Our STN: BL 125566/1034

SUPPLEMENT APPROVAL
PMC FULFILLED
October 10, 2025

Takeda Pharmaceuticals U.S.A., Inc.
Attention: Mercyanne Publico, MS
500 Kendall Street
Cambridge, MA 02142

Dear Mercyanne Publico:

We have approved your request received April 10, 2025, to supplement your Biologics License Application (BLA) submitted under section 351(a) of the Public Health Service Act for Antihemophilic Factor (Recombinant), PEGylated (ADYNOVATE) by providing the final clinical study report (CSR), along with the proposed labelling update to the USPI. The USPI was updated for immunogenicity, adverse reactions, and pharmacokinetics.

LABELING

We hereby approve the draft content of labeling Package Insert submitted under amendment 10, dated October 9, 2025.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the final content of labeling (21 CFR 601.14) in Structured Product Labeling (SPL) format via the FDA automated drug registration and listing system, (eLIST) as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the Package Insert submitted on October 9, 2025. Information on submitting SPL files using eLIST may be found in the guidance for industry *SPL Standard for Content of Labeling Technical Qs and As* at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

All final labeling should be submitted as Product Correspondence to this BLA, STN BL 125566 at the time of use and include implementation information on Form FDA 356h.

ADVERTISING AND PROMOTIONAL LABELING

You may submit two draft copies of the proposed introductory advertising and promotional labeling with Form FDA 2253 to the Advertising and Promotional Labeling Branch at the following address:

Food and Drug Administration
Center for Biologics Evaluation and Research
Document Control Center
10903 New Hampshire Ave.
WO71–G112
Silver Spring, MD 20993-0002

You must submit copies of your final advertising and promotional labeling at the time of initial dissemination or publication, accompanied by Form FDA 2253 (21 CFR 601.12(f)(4)).

All promotional claims must be consistent with and not contrary to approved labeling. You should not make a comparative promotional claim or claim of superiority over other products unless you have substantial evidence or substantial clinical experience to support such claims (21 CFR 202.1(e)(6)).

FULFILLED POSTMARKETING REQUIREMENT/COMMITMENTS

This submission fulfills your postmarketing commitment (PMC) #7 identified in the November 13, 2015, approval letter for BLA STN BL 125566/0 for Antihemophilic Factor (Recombinant), PEGylated (ADYNOVATE). The commitment addressed in this submission is as follows:

PMC #7: You have committed to conducting "A phase 3, multi-center, open label study to investigate safety and immunogenicity of ADYNOVATE in previously untreated patients (PUPs)" [clinical study 261203]. This study will evaluate on-demand treatment and control of bleeding episodes in the setting of routine prophylaxis to reduce the frequency of bleeding episodes, as well as the perioperative management of bleeding.

Final protocol submission date: December 31, 2015

Study/trial completion date: December 31, 2022

Final Report Submission date: September 30, 2023

This completes all of your PMRs and PMCs. As such, your **Annual Status Report of Postmarketing Requirements/Commitments** is no longer required until such time a new Requirement or Commitment subject to the reporting requirements of section 506B of the Federal Food, Drug, and Cosmetic Act is issued.

We will include information contained in the above-referenced supplement in your BLA file.

Sincerely,

Asha Das, MD
Acting Director
Division of Clinical Evaluation Hematology
Office of Clinical Evaluation
Office of Therapeutic Products
Center for Biologics Evaluation and Research