m.	<b>APPLICANT PRESENTATIONS</b>	<b>Otsuka Pharmaceutical Company, Ltd.</b>
	Introduction	<b>Mary Hobart, PhD</b> Senior Vice President Global Regulatory Affairs Otsuka Pharmaceutical Company, Ltd.
	Background and Unmet Need	<b>Arash Javanbakht, MD</b> Founding Director Stress, Trauma, and Anxiety Research Clinic (STARC) Wayne State University School of Medicine
	Efficacy	<b>John Kraus, MD, PhD</b> Executive Vice President and Chief Medical Officer Otsuka Pharmaceutical Company, Ltd.  <b>Jason Connor, PhD</b> President & Lead Statistical Scientist ConfluenceStat LLC
	Safety	<b>Thomas Thompson, MD</b> Vice President, Global Clinical Development Therapeutic Head, CNS Otsuka Pharmaceutical Company, Ltd.
	Clinical Perspective	<b>Kathleen Brady, MD, PhD</b> Distinguished University Professor Medical University of South Carolina

Director, South Carolina Clinical and  
Translational Research Institute

Benefit/ Risk Summary

**Mary Hobart, PhD**

10:25 a.m. Clarifying Questions to Applicant

10:55 a.m. **BREAK**

11:05 a.m. **FDA PRESENTATIONS**

Brexpiprazole for the treatment of  
posttraumatic stress disorder (PTSD) in  
adults, in combination with sertraline

**Roberta Rasetti, MD, PhD**  
Clinical Reviewer  
DP, ON, OND, CDER, FDA

**Yiming Chen, PhD**  
Statistical Reviewer  
Division of Biometrics I  
Office of Biostatistics  
Office of Translational Sciences  
CDER, FDA

12:05 p.m. Clarifying Questions to FDA

12:35 p.m. **LUNCH**

1:30 p.m. **OPEN PUBLIC HEARING**

2:30 p.m. Questions to the Committee/Committee Discussion

4:00 p.m. **ADJOURNMENT**

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***Questions to the Committee:***

1. **DISCUSSION:** Discuss the strength of evidence provided by the two phase 3 studies 00071 and 00072, in particular discuss the impact of the discordant results on your overall assessment of efficacy.

***Committee Discussion:*** Panel members discussed that the combination therapy appeared to work better in patients with a poor response to sertraline, whereas it appeared less effective in those with a better response to sertraline alone. Members also noted that genetic or other response factors could have influenced the differing outcomes; however, neither trial specifically evaluated these factors. Additionally, some panelists discussed the importance of including a broader population, particularly military populations, in future studies. Please see the transcript for details of the committee discussion.

2. **DISCUSSION:** Discuss your view on the contribution of Study 00061 on the overall evidence of effectiveness.

*Committee Discussion:* Panel members discussed that study 00061 was difficult to use to determine the drug's effectiveness or to serve as a substitute for study 00072. However, they noted that study 00061 provided some evidence of a low to moderate effect, suggesting that the combination could be effective. Please see the transcript for details of the committee discussion.

3. **DISCUSSION:** Based on available data, and with consideration of the known risks of brexpiprazole and sertraline individually, discuss the acceptability of the proposed concurrent initiation treatment paradigm.

*Committee Discussion:* Overall, panel members discussed that, in the real-world co-initiation may not reflect how patients will use this treatment. They noted that patients are likely to start with sertraline and then add brexpiprazole, as third-party payers could dictate this sequencing. Panel members also noted that that co-initiation could increase risks associated with brexpiprazole such as weight gain, akathisia, and extrapyramidal symptoms (EPS). Additionally, panel members questioned whether the efficacy, showing only a five-point benefit was strong enough to support clinicians adopting co-initiation as a standard approach. Please see the transcript for details of the committee discussion.

4. **VOTE:** Based on the available data presented, has the efficacy of brexpiprazole, when initiated concurrently with sertraline, been established for the treatment of PTSD?

Please provide your rationale and indicate the specific information (e.g., statistical analyses, other data) on which you base your vote.

**Vote Result:      Yes: 1              No: 10              Abstain: 0**

*Committee Discussion:* The majority of the panel voted "No," stating that the current evidence did not establish efficacy. Panel members discussed that while study 00071 showed supportive results, study 00072 yielded negative findings, and study 00061 provided only limited evidence. The panel noted that the mixed results created uncertainty about the overall risk-benefit profile. Additional concerns were raised regarding the absence of clear plans for managing Type 1 error in study 00061, and some members suggested including combat veterans with PTSD in future studies. Overall, panel members noted that an additional well-designed phase 3 trial may be necessary to strengthen the evidence. Please see the transcript for details of the committee discussion.

The meeting was adjourned at approximately 3:55 p.m.