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

DATE: August 22, 2018

TO: Rachel Sherman, M.D., M.P.H.
Principal Deputy Commissioner
Office of the Commissioner, Food and Drug Administration

THROUGH: Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of Special Medical Programs

FROM: Jayne E. Peterson, B.S. Pharm., J.D.
Director, Division of Advisory Committee and Consultant Management
Office of Executive Programs
Center for Drug Evaluation and Research

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

Committees: Gastrointestinal Drugs Advisory Committee (GIDAC) and
Drug Safety and Risk Management (DSaRM) Advisory Committee

Meeting date: October 17, 2018

Description of the Particular Matter to Which the Waiver Applies:

Dr. Benjamin Lebwohl is a standing voting member of the Gastrointestinal Drugs Advisory Committee (GIDAC), who is attending the October 17, 2018, joint meeting of the GIDAC and the Drug Safety and Risk Management Advisory Committee (DSaRM). The GIDAC'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. The DSaRM's function is to review and evaluate information on risk management, risk communication, and quantitative evaluation of spontaneous reports for drugs for human use and for any other product for which the Food and Drug Administration has regulatory responsibility. The Committee also advises the Commissioner of Food and Drugs regarding the scientific and medical evaluation of all information gathered by the Department of Health and Human Services and the Department of Justice about the safety, efficacy, and abuse potential of drugs or other substances, and recommends actions to be taken by the Department of Health and Human Services with regard to the marketing, investigation, and control of such drugs or other substances.

The committees will meet on October 17, 2018, to discuss supplemental new drug application (sNDA) 021200, supplement 015, for tegaserod maleate (ZELNORM) tablets for oral administration, submitted by Sloan Pharma S.a.r.l, Bertrange, Cham Branch, a wholly-owned subsidiary of US Worldmeds, proposed for the treatment of women with irritable bowel syndrome with constipation (IBS-C) who do not have a history of cardiovascular ischemic disease, such as myocardial infarction, stroke, transient ischemic attack, or angina, and who do not have more than one risk factor for cardiovascular disease. The topic of this meeting is a particular matter involving specific parties.

Type, Nature, and Magnitude of the Financial Interest(s):

Dr. Lebwohl reported a financial interest in (b) (6) a healthcare sector mutual fund. The value of his holding in this fund is between $200,000 - $300,000. At the writing of this waiver, this fund contained assets in five competing/affected firms: (b) (6) The top 25 holdings of the fund include – (b) (6) – representing approximately 5.38% and 5.11%, respectively, of the underlying value of the fund. (b) (6) are not in the top 25 holdings; each representing less than 1.44%.

Under a regulatory exemption issued by the Office of Government Ethics, an employee may participate in any particular matter affecting one or more holdings of 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 funds in which there is a disqualifying financial interest and which concentrate in the same sector does not exceed $50,000. Because Dr. Lebwohl's financial interest in the (b) (6) exceeds that amount, he has disqualifying financial interests based on the fund's holding of the above-listed companies.

Basis for Granting the Waiver:

The primary issue for discussion at this meeting will be the benefit/risk profile of the use of tegaserod, given the potential cardiovascular risks associated with this class of products. The proposed population for reintroduction of tegaserod to the market is supported both by data from clinical trials and epidemiologic data. Therefore, a productive discussion and assessment of the data depends on having experts with a strong expertise in clinical gastroenterology, with experience treating adult patients with IBS-C and chronic idiopathic constipation (CIC), combined with an understanding of how to interpret epidemiological data. Dr. Lebwohl has unique qualifications and specialized expertise needed for the evaluation and interpretation of the type and nature of clinical trial and especially epidemiologic data that will be presented. Dr. Lebwohl's background in these areas will allow for valuable contribution to the discussion.

Dr. Lebwohl has unique qualifications and specialized expertise needed for this particular matter.

Benjamin Lebwohl, M.D., M.S., received his medical degree from Columbia University College of Physicians and Surgeons and later received his Masters of Science in Biostatics from Columbia University, Mailman School of Public Health. He is an Assistant Professor of

Medicine and Epidemiology at Columbia University College of Physicians & Surgeons; Director of Clinical Research, Celiac Disease Center at Columbia University and an Assistant Attending at New York-Presbyterian/Columbia University Medical Center. Dr. Lebwohl was awarded a two-year fellowship at NIH, where he studied colorectal cancer prevention. Dr. Lebwohl was a Gerstner Scholar (2014-2017) at Columbia, studying the impact of gluten exposure on the microbiome in patients with celiac disease and non-celiac gluten sensitivity. He is also the recipient of the American Gastroenterology Association Research Scholar Award (2014-2017), collaborating with the Channing Laboratory at Harvard to study risk factors for celiac disease and the health effects of gluten in large cohort studies.

