FOOD AND DRUG ADMINISTRATION (FDA)
Center for Drug Evaluation and Research (CDER)

Pharmaceutical Science and Clinical Pharmacology (PSCP) Advisory Committee Meeting
FDA White Oak Campus, Building 31 Conference Center, the Great Room (Rm. 1503)
10903 New Hampshire Avenue, Silver Spring, Maryland
May 7, 2019

DRAFT AGENDA

The committee will discuss the following topics: (1) approaches to evaluate the effect of renal impairment on drug exposure, and (2) best practice considerations for translating pharmacokinetic (PK) information into dose individualization instructions. Regarding topic 1, many registration trials exclude patients with advanced kidney disease, and product labeling dosing instructions for these patients are commonly derived from our understanding of the change in the PK in individuals with varying degrees of renal function. The most common current approach to determine dosing instructions for patients with varying degrees of renal function begins with a stand-alone renal impairment study, either full design or reduced design. In addition to stand-alone renal impairment studies, drug development programs often use the findings from population PK (POPPK) analyses, which leverage the PK information across all the studies available in a drug development program. An alternative approach to consider is for drug development programs to predict the impact of renal impairment on the PK of the drug, either based on the understanding of the PK of a new molecular entity or using physiologic based PK (PBPK) models, without a stand-alone renal impairment study. Patients with impaired renal function can then be included in later stage clinical trials, with prospective dose adjustment incorporated if deemed necessary based the predictions. The dosing should be confirmed based on analysis of PK samples from the late stage trials (sparse PK, POPPK analysis). Regarding topic 2, dose individualization is typically achieved by applying the concept of 'exposure-matching' under the assumption that such a maneuver will result in a benefit-risk similar to that observed in the registration trials. The committee will discuss the application of 'exposure matching,' including the necessary assumptions and any limitations.

9:00 a.m.	Call to Order and Introduction of Committee	**Andre Terzic, MD, PhD, FAHA** Chairperson, PSCP
9:05 a.m.	Conflict of Interest Statement	**Jay Fajiculay, PharmD** Designated Federal Officer, PSCP
9:15 a.m.	FDA Opening Remarks	**Kellie Reynolds, PharmD** Deputy Director Division of Clinical Pharmacology IV Office of Clinical Pharmacology (OCP) Office of Translational Sciences (OTS), CDER, FDA
9:25 a.m.	**FDA PRESENTATIONS**	
	Determination of Dosing Instructions for Patients with Renal Impairment: Current Paradigm	**Martina Sahre, PhD** Policy Lead Guidance and Policy Team OCP, OTS, CDER, FDA
	Translation of Findings to Dosing Recommendations	**Rajanikanth (Raj) Madabushi, PhD** Team Leader, Guidance and Policy Team OCP, OTS, CDER, FDA
10:25 a.m.	Clarifying Questions to Presenters	
10:40 a.m.	**BREAK**	

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DRAFT AGENDA (cont.)

10:55 a.m.	**INDUSTRY PRESENTATION**	
	Industry Perspectives on Approaches to Evaluate the Effect of Renal Impairment on Drug Exposure	**Richard A. Graham, PhD** **International Consortium for Innovation & Quality in Pharmaceutical Development** **Vice President, Head of Clinical Pharmacology** **Theravance Biopharma**
11:45 a.m.	Clarifying Questions to Presenter	
12:00 p.m.	**LUNCH**	
1:00 p.m.	**OPEN PUBLIC HEARING**	
2:00 p.m.	Questions to the Committee/ Committee Discussion	
3:00 p.m.	**BREAK**	
3:10 p.m.	Questions to the Committee/ Committee Discussion (cont.)	
4:00 p.m.	**ADJOURNMENT**	

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