Important Drug Safety Notice

TO ALL PARTICIPATING PHARMACIES

Circular Letter MC25-025-CG
December 24, 2025

FDA announced that, has received postmarketing safety data on thromboembolic events, including serious and fatal outcomes, in patients treated with Andexxa (coagulation factor Xa (recombinant), inactivated-zhzo). Based on available data, the serious risks including the increase in thromboembolic events are such that the FDA considers the risks of the product to outweigh its benefits. The FDA has communicated this position to AstraZeneca, and the company has submitted a request to voluntarily withdraw the BLA for the product for commercial reasons. Additionally, the company has confirmed that it will end U.S. commercial sales today, December 22, 2025. Andexxa will no longer be manufactured for or sold in the U.S. by AstraZeneca after December 22, 2025.

RECOMMENDATIONS

1. Consumers should contact their physician or healthcare provider.

2. Expect patients to visit your pharmacy asking for information on this safety issue and prepare your pharmacy staff on how to handle the situation.

MC-Rx Pharmacy Services Department

T. (800) 377-1037
1267 Professional Pkwy, Gainesville, GA 30507
T. (787) 286-6032
Call Box 4908, Caguas, P.R. 00726
MC-Rx.com

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Update on the Safety of Andexxa by AstraZeneca: FDA Safety Communication

AUDIENCE: Patient, Health Care Professional, Pharmacy, Hematology

ISSUE: Since approval, the FDA has received postmarketing safety data on thromboembolic events, including serious and fatal outcomes, in patients treated with Andexxa (coagulation factor Xa (recombinant), inactivated-zhzo). Based on available data, the serious risks including the increase in thromboembolic events are such that the FDA considers the risks of the product to outweigh its benefits. The FDA has communicated this position to AstraZeneca, and the company has submitted a request to voluntarily withdraw the BLA for the product for commercial reasons.

Additionally, the company has confirmed that it will end U.S. commercial sales today, December 22, 2025. Andexxa will no longer be manufactured for or sold in the U.S. by AstraZeneca after December 22, 2025.

Continuous monitoring and assessment of the safety of all biological products, including Andexxa, is an FDA priority, and we remain committed to informing the public when we learn new information about these products.

BACKGROUND: The FDA initially granted accelerated approval (AA) of Andexxa, a recombinant modified human factor Xa (FXa) protein, in 2018, indicated for patients treated with rivaroxaban or apixaban when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding. Initial approval included a Boxed Warning for thromboembolic risks. AA was granted based on the change from baseline in anti-activated FXa (anti-FXa) activity in healthy volunteers, as a surrogate endpoint reasonably likely to predict clinical benefit.

At the time of AA of Andexxa, AstraZeneca (Applicant) was subject to a requirement to conduct a randomized controlled trial (NCT03661528) to verify the clinical benefit of