Food and Drug Administration
Center for Drug Evaluation and Research

Final Summary Minutes of the Dermatologic and Ophthalmic Drugs Advisory Committee Meeting
December 13, 2019

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

Topic: The committee discussed biologics license application (BLA) 761143, teprotumumab solution for intravenous use, submitted by Horizon Pharma Ireland, Ltd., proposed for the treatment of active thyroid eye disease.

These summary minutes for the December 13, 2019 meeting of the Dermatologic and Ophthalmic Drugs Advisory Committee of the Food and Drug Administration were approved on January 22, 2020.

I certify that I attended the December 13, 2019 meeting of the Dermatologic and Ophthalmic Drugs Advisory Committee of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	**/s/**
Jay R. Fajiculay, PharmD	James Chodosh, MD, MPH
Acting Designated Federal Officer, DODAC	*Chairperson, DODAC*

Final Summary Minutes of the Dermatologic and Ophthalmic Drugs Advisory Committee Meeting
December 13, 2019

The Dermatologic and Ophthalmic Drugs Advisory Committee (DODAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on December 13, 2019, at the FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503), 10903 New Hampshire Avenue, Silver Spring, Maryland. Prior to the meeting, the members and temporary voting members were provided the briefing materials from the FDA and Horizon Pharma Ireland, Ltd. The meeting was called to order by James Chodosh, MD (Chairperson). The conflict of interest statement was read into the record by Jay Fajiculay, PharmD (Acting Designated Federal Officer). There were approximately 100 people in attendance. There were 11 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 biologics license application (BLA) 761143, teprotumumab solution for intravenous use, submitted by Horizon Pharma Ireland, Ltd., proposed for the treatment of active thyroid eye disease.

Attendance:
Dermatologic and Ophthalmic Drugs Advisory Committee Members Present (Voting):
James Chodosh, MD, MPH (Chairperson); Sidney Gicheru, MD; Mary Elizabeth Hartnett, MD; Timothy Murray, MD, MBA, FACS; Christina Y. Weng, MD, MBA

Dermatologic and Ophthalmic Drugs Advisory Committee Members Not Present (Voting):
Korey Capozza, MPH (Consumer Representative); Ken Katz, MD, MSc, MCSE (Dermatology Chairperson); Elaine Siegfried, MD; Megha Tollefson, MD

Dermatologic and Ophthalmic Drugs Advisory Committee Member Present (Non-Voting):
Ercem Atillasoy, MD (Industry Representative)

Temporary Members (Voting): Erica Brittain, PhD; Kenneth D. Burman, MD; Tonya S. King, PhD; Cecilia C. Low Wang, MD; Jennifer Schwartzott, MS (Patient Representative); John F. Stamler, MD, PhD; David Yoo, MD

FDA Participants (Non-Voting):
Peter Stein, MD; Wiley Chambers, MD

Acting Designated Federal Officer (Non-Voting): Jay Fajiculay, PharmD

Open Public Hearing Speakers: Nancy Patterson, PhD (Graves' Disease and Thyroid Foundation); Kathleen A. Arntsen (Lupus and Allied Diseases Association, Inc.); Fatemeh Rajaii, MD, PhD; Terry Smith, MD; Ron Barela; Susan Schatz; Wendy Labadie; Judy Bachman;

Randall Rutta (American Autoimmune Related Diseases Association); Karen Williams (Organization of Rare Diseases); Sara Brown (Prevent Blindness)

The agenda was as follows:

Call to Order and Introduction of Committee	**James Chodosh, MD** Chairperson, DODAC
Conflict of Interest Statement	**Jay R. Fajiculay, PharmD** Designated Federal Officer (Acting), DODAC
FDA Opening Remarks	**Wiley A. Chambers, MD** Deputy Director Division of Transplant and Ophthalmology Products Office of New Drugs, CDER, FDA
APPLICANT PRESENTATIONS	**Horizon Pharma Ireland, Ltd.**
Introduction	**Timothy P. Walbert** Chairman, President and Chief Executive Officer Horizon Therapeutics
Unmet Medical Need	**Raymond S. Douglas, MD, PhD** Director of Orbital and Thyroid Eye Disease Program Cedars-Sinai Medical Center
Teprotumumab Mechanism and Program Overview	**Shao-Lee Lin, MD, PhD** Executive Vice President, Head of Research and Development, Chief Scientific Officer Horizon Therapeutics
Efficacy and Safety	**Elizabeth H.Z. Thompson, PhD** Vice President, Clinical Development, Rare Disease Horizon Therapeutics
Clinical Perspective	**Raymond S. Douglas, MD, PhD**
Clarifying Questions to the Applicant	
BREAK	
Clarifying Questions to the Applicant (continued)	

FDA PRESENTATION

FDA Clinical Review of Teprotumumab	**Wiley A. Chambers, MD**

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:** Please discuss the expected onset and duration of effect following the administration of teprotumumab. Please also include in your discussion whether there is a potential safety concern with repeated courses of treatment.

