



Our STN: BL 125795/81

SAFETY LABELING CHANGE ORDER

May 20, 2026

Takeda Pharmaceuticals U.S.A., Inc.
Attention: Arjun Singh Channi
125 Binney Street
Cambridge, MA 01242

Dear Mr. Channi:

Please refer to your Biologics License Application (BLA) submitted under section 351(a) of the Public Health Service Act for ADAMTS13, recombinant-krhn [ADZYNMA].

On February 5, 2026, we sent you a Safety Labeling Change Notification letter invoking our authority under section 505(o)(4) of the Federal Food, Drug, and Cosmetic Act to require safety related label changes to the labeling of ADZYNMA to address the safety information related to the development of neutralizing antibodies to ADAMTS13, associated with serious outcomes including death. The decision to require safety labeling changes was based on new safety information about this risk identified since this product was approved. In accordance with section 505(o)(4) of the FDCA, you were directed to submit, within 30 days of the date of that letter, a supplement proposing changes to the approved labeling, or notify FDA that you do not believe a labeling change is warranted and submit a statement detailing the reasons why such a change is not warranted.¹

On March 6, 2026, you submitted a prior approval supplement proposing changes to the approved labeling to reflect the new safety information.

Section 505(o) requires FDA to promptly review your submission and initiate discussions if necessary. You were contacted on March 11, 2026, to initiate discussions of your submission. The 30-day discussion period was extended in our letter dated April 3, 2026, to allow us to complete our review and reach agreement on the content of the labeling. We also refer to modified proposed labeling language that was sent to you by email on March 31, 2026, April 24, 2026, and May 1, 2026, and to your amendment responses received on April 2, 2026 and May 6, 2026².

¹ You are also required to conduct post-marketing required (PMR) studies to evaluate and characterize the risks of developing antibodies to ADAMTS13 following exposure to ADZYNMA. The PMR studies are not addressed in this Order.

² Formal amendment submission receipt dates. Submissions identical to email responses received April 1, 2026, and May 4, 2026, respectively.

We have completed the review of your submission, initiated discussions of your submission, and did not reach agreement. For the reasons in our February 5, 2026, Safety Labeling Change Notification letter (attached), we find that your proposed labeling changes do not adequately address the new safety information described above.

Under the authority of Section 505(o)(4)(E) of the FDCA, we are ordering you to make all the changes to the labeling listed in the February 5, 2026, Safety Labeling Change Notification letter and as modified in accordance with our emails dated March 31, 2026, April 24, 2026, and May 1, 2026, including the changes to add a Boxed Warning, revise Section 5.2, and revise Section 12.6.

Pursuant to Section 505(o)(4)(E), a changes being effected (CBE) supplement containing all of the changes to the labeling that are listed in the February 5, 2026, Safety Labeling Change Notification letter and as modified in accordance with our emails dated March 31, 2026, April 24, 2026, and May 1, 2026, must be received by FDA by June 4, 2026, for ADZYNMA.

Prominently identify the submission with the following wording in bold capital letters at the top of the first page of the submission:

SAFETY LABELING CHANGES UNDER 505(o)(4) – CHANGES BEING EFFECTED

Alternatively, within 5 days from the date of this letter, you may appeal this Order using the Agency's established formal dispute resolution process in 21 CFR 10.75 and the Guidance for Industry Formal Dispute Resolution: Appeals Above the Division Level at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents/formal-dispute-resolution-sponsor-appeals-above-division-level-guidance-industry-and-review-staff>. The appeal should be submitted as a correspondence to your BLA 125795. Identify the submission as “**Formal Dispute Resolution Request**”.

Failure to respond to this Order within the specified timeframes is a violation of section 505(o)(4) of the FDCA. Under section 303(f)(4) of the FDCA, 21 U.S.C. 333(f)(4), an application holder that is in violation of Safety Labeling Change requirements is subject to civil monetary penalties. Further, such a violation would cause your product to be misbranded under section 502(z) of the Act, 21 U.S.C. 352(z). Violations of these requirements may be subject to additional enforcement actions, included but not limited to seizure of your product and injunction.

If you have any questions, please contact the Regulatory Project Manager, Cara Pardon, at (240) 994-8449 or by email at cara.pardon@fda.hhs.gov.

Sincerely,

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

ENCLOSURE:
Safety Labeling Change Notification Letter