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

DATE: February 8, 2018

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

THROUGH: Russell Fortney
Director (Acting), 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
Center for Drug Evaluation and Research

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

Committee: Gastrointestinal Drugs Advisory Committee (GIDAC)

Meeting date: March 8, 2018

Description of the Particular Matter to Which the Waiver Applies:

Dr. Lebwohl is a standing voting member of the Gastrointestinal Drugs Advisory Committee. 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.

The committee will meet on March 8, 2018, to discuss supplemental new drug application (sNDA) 203214, supplement 18, Xeljanz (tofacitinib) 5 mg and 10 mg tablets, submitted by Pfizer Inc., proposed for the treatment of adult patients with moderately to severely active ulcerative colitis who have demonstrated an inadequate response, loss of response or intolerance to corticosteroids, azathioprine, 6-mercaptopurine or tumor necrosis factor (TNF) inhibitor therapy. 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 six competing/affected firms – [redacted] – representing approximately [redacted], respectively, of the underlying value of the fund.

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 [redacted] 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 GIDAC meeting will be the benefit/risk assessment of the use of tofacitinib 10mg twice a day dosing, beyond the 8 weeks of initial induction treatment. The proposed dose is above the maximum recommended dosage for the current approved uses; therefore, the key discussion point will be whether safety and efficacy data supports the long-term use of the 10 mg twice daily dosage in refractory (prior tumor-necrosis factor inhibitor failure) ulcerative colitis (UC) patients.

UC is a disease affecting the colon and the primary endpoint for trials for drugs intended to treat UC includes measurement of findings on colonoscopy. A fruitful discussion of these matters depends upon having strong expertise in this area and hearing many perspectives. It will be critical to have Dr. Lebwohl's expertise in adult gastroenterology, including evaluation and treatment of colon and rectal disease, to ensure the success of this advisory committee meeting. UC is a disease affecting the colon; the primary endpoint for trials for drugs intended to treat UC includes measurement of findings on colonoscopy.

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, gastrointestinal endoscopy procedures, colonoscopy, colon and rectal disease, colon cancer screening and prevention, and

celiac disease. Dr. Lebwohl collaborates with Columbia University – Celiac Disease Center 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 New York City 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.

It is particularly important to include Dr. Lebwohl in the upcoming GIDAC meeting, given his experience in adult gastroenterology, gastrointestinal endoscopy procedures, colonoscopy, and his work in developing a system for the measurement of colonoscopy quality indicators. In the review Division's search for gastroenterology experts, Dr. Lebwohl's work in measurement of colonoscopy quality indicators stood out. His background in epidemiology and biostatistics will be valuable to the discussion centering on aspects of the adequacy of the efficacy data for tofacitinib to support a potential approval, and in providing thoughtful evaluation of the risk/benefit profile for this product. In addition, 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, tofactinib, for UC. Although there are a number of gastroenterologists scheduled to attend this meeting, Dr. Lebwohl is the only invited expert with experience in the development of a system for measuring colonoscopy quality indicators, including the adenoma detection rate. 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 does not expect that the meeting is likely to receive significant public interest, (non-trade) press interest, or Congressional interest.

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

UC is a chronic, idiopathic inflammatory disease that affects the colon, most commonly afflicting adults aged 30–40 years and resulting in disability. It is characterized by relapsing and remitting mucosal inflammation, starting in the rectum and extending to proximal segments of the colon. The annual direct and indirect costs related to UC are estimated to be as high as $8 – $15 billion in the USA.

Although several treatment options are available, none of them are curative. This leads to most patients experiencing periods of illness after intervals of remission. Goals of treatment are induction and maintenance of remission of symptoms to provide an improved quality of life, reduction in need for long-term corticosteroids, and minimization of cancer risk. Currently, agents approved for moderate-severe active UC that have demonstrated an inadequate response, loss of response or intolerance to corticosteroids, are azathioprine, 6-mercaptopurine (6-MP) or TNF inhibitor therapy, such as infliximab, vedolizumab, golimumab, and adalimumab. These agents require intravenous or subcutaneous administration. However, tofacitinib, the product at issue, is an oral medication proposed to be administered twice daily. This product, if approved, represents the first systemic immunosuppressant in a new drug class, and the first oral treatment option available to patients with severe UC disease. 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:

__X__ 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.

Kathleen Davies -S

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for Rachel Sherman

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

February 15, 2018
Date