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APPLICATION NUMBER:

207925Orig1s000

PHARMACOLOGY REVIEW(S)

INTEROFFICE MEMO

TO: NDA 207-925
Ivacaftor Granules
Kalydeco Granules (Proposed Proprietary Name)

FROM: Marcie Wood, Ph.D.
Supervisory Pharmacologist
Division of Pulmonary, Allergy, and Rheumatology Products

DATE: February 19, 2015

NDA 207-925 for ivacaftor granules was submitted on September 17, 2014, to support a proposed indication for the treatment of cystic fibrosis in patients 2 years of age and older who have one of the following mutations in the CFTR gene: G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R, or R117H. Proposed doses are 50 mg q12h (100 mg/day) for patients < 14 kg and 75 mg q12h (150 mg/day) for patients ≥ 14 kg. Ivacaftor tablets are currently approved for the treatment of cystic fibrosis in patients 6 years of age and older with the G551D, G1244E, G1349D, G178R, G551S, S1251N, S1255P, S549N, S549R, or R117H CFTR gene mutation at a dose of 150 mg q12h (300 mg/day). Ivacaftor is a CFTR potentiator.

Ivacaftor granules contain ivacaftor drug substance, (b) (4) the following excipients: colloidal silicon dioxide, croscarmellose sodium, lactose monohydrate, mannitol, magnesium stearate, and sucralose. The composition of ivacaftor granules is provided in the table below. There are no nonclinical concerns for the qualitative or quantitative composition of ivacaftor granules.

Composition of Ivacaftor Granules

Component	Quality Standard	Component Function	Amount per 50 mg unit dose (mg)	Amount per 75 mg unit dose (mg)	Content (% w/w)
Ivacaftor (b) (4)	NDA 203188	Active	(b) (4)	(b) (4)	(b) (4)
Lactose monohydrate	USP/NF	(b) (4)	(b) (4)	(b) (4)	(b) (4)
Mannitol	USP/NF				
Sucralose	USP/NF				
Croscarmellose sodium	USP/NF				
Colloidal silicon dioxide	USP/NF				
Magnesium stearate	USP/NF				
Total	---				

No new nonclinical ivacaftor studies were submitted for review in the current NDA. The sponsor (Vertex Pharmaceuticals, Inc.) referenced nonclinical information contained in NDA 203-188 for ivacaftor tablets. All pivotal nonclinical data was previously reviewed under NDA 203-188. Refer to the nonclinical reviews by Dr. Marcie Wood and Dr. Timothy Robison.

Labeling: No changes are currently proposed to the nonclinical sections of the label.

Recommendation: There are no outstanding pharmacology or toxicology issues for this NDA application, and this NDA is recommended for approval from the nonclinical perspective.

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/s/

MARCIE L WOOD
02/19/2015