   Committee Discussion: *The committee discussed that the data presented showed a variable expected time of teprotumumab-effect onset and duration of effect following administration. Some members expressed concern that the limited number of clinical trial subjects may not provide a full picture regarding the totality of adverse events potentially associated with repeated courses of treatment with the drug, or potential side effects of long-term teprotumumab use. The committee members also noted specific concerns regarding high blood sugar and hearing loss. Please see the transcript for details of the committee discussion.*

2. **DISCUSSION:** Please discuss any safety limitations or safety labeling that should result from the relatively small database of patients in this orphan indication for teprotumumab.

   Committee Discussion: *The committee discussed that the labeling should include safety concerns such as use in pregnancy, blood sugar monitoring and the potential for hearing loss. Some members stated they would be interested to learn what types of hearing loss were identified and at what time point after teprotumumab administration. Some members stated the product should be avoided in patients with known irritable bowel disease. Please see the transcript for details of the committee discussion.*

3. **DISCUSSION:** Please discuss whether the term "Active" as used in the proposed indication is informative to clinicians and patients considering use of the product.

   Committee Discussion: *The committee discussed that the term "Active" as used in the proposed indication would be useful for clinicians; however, it would need to be defined in labeling to aid clinicians to appropriately classify patients as having "Active" thyroid eye disease. The committee offered various examples of how to classify "Active." One member suggested that the Agency could consider potentially using the product only in conjunction with an ophthalmologist or endocrinologist to monitor treatment progress or potential adverse events experienced. Please see the transcript for details of the committee discussion.*

4. **DISCUSSION:** Please discuss the need for glucose monitoring after initiation of teprotumumab administration. If needed, please discuss the recommended timing of any monitoring.

   Committee Discussion: *The committee discussed that the data provided did not contain enough information to appropriately identify a schedule for glucose monitoring after initiation of teprotumumab administration. However, a general consensus for baseline glucose testing, fasting glucose testing every couple of months with repeated infusions, and glucose monitoring after discontinuation of teprotumumab were discussed. Please see the transcript for details of the committee discussion.*

5. **DISCUSSION:** Please discuss your level of concern with the episodes and frequency of reported:

   a. muscle spasms

      Committee Discussion: *The committee agreed that muscle spasms were not too concerning and should be included in the Adverse Reactions section of the product label. Please see the transcript for details of the committee discussion.*

   b. hypoacusis/loss of hearing

      Committee Discussion: *The committee suggested that hearing loss be included in the Warnings and Precautions section of the product label since this side effect may affect a patient's decision to use teprotumumab, especially if the patient had prior hearing loss or has a family history of hearing loss. Please see the transcript for details of the committee discussion.*

   c. diarrhea/inflammatory bowel disease

      Committee Discussion: *The committee noted that while diarrhea should be included in the Adverse Reactions section of the product label, irritable bowel disease could be considered for inclusion in the Warning and Precautions section. Please see the transcript for details of the committee discussion.*

d. infection rate

Committee Discussion: *The committee stated that infection rates should be included in the Adverse Reactions section of the product label. Please see the transcript for details of the committee discussion.*

e. alopecia

Committee Discussion: *The committee stated that alopecia should be included in the Adverse Reactions section of the product label. Please see the transcript for details of the committee discussion.*

6. **VOTE:** Do the potential benefits of using teprotumumab as recommended outweigh the potential risks associated with the use of the drug product for the intended population?

Vote Result: Yes: 12 No: 0 Abstain: 0

Committee Discussion: *The committee unanimously voted "Yes", that the potential benefits of using teprotumumab as recommended outweigh the potential risks associated with the use of the drug product for the intended population. The committee acknowledged that there are currently no products available on the market to treat thyroid eye disease, and that the benefits of teprotumumab use outweigh the adverse events observed in clinical trials. Some committee members suggested that the Applicant conduct a clinical trial with a greater number of subjects to identify any additional adverse event that may have not been identified from the limited data presented. The committee also recommended that the Applicant work with the Agency to identify post-marketing commitments such as appropriate labeling or use of a registry. Please see the transcript for details of the committee discussion.*

7. **DISCUSSION:** If teprotumumab is approved, are there specific recommendations for the labeling?

Committee Discussion: *The committee had no further recommendations than what was already discussed previously.*

The meeting was adjourned at approximately 3:22 p.m.