Food and Drug Administration
Center for Drug Evaluation and Research

Summary Minutes of the Antimicrobial Drugs Advisory Committee Meeting
June 8, 2023

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 committee discussed biologics license application (BLA) 761328, for nirsevimab, a long-acting respiratory syncytial virus (RSV) F protein inhibitor monoclonal antibody for intramuscular use, submitted by AstraZeneca AB. The proposed indication is prevention of RSV lower respiratory tract disease in:

- Neonates and infants born during or entering their first RSV season.
- Children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

These summary minutes for the June 8, 2023 meeting of the AMDAC of the Food and Drug Administration were approved on August 2, 2023.

I certify that I attended the June 8, 2023 meeting of the AMDAC of the Food and Drug Administration and that these minutes accurately reflect what transpired.

/s/	**/s/**
She-Chia Jankowski, PharmD	Lindsey R. Baden, MD
Designated Federal Officer, AMDAC	Chairperson, AMDAC

Summary Minutes of the Antimicrobial Drugs Advisory Committee Meeting
June 8, 2023

The Antimicrobial Drugs Advisory Committee (AMDAC) of the Food and Drug Administration, Center for Drug Evaluation and Research met on June 8, 2023. 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 from the FDA, and AstraZeneca Pharmaceuticals LP. The meeting was called to order by Lindsey R. Baden, MD (Chairperson). The conflict of interest statement was read into the record by She-Chia Jankowski, PharmD (Designated Federal Officer). There were approximately 588 people online. There were three 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) 761328, for nirsevimab, a long-acting respiratory syncytial virus (RSV) F protein inhibitor monoclonal antibody for intramuscular use, submitted by AstraZeneca AB. The proposed indication is prevention of RSV lower respiratory tract disease in:

- Neonates and infants born during or entering their first RSV season.
- Children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season.

Attendance:
AMDAC Members Present (Voting): Lindsey R. Baden, MD (Chairperson); Michael D. Green, MD, MPH; W. David Hardy, MD, AAHIVS; Sally A. Hunsberger, PhD; Ighovwerha Ofotokun, MD, MSc; Nimish Patel, PharmD, PhD; Federico Perez, MD, MS; George K. Siberry, MD, MPH; Roblena E. Walker, PhD (Consumer Representative)

AMDAC Member Present (Non-Voting): Richa S. Chandra, MD, MBA (Industry Representative)

AMDAC Members Not Present (Voting): Richard A. Murphy, MD, MPH; Sankar Swaminathan, MD

Temporary Members (Voting): Mary Cataletto, MD, MMM; Douglas S. Diekema, MD, MPH; Peter L. Havens, MD, MS; Rohan Hazra, MD; Mary Anne Jackson, MD, FAAP, FIDSA, FPIDS; Karen L. Kotloff, MD; Steven Krug, MD; Tamorah Lewis, MD, PhD; Meredith McMorrow, MD, MPH; Stacey Stokes, MD, MPH; Jasmine Shackleford Thomas (Patient Representative); Benjamin Wilfond, MD

FDA Participants (Non-Voting): John Farley, MD, MPH; Yodit Belew, MD; Melisse Baylor, MD; Justin Earp, PhD; Neha Gada, PharmD, BCPS; Anna Kettermann, Dipl.-Math, MA; Yang Zhao, PhD

Designated Federal Officer (Non-Voting): She-Chia Jankowski, PharmD

Open Public Hearing Speaker: DeEtta Lee; Jennifer Sonney, PhD; Bill Vacca

The agenda was as follows:

Call to Order	**Lindsey R. Baden, MD** Chairperson, AMDAC
Introduction of Committee and Conflict of Interest Statement	**She-Chia Jankowski, PharmD** Designated Federal Officer, AMDAC
FDA Opening Remarks	**John Farley, MD, MPH** Director Office of Infectious Diseases (OID) Office of New Drugs (OND), CDER, FDA
APPLICANT PRESENTATIONS	**AstraZeneca AB**
Introduction	**Tonya Villafana, PhD, MPH** Vice President, Global Franchise Head Vaccines and Immune Therapies AstraZeneca
Efficacy	**Amanda Leach, MRCPCH** Global Clinical Head AstraZeneca
Safety	**Manish Shroff, MBBS, MS, MBA** Senior Director Global Patient Safety, AstraZeneca
Clinical Perspective	**William Muller, MD, PhD** Professor, Pediatrics, Northwestern University Feinberg School of Medicine Scientific Director, Office of Clinical and Community Trials, Ann & Robert H. Lurie Children's Hospital of Chicago
Benefit-Risk & Conclusions	**Tonya Villafana, PhD, MPH**
FDA PRESENTATION	
Overview	**Melisse Baylor, MD** Clinical Reviewer Division of Antivirals (DAV) OID, OND, CDER, FDA

FDA PRESENTATIONS (CONT.)

