CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

204553Orig1s000

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

IND 064892

MEETING MINUTES

Janssen Research & Development, LLC
Attention: Huy Q. Truong, MS
Associate Director, Global Regulatory Affairs
920 U.S. Highway 202 South, PO Box 300
Raritan, NJ 08869

Dear Mr. Truong:[1]

Please refer to your investigational new drug application (IND) submitted under section 505(i) of the Federal Food, Drug, and Cosmetic Act for rivaroxaban.

We also refer to the meeting between representatives of your firm and the FDA on August 6, 2019. The purpose of the meeting was to discuss the planned New Drug Application submission for two proposed pediatric indications supported by the development program in the treatment and thromboprophylaxis of venous thromboembolism (VTE) and discuss the new pediatric formulation (granule for oral suspension).

A copy of the official minutes of the meeting is enclosed for your information. Please notify us of any significant differences in understanding regarding the meeting outcomes.

If you have any questions, contact Katie Chon, Regulatory Project Manager, at katie.chon@fda.hhs.gov or (240) 402-6578.

Sincerely,

{See appended electronic signature page}

Tanya M. Wroblewski, MD
Clinical Team Leader
Division of Hematology Products
Office of Hematology and Oncology Products
Center for Drug Evaluation and Research

Enclosure:

- Meeting Minutes

[1] We update guidances periodically. For the most recent version of a guidance, check the FDA Guidance Documents Database https://www.fda.gov/RegulatoryInformation/Guidances/default.htm.

MEMORANDUM OF MEETING MINUTES

Meeting Type: B
Meeting Category: Pre-NDA

Meeting Date and Time: August 6, 2019 10:00 AM – 11:00 AM EST
Meeting Location: 10903 New Hampshire Avenue
White Oak Building 22, Conference Room: 1315
Silver Spring, Maryland 20903

Application Number: IND 064892
Product Name: Rivaroxaban tablets
Indication: Xarelto is indicated for the treatment of venous thromboembolism (VTE) and the reduction in the risk of recurrent VTE in children from birth to < 18 years of age following initiation of standard anticoagulation treatment.

Xarelto is indicated for the thromboprophylaxis in children 2 years to 8 years of age with congenital heart disease (CHD) who have undergone Fontan procedure.
Sponsor Name: Janssen Research & Development, LLC (Janssen or JRD)

Meeting Chair: Tanya Wroblewski, MD
Meeting Recorder: Katie Chon, PharmD, RPh

FDA ATTENDEES

Office of Hematology and Oncology Products (OHOP)/Division of Hematology Products (DHP)
Ann Farrell, MD, Director
Tanya Wroblewski, MD, Clinical Team Leader
Laurel Menapace, MD, Medical Officer
Lori Ehrlich, MD, Medical Officer
Katie Chon, PharmD, RPh, Regulatory Project Manager

Office of Biostatistics/Division of Biometrics V
Alexei Ionan, PhD, Statistical Reviewer

Office of Clinical Pharmacology(OCP)/Division of Clinical Pharmacology I
Venkateswaran Chithambaram-Pillai, PhD, Clinical Pharmacologist

OCP/Division of Applied Regulatory Science
Jeffry Florian, PhD, General Health Scientist

OCP/Division of Pharmacometrics
Xinyuan Zhang, PhD, Pharmacology reviewer

Office of Pharmaceutical Quality
Ramesh Raghavachari, PhD, Team Leader
Sherita McLamore, PhD, Team Leader
Emily Wu PhD, Product Quality Reviewer

Office of Surveillance and Epidemiology/Division of Medication Error Prevention and Analysis
Mishale Mistry, PharmD, MPH, Associate Director

Office of Device Evaluation/Division of Anesthesiology, General Hospital, Respiratory, Infection Control, and Dental Devices
Rita Lin, MS, RAC, Human Factors Engineer

SPONSOR ATTENDEES
James Buckley, MS, Director, JRD Global CMC Regulatory Affairs
Angela Falzone, PhD, Scientific Director, JRD CMC Leader
Kimberly Nessel, MS, Scientific Director, JRD Cardiovascular and Metabolism
L Miriam Pina, MD, Senior Director, JRD Project Physician
Branden Reid, PhD, Associate Director, JRD Global CMC Regulatory Affairs, Medical Devices and Combination Products
Huy Q Truong, MS, Associate Director, JRD Global Regulatory Affairs

Bayer Pharmaceuticals (Sponsor's collaborator)
Matthew Gale, PhD, Statistical and Programming Lead
Artur Lutfullin, MD, Senior Global Regulatory Strategist
Miriam Tamm, PhD, Senior Statistician, Integrated Analysis Statistics

(Via teleconference):
Penny Zhu, PhD, Associate Scientist Director, JRD Pharmacometrics, Global Clinical Pharmacology

Bayer Pharmaceuticals (Sponsor collaborator):
Dagmar Kubitza, MD, Head Pharmacodynamics Cardiovascular, Clinical Pharmacology Cardiovascular/Hematology
Akos F Pap, PhD, Project Statistician
William Smith, MD, Global Clinical Lead
Thomas Uhlich, PhD, CMC Technical Development Team Leader, Global Chemical and Pharmaceutical Development
Katrin Coboeken, PhD, Scientist Systems Pharmacology (Modelling)
Madhurima Maajumder, PhD, Study Statistician for Einstein Jr Phase 3 study

1.0 BACKGROUND

Rivaroxaban is an oral Factor Xa inhibitor indicated:

- to reduce the risk of stroke and systemic embolism in patients with nonvalvular atrial fibrillation
- for the treatment of deep vein thrombosis (DVT)
- for the treatment of pulmonary embolism (PE)
- for the reduction in the risk of recurrence of DVT and/or PE in patients at continued risk for recurrent DVT and/or PE after completion of initial treatment lasting at least 6 months
- for the prophylaxis of DVT, which may lead to PE in patients undergoing knee or hip replacement surgery
- in combination with aspirin, to reduce the risk of major cardiovascular events (cardiovascular (CV) death, myocardial infarction (MI) and stroke) in patients with chronic coronary artery disease (CAD) or peripheral artery disease (PAD)

The proposed indications the Sponsor is seeking are the following:

- Xarelto is indicated for the treatment of venous thromboembolism (VTE) and the reduction in the risk of recurrent VTE in children from birth to < 18 years of age following initiation of standard anticoagulation treatment.
- Xarelto is indicated for the thromboprophylaxis in children 2 years to (b) (4) with congenital heart disease (CHD) who have undergone Fontan procedure.

On May 29, 2015, Janssen submitted a Proposed Pediatric Study Request (PPSR) for rivaroxaban and on June 8, 2017, the Agency issued a formal Written Request (WR). On March 23, 2018, the Agency issued a WR – Amendment 1.

On May 22, 2019, the Sponsor requested a meeting to discuss their planned New Drug Application (NDA) for two proposed pediatric indications supported by the development program in the treatment and thromboprophylaxis of venous thromboembolism (VTE) and discuss the new pediatric formulation (granule for oral suspension). In addition, the Sponsor seeks guidance on the proposed stability package and testing including the planned assessment in the support of the filing for registration of the commercial product and the oral dosing device, the planned timing and contents of the NDA submission.

FDA sent Preliminary Comments to Janssen on July 31, 2019.

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