



## Waiver to Allow Participation in a Food and Drug Administration Advisory Committee

DATE: July 18, 2024

TO: Rachel Bressler  
Acting Director, Advisory Committee Oversight and Management Staff  
Office of the Chief Scientist

FROM: Byron Marshall  
Director, Division of Advisory Committee and Consultant Management  
Office of Executive Programs  
Center for Drug Evaluation and Research

Name of Advisory Committee Meeting Voting Member: **Benjamin Lebwohl, M.D., M.S.**

Committee: Gastrointestinal Drugs Advisory Committee

Meeting date: September 13, 2024

Description of the Particular Matter to Which the Waiver Applies:

Benjamin Lebwohl, M.D., M.S., is a standing voting member and Chairperson of the Gastrointestinal Drugs Advisory Committee (GIDAC). The committee's function is to review and evaluate available data concerning the safety and effectiveness of marketed and investigational human drug products for use in the treatment of gastrointestinal diseases and make appropriate recommendations to the Commissioner of Food and Drugs.

On September 13, 2024, the committee will discuss supplemental new drug application (sNDA) 207999 S-011, for Ocaliva (obeticholic acid) 5 mg titrated to 10 mg oral tablets, administered once a day, submitted by Intercept Pharmaceuticals, Inc., to fulfill the accelerated approval postmarketing requirements specified in the Ocaliva approval letter dated May 27, 2016. The sNDA included data proposed to describe and verify clinical benefit for the indication for the treatment of adult patients with primary biliary cholangitis (PBC) without cirrhosis or with compensated cirrhosis who do not have evidence of portal hypertension, either in combination with ursodeoxycholic acid (UDCA) with an inadequate response to UDCA or as monotherapy in patients unable to tolerate UDCA. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest:

Dr. Lebowhl reported a financial interest in [REDACTED] (b) (6), a healthcare sector mutual fund. The value of his holding in this fund is between \$300,000 and \$500,000. Based on the most current publicly available information at the time of writing this waiver, this fund invests less than 1.3% of its assets in [REDACTED] (b) (6), a competing firm.

Under the regulatory exemption issued by the Office of Government Ethics (5 CFR § 2640.201(b)), an employee may participate in any particular matter affecting one or more holdings in a sector mutual fund where the disqualifying financial interest in the matter arises because of ownership of an interest in the fund and the aggregate market value of interests in all related funds (specifically, those in which there is a disqualifying financial interest and which concentrate in the same sector) does not exceed \$50,000. Because Dr. Lebowhl's financial interest in the [REDACTED] (b) (6) fund exceeds that amount, he cannot avail himself of that exemption and must seek a waiver.

Basis for Granting the Waiver:

*Dr. Benjamin Lebowhl has unique qualifications and specialized expertise needed for this particular matter.*

Dr. Benjamin Lebowhl is Professor of Medicine and Epidemiology, and Director of Clinical Research of the Celiac Disease Center at the Columbia University Irving Medical Center.

Dr. Lebowhl received his medical degree from Columbia College of Physicians and Surgeons, and then completed his internship, residency, and chief residency in internal medicine at Columbia. He stayed at Columbia as a fellow in Digestive and Liver Disease, during which time he obtained a Master's in Patient Oriented Research from the Department of Biostatistics at the Mailman School of Public Health. He was a post-doctoral fellow in a National Cancer Institute-funded Training Program in Cancer-Related Population Sciences under the mentorship of Alfred Neugut. He joined the faculty of the Celiac Disease Center at Columbia University in 2010.

Dr. Lebowhl is a past president of the Society for the Study of Celiac Disease, and is the Director of Clinical Research at the Celiac Disease Center at Columbia University, where he collaborates with investigators in the United States and abroad in epidemiology, patterns of care, natural history, and therapeutics. Dr. Lebowhl's second and related research interest is quality of endoscopy, including improving the detection of colorectal adenomas. He has co-authored more than 300 peer-reviewed publications. His research is supported by the National Institutes of Health, and past research funding includes the American Gastroenterological Association, the Celiac Disease Foundation, and the American Scandinavian Foundation.