	Yang Zhao, PhD Clinical Pharmacology Reviewer Division of Infectious Disease Pharmacology Office of Clinical Pharmacology (OCP) Office of Translational Science (OTS) CDER, FDA
Efficacy and Safety Issues	**Anna Kettermann, Dipl.-Math, MA** Statistics Reviewer Division of Biostatistics IV Office of Biostatistics OTS, CDER, FDA
	Melisse Baylor, MD
	Justin Earp, PhD Pharmacometrics Reviewer Division of Pharmacometrics OCP, OTS, CDER, FDA
Proposed Pharmacovigilance Strategy	**Neha Gada, PharmD, BCPS** Cross Discipline Safety Advisor Office of Pharmacovigilance and Epidemiology Office of Surveillance and Epidemiology CDER, FDA
Overall Summary	**Melisse Baylor, MD**
Clarifying Questions	

LUNCH

OPEN PUBLIC HEARING

Charge to the Committee	**Yodit Belew, MD** Associate Director for Therapeutic Review DAV, OID, OND, CDER, FDA

BREAK

Questions to the Committee/Committee Discussion

ADJOURNMENT

Questions to the Committee:

1. **VOTE:** Is the overall benefit-risk assessment favorable for the use of nirsevimab for the prevention of respiratory syncytial virus (RSV) lower respiratory disease in neonates and infants born during or entering their first RSV season?
    a. If yes, please discuss your rationale.
    b. If no, please comment on what additional clinical data are needed to support this indication.

    Vote Result: Yes: 21 No: 0 Abstain: 0

    Committee Discussion: *The Committee members unanimously voted "Yes", indicating that the overall benefit-risk assessment is favorable for the use of nirsevimab for the proposed indication of the prevention of RSV lower respiratory tract disease in neonates and infants born during or entering their first RSV season. The Committee was encouraged by the robust efficacy of nirsevimab and reassured by the size of the safety database and safety assessments. Furthermore, the Committee members emphasized a need for RSV treatments and preventions in neonates and infants, as RSV could lead to significant illness, hospitalization and deaths for young children. Please see the transcript for details of the Committee's discussion.*

2. **DISCUSSION:** Please comment on the benefits and risks for nirsevimab when assessed by chronological and gestational age groups. Discuss the population or subpopulation for whom nirsevimab administration in the first RSV season would be most appropriate.

    Committee Discussion: *The Committee noted that safety data were reassuring across the cohorts and the single dose strategy would be operationally very valuable. With respect to efficacy of nirsevimab to prevent RSV lower respiratory tract disease in neonates and infants born during or entering their first RSV season, the Committee generally agreed that nirsevimab was effective across the various chronological and gestational age groups. The Committee members acklowledged that smaller number of participants in the 6 to less than 12 months old age group were enrolled in the trials. Some Committee members suggested that additional pharmacokinetic data would be helpful to assess the efficacy of nirsevimab in this subgroup. The majority of the Committee members noted differences in geographic locations and RSV seasonality may complicate nirsevimab dosing strategy, but that organizations such as the American Academy of Pediatricians and the ACIP could adequately address dosing scheduling recommendations. Please see the transcript for details of the Committee's discussion.*

3. **VOTE:** Is the overall benefit-risk assessment favorable for the use of nirsevimab for the prevention of RSV lower respiratory tract disease in children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season?
    a. If yes, please discuss your rationale.

b. If no, please comment on what additional clinical data are needed to support this indication.

Vote Result: **Yes: 19** **No: 2** **Abstain: 0**

Committee Discussion: *The majority of the Committee members voted "Yes", indicating that the overall benefit-risk assessment is favorable for the use of nirsevimab for the proposed indication of the prevention of RSV lower respiratory tract disease in children up to 24 months of age who remain vulnerable to severe RSV disease through their second RSV season. Most Committee members noted that the extrapolation of efficacy to this high risk subgroup was reasonable with minimal safety risks; and the Committee reiterated its support and encouragement for the post-marketing survillence strategies. Two Committee members voted "No", indicating that the extrapolation was somewhat questionable and would like to see additional data in this high risk subgroup, and in particular, for the congenital heart disease population. Please see the transcript for details of the Committee's discussion.*

4. **DISCUSSION:** In the context of potential, future availability of maternal RSV vaccine to protect infants from RSV disease during their first RSV season, what additional data may be helpful to inform future recommendations regarding the use of nirsevimab in infants born to mothers who received RSV vaccination?

Committee Discussion: *The Committee recommended that additional data is needed to inform the use of nirsevimab in infants born to mothers who received RSV vaccination, and help with resources considerations in the context of RSV prevention recommendations. Several Committee members commented that more information on durability of response was needed for the maternal RSV vaccine and for nirsevimab. The Committee suggested several study designs, including studies that evaluate immune biomarkers, or real-world use studies. Other suggestions included conducting studies based on stratification by gestational age groups and maternal vaccination status to best determine the role of nirsevimab in this context. In addition, some Committee members emphasized the importance of including high risk infants and children in these studies, particularly infants or children with congenital heart disease. Please see the transcript for details of the Committee's discussion.*

The meeting was adjourned at approximately 4:45 p.m. Eastern Time.