His current areas of clinical expertise include upper endoscopy, GI endoscopy procedure, colonoscopy, colon and rectal disease, colon cancer screening and prevention, and celiac disease. Dr. Lebwohl collaborates with Columbia University – Celiac Disease Center and abroad in the areas of the epidemiology, patterns of care, and natural history of celiac disease. His second related research interest is quality of endoscopy, including bowel preparation prior to colonoscopy, improving the detection of colorectal adenomas, and improving the diagnostic yield of biopsy of the small intestine. Since 2011, Dr. Lebwohl has been involved with the Screening Colonoscopy Report Cards program at the NYC Department of Health and Mental Hygiene. He helped to develop a system for the measurement of colonoscopy quality indicators, including the adenoma detection rate, which is widely regarded as the most important process measure in screening colonoscopy.

In addition to his expertise in gastroenterology, Dr. Lebwohl's background in epidemiology and biostatistics will be valuable to the advisory committee discussion centering on aspects of the adequacy and strength of the efficacy data for tegaserod to support potential approval, and in providing thoughtful evaluation of the risk/benefit profile for this product and broader public health considerations. Furthermore, as an experienced member of the GIDAC, it will be essential to have his perspective, complementary to other members who may be participating for the first time in a GIDAC meeting.

Multiple experts are needed.

Multiple gastroenterologists were invited to attend this meeting to allow for a diverse panel of experts that would include those who treat adults and pediatric patients; this would help provide a balanced assessment of the acceptability of the known and anticipated risks associated with the proposed treatment with tegasserod. Although there are a number of gastroenterologists scheduled to attend this meeting, Dr. Lebwohl is the only invited expert with a combination of expertise in adult gastroenterology, biostatistics, and epidemiology. His expertise in this area allows him to bring a unique persepective and contribution to the discussion. Having a diverse collection of professional experiences represented on the panel would provide an opportunity for a robust and productive discussion of the meeting topic.

The particular matter is not sensitive.

The meeting topic is not considered to be sensitive. The Division responsible for review of this product does not expect that the meeting is likely to receive congressional interest. However, the Division considers the possibility that a reintroduction of Zelnorm into the U.S. market will be of great interest to the public.

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

IBS is one of the two most common functional gastrointestinal disorders worldwide (besides CIC). These disorders significantly impair patients' quality of life. IBS is defined by abdominal discomfort associated with altered bowel habits. It has a global prevalence of 11%, with all regions of the world being affected by this disorder at similar rates. IBS is more common in females and younger adults of less than 50 years of age. Sometimes the pain from IBS can be so severe that it's disabling, and patients can't do routine things. Depression, anxiety and other psychological conditions are also common in people with IBS. The exact cause of IBS is not well understood, and there is no known cure. Given its prevalence, the frequency of sometimes debilitating symptoms, and the fact that IBS typically occurs in younger adulthood, the indirect costs associated with loss of productivity and work absenteeism is considerable. In addition, there are direct medical expenses related to additional medical tests and the use of various medical and nonmedical remedies that may have limited impact. First line treatment in most cases includes non-prescription options such as fiber products (psyllium) or nondrug interventions. Over-the-counter (OTC) therapies and nondrug interventions are not specifically approved for IBS-C. Following OTC options, only three prescription drugs are approved: lubiprostone, linaclotide and plecanatide. Dr. Lebwohl's vast experiences in gastroenterology, endoscopy, colonoscopy and colon diseases coupled with his background in epidemiology and biostatics will ensure a fruitful discussion and a broader public health consideration.

Accordingly, I recommend that you grant Dr. Benjamin Lebwohl, a standing 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 Special Government Employee's Ability to Act:

_____ Non-voting

_____ Other (specify):

_____

_____

_____ Denied – The individual may not participate.

Russell Fortney -S

Digitally signed by Russell Fortney -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, 0.9.2342.19200300.100.1.1=1300191216, cn=Russell Fortney -S
Date: 2018.09.25 09:47:51 -04'00'

for Rachel Sherman, M.D., M.P.H.
Principal Deputy Commissioner
Office of the Commissioner, Food and Drug Administration

September 25, 2018
Date