Dr. Lebowhl is the Louis and Gloria Flanzer Scholar at Columbia University Irving Medical Center. He serves as Chair of the Gastrointestinal Drugs Advisory Committee of the United States Food and Drug Administration. He is heavily involved in medical education and lectures regularly to trainees on topics including celiac disease, evidence-based medicine, clinical decision

making, pseudoscience, diarrhea, and colorectal cancer screening.

*The particular matter is considered sensitive.*

This topic is considered to be sensitive, as the FDA Division with responsibility for review of this product expects that the meeting may receive significant public interest and non-trade press interest.

*Dr. Lebwohl's expertise in this particular matter is necessary in the interest of public health.*

Primary biliary cholangitis (PBC), previously known as primary biliary cirrhosis, is an autoimmune disorder that leads to the gradual destruction of intrahepatic bile ducts, resulting in periportal inflammation and cholestasis. Prolonged hepatic cholestasis subsequently leads to cirrhosis and portal hypertension. Researchers theorize that patients with primary biliary cirrhosis have both genetic predisposition with the right environmental trigger. The prevalence of the disease is 100-fold higher in first degree relatives of the index patient, which strongly suggests a genetic predisposition.

PBC is rare, with a reported prevalence of 19 to 402 cases per million persons. The vast majority of patients (90 to 95 percent) are women, and most patients are diagnosed between the ages of 30 and 65 years (often in their 40s or 50s). The age and sex-adjusted prevalences per 100,000 persons are 65.4 for women and 12.1 for men. PBC prevalence appears to vary geographically and is most common in northern Europe and North America.

The incidence of PBC is estimated to be 2.7 per 100,000 person-years (4.5 per 100,000 person-years for women and 0.7 per 100,000 person-years for men). The true incidence of primary biliary cholangitis is rising as more screening tests such as liver chemistry and lipid profile are performed in otherwise healthy persons.

There is no cure for PBC. The goal of therapy is to prevent the disease progression and manage the symptoms and complications related to chronic cholestasis.

In the interest of public health, it is important that the Agency has available the unique expertise that Dr. Lebwohl will provide for the discussion of the particular matter before the committee.

*Any potential for a conflict of interest is greatly outweighed by the strong need for Dr. Lebwohl's expertise in this matter.*

Dr. Lebwohl has been a standing member of the committee since 2017 and Chairperson since 2021. Dr. Lebwohl's expertise in gastroenterology in combination with his training in epidemiology allows him to bring a unique perspective and contribution to the discussion. His diverse collection of professional experiences and previous experiences with AC meetings as a standing member and Chairperson of the GIDAC will be invaluable to a robust and productive discussion of the application coming before the committee. Furthermore, the underlying value of (b) (6) stock in Dr. Lebwohl's (b) (6) interests constitutes a value, if held individually, that would meet the *de minimus* exemption for individual securities under 5 C.F.R. § 2640.202(a).

Accordingly, I recommend that you grant Dr. Benjamin Lebwohl, voting member of the Gastrointestinal Drugs Advisory Committee, a waiver from the conflict of interest prohibitions of 18 U.S.C. § 208(a).

Certification:

The individual may participate, pursuant to 18 U.S.C. 208(b)(3) – The need for the individual’s services outweighs the potential for a conflict of interest created by the financial interest involved.

Limitations on the Regular Government Employee’s or Special Government Employee’s Ability to Act:

Non-voting

Other (specify):

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Denied – The individual may not participate.

Michael F. Ortwerth -S Digitally signed by Michael F. Ortwerth -S *for*  
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08/26/2024

Rachel Bressler  
Acting Director  
Advisory Committee Oversight and Management Staff  
Office of the Chief Scientist

Date