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

DATE: August 20, 2020

TO: Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of the Chief Scientist

FROM: Marieann Brill
Associate Director for Regulatory Affairs/Designated Federal Officer
Office of Pediatric Therapeutics

Name of Advisory Committee Meeting Temporary Member: **Jeffrey R. Strawn, M.D., F.A.A.C.A.P.**

Committee: Pediatric Advisory Committee

Meeting date: September 15, 2020

Description of the Particular Matter to Which the Waiver Applies:

The Pediatric Advisory Committee (PAC) is chartered to provide advice and make recommendations regarding FDA-regulated pediatric research including the identification of research priorities related to pediatric therapeutics. In addition, the PAC reviews adverse event reports for drugs and biologics that have had pediatric labeling based on studies conducted under the Best Pharmaceuticals for Children Act (BPCA) (21 U.S.C. § 355a) and/or the Pediatric Research Equity Act (PREA) (21 U.S.C. § 355b).

The role of the PAC is legislated by BPCA and PREA. The PAC does not provide advice to FDA with respect to approval of any specific FDA-regulated product.

The PAC will meet on September 15, 2020, to discuss pediatric-focused safety reviews for Adzenys ER, Mydayis, Vyvanse, Orencia, and a number of other products. Since these products will be discussed before the committee, the PAC will be asked to vote and make recommendations. Below are the indications for use for the following products:

- Adzenys ER (amphetamine) is indicated for treatment of attention deficit hyperactivity disorder (ADHD) in patients 6 years and older; and is marketed by Neos Therapeutics Inc.
- Mydayis (mixed salts of a single-entity amphetamine) is indicated for the treatment of ADHD in patients 13 years and older; and is marketed by Shire Development LLC

- Vyvanse (lisdexamfetamine dimesylate) is indicated for ADHD in patients 6 years and older; and is marketed by Shire Development LLC
- Orencia (abatacept) is indicated for Polyarticular Juvenile Idiopathic Arthritis; and is marketed by Bristol Myers Squibb

There will be a discussion regarding acute dystonia associated with the use of ADHD medications (including methylphenidate products, amphetamine products, and atomoxetine). Additionally, there will be a discussion regarding acute hyperkinetic movement disorder associated with the combined use of ADHD stimulants and antipsychotics (including first-generation antipsychotics and second-generation antipsychotics). The following products will be used as examples during this discussion:

- Abilify (aripiprazole) is indicated for schizophrenia, acute treatment of manic and mixed episodes associated with bipolar I, agitation associated with schizophrenia or bipolar mania, adjunctive treatment of major depressive disorder, treatment of irritability associated with autistic disorder, and treatment of Tourette's disorder. Abilify is marketed by Otsuka Pharmaceutical Company.
- Adderall XR (mixed salt of single entity amphetamine) is indicated for ADHD; and is marketed by Shire
- Concerta (methylphenidate HCL) is indicated for ADHD; and is marketed by Janssen Pharmaceuticals Inc.
- Risperdal (risperidone) is indicated for the treatment of schizophrenia, as monotherapy or adjunctive therapy with lithium or valproate, for the treatment of acute maniac or mixed episodes associated with Bipolar I Disorder, and treatment of irritability associated with autistic disorder. Risperdal is marketed by Janssen Pharmaceuticals Inc.
- Strattera (atomoxetine hydrochloride) is indicated for ADHD; and is marketed by Eli Lilly and Co.

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

Dr. Strawn has identified a financial interest of his employer which can be affected by the particular matter before the committee. That financial interest is imputed to him under the federal conflict of interest statute, 18 U.S.C. § 208.

Dr. Strawn's [redacted] (b) (4) with Patient Centered Outcomes Initiative (PCORI) to conduct studies related to aripiprazole:

> Augmentation versus switch: comparative effectiveness research for antidepressant incomplete and non-responders with treatment resistant depression (ASCERTAIN-TRD). This is a multi-site, randomized, open-label, effectiveness trial comparing three treatment arms for major depressive disorder (MDD) patients with TRD who are currently on ongoing, stable and adequate antidepressant therapy (ADT). Adequate ADT is defined as a therapeutically sufficient dose for a sufficient treatment period, which would be expected to be effective as listed in the Massachusetts General Hospital (MGH) Antidepressant Treatment Response Questionnaire (ATRQ). Patients will be randomized in a 1:1:1 fashion to one of three open-label treatment arms: a) aripiprazole augmentation, b) repetitive transcranial magnetic stimulation (rTMS) augmentation, and c) switching to venlafaxine XR

or duloxetine. The study population is 18 to 80 years old (adults). Dr. Strawn serves as a sub-investigator; specifically, he is a back-up physician for conducting TMS. (b) (4) has received (b) (4) since the study started in March 2019. Dr. Strawn does not receive any remuneration for this study. The study is expected to end in October 2020.

