April 13, 2023

RESPONSE TO PREA NON-COMPLIANCE LETTER

Ann Farrell, MD; Director
Division of Nonmalignant Hematology
Office of Cardiology, Hematology, Endocrinology, and Nephrology
Food and Drug Administration
Center for Drug Evaluation and Research
5901-B Ammendale Road
Beltsville, MD 20705-1266

RE: ARIXTRA® (FONDAPARINUX SODIUM) SOLUTION FOR SUBCUTANEOUS INJECTION
2.5 mg/0.5 mL, 5 mg/0.4 mL, 7.5 mg/0.6 mL, 10 mg/0.8 mL
NDA 021345
SEQUENCE NUMBER: 0141

Dear Dr. Farrell:

Reference is made to NDA 021345 for Arixtra® (fondaparinux sodium injection) Solution held by Mylan Ireland Limited (Mylan), a Viatris Company[1], as well as IND 051126 held by Aspen Global, Inc. The product is approved for the treatment of acute deep vein thrombosis and acute pulmonary embolism when administered in conjunction with warfarin sodium in adults. Reference is also made to PMRs 2151-1 and 2151-2 for the evaluation of Arixtra in pediatric patients aged 1-16 years, which had a deferral extension due date of December 31, 2022, granted by the FDA on May 14, 2021.

This correspondence is submitted in response to the PREA Non-Compliance Letter received from the FDA on February 28, 2023. Mylan acknowledges that it was unable to fulfill all facets of the PMRs to support a comprehensive pediatric supplement by the due date of December 31, 2022, and on December 14, 2022, requested an extension of PMRs 2151-1 and 2151-2 until September 2023.

As explained in our previous correspondence dated June 16, 2020, historically there have been significant challenges with conducting a clinical study in pediatric patients. Since acquiring the application from the previous sponsors, Mylan has been diligently working to overcome these challenges and complete the PMRs. The recent delays in fulfilling PMRs 2151-1 and 2151-2 are the result of numerous setbacks encountered in supply chains (such as procuring the necessary types and volumes of syringes for testing), as well as delays and logistical challenges with our vendors and partners. Additionally, modifications to Mylan's pediatric proposal based upon the Agency's feedback increased the scope and volume of the anticipated work required to fulfill these PMRs, which impacted our planned timeline for the completion of our research and development activities. Agreement with the Agency on the contents of the future submission of the pediatric efficacy supplement was reached only in April 2022.

[1] Mylan Ireland Limited is independently operated and is an indirect, wholly owned subsidiary of Viatris Inc.

Mylan is fully committed to ensuring that PMRs 2151-1 and 2151-2 are fulfilled as soon as possible and expects to complete the tasks necessary to submit a high-quality pediatric supplement in September 2023. Mylan's ongoing work to support PMRs 2151-1 and 2151-2 includes the following:

- extensive data collection from the study site's pediatric patient records
- database management including incremental data transfers between Mylan and the study site
- source document verification, query generation, and query resolution
- finalization of the clinical database in collaboration with the study site
- statistical analysis of the clinical data and writing of the retrospective pediatric clinical study report
- in-use stability testing and reporting
- microbial challenge study and reporting
- final human factors assessment including use-related risk assessment
- (b) (4)

All files in this product correspondence have been scanned utilizing Symantec antivirus software and are free of known viruses. All inquiries regarding this correspondence should be directed to the responsible officials listed in Form FDA 356h.

Sincerely,

<Please see following page for signature manifestation.>

Robert Barto
Senior Director, Regulatory Affairs

RB/bjm

Document me Cover Letter - 003087974

Title Cover Letter - 0141 - Product Correspondence - Response to PREA on-Compliance Letter - 13-Apr-2023

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