This study involves a product, aripiprazole, that will be under discussion by the PAC. Although the committee will not be looking at safety reviews of aripiprazole, it will be discussing that product in the context of its use in different treatment scenarios. Out of an abundance of caution, we are seeking a waiver to permit Dr. Strawn's participation.

Basis for Granting the Waiver:

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

Dr. Jeffrey Strawn M.D. is a child and adolescent psychiatry expert and is serving as a temporary voting member of the PAC. He earned his medical degree from the University of Cincinnati College of Medicine and completed his residency at the University Hospital, Cincinnati, Ohio. He completed a fellowship in child and adolescent psychiatry at the Cincinnati Children's Hospital Medical Center. Dr. Strawn is a diplomate of the American Board of Psychiatry and Neurology in both psychiatry and child and adolescent psychiatry. In addition to the positions listed above, Dr. Strawn is a Medical Staff member at the Cincinnati Children's Hospital Medical Center and an Attending Psychiatrist at the UC Health – University of Cincinnati Medical Center. He is also a Medical Director at the University of Cincinnati, Department of Psychiatry and Behavioral Neuroscience, Resident Psychotherapy Clinic – Adolescent Division. Dr. Strawn's academic appointments include Associate Vice Chair of Research and an Associate Professor of Psychiatry, Department of Psychiatry and Behavioral Neuroscience at the University of Cincinnati (UC). He is also an Associate Professor of Clinical Pharmacology, Department of Pediatrics at the Cincinnati Children's Hospital Medical Center and an Associate Professor of Pediatrics, Department of Pediatrics at the University of Cincinnati and Cincinnati Children's Hospital Medical Center.

Dr. Strawn's initial work examined the neurophysiology, neurochemistry and neuroanatomy of anxiety disorders in children and adolescents. Moreover, he worked in predictive models of antidepressant response and tolerability in youth and in conducting clinical trials in pediatric anxiety and depressive disorders. In this capacity, Dr. Strawn worked to increase the evidence base for treatment interventions in youth and has extensive expertise in the conduct of double blind, placebo-controlled trials in youth. His work also examines the tolerability of treatments for pediatric anxiety disorders using network meta-analyses and Bayesian approaches. Collectively, Dr. Strawn has published more than 120 peer-reviewed articles that largely focus on the treatment of pediatric anxiety and depressive disorders, on antidepressant efficacy and tolerability in youth and on the pharmacology of antidepressant medications in youth. It is this clinical experience which enriches Dr. Strawn with the day-to-day understanding of antidepressant efficacy and tolerability in pediatric patients, pharmacogenomics, clinical trial design/interpretation in pediatric affective and anxiety disorders and pediatric anxiety disorders.

The particular matter is not sensitive.

The PAC will discuss matters related to the pediatric-focused safety reviews for Adzenys ER (amphetamine), Mydayis (mixed salts of a single-entity amphetamine), Vyvanse (lisdexamfetamine dimesylate), Orencia (abatacept), and a number of other products. There will be a discussion regarding acute dystonia associated with the use of ADHD medications (including methylphenidate products, amphetamine products, and atomoxetine). Additionally, there will be discussions regarding acute hyperkinetic movement disorder associated with the combined use of ADHD stimulants and antipsychotics (including first-generation antipsychotics and second-generation antipsychotics). Abilify (aripiprazole), Adderall XR (mixed salt of single entity amphetamine), Concerta (methylphenidate HCL), Risperdal (risperidone), and Strattera (atomoxetine hydrochloride) will be used as examples during this part of the discussion. Based on the profile of adverse events reported for these products, the discussions at this meeting are not considered sensitive.

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

It is important to have someone with expertise in child and adolescent psychiatry to review pediatric adverse events, discuss acute dystonia associated with the use of ADHD medications (including methylphenidate products, amphetamine products, and atomoxetine), and discuss acute hyperkinetic movement disorder associated with the combined use of ADHD stimulants and antipsychotics (including first-generation antipsychotics and second-generation antipsychotics). In the interest of public health, it is critical that FDA has available the expertise that Dr. Strawn will provide to the committee.

Accordingly, I recommend that you grant Dr. Jeffrey Strawn, a temporary voting member of the Pediatric 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.

Russell Fortney -S Digitally signed by Russell Fortney -S
Date: 2020.08.27 15:17:30 -04'00'

August 27, 2020

Russell Fortney
Director, Advisory Committee Oversight and Management Staff
Office of the Chief Scientist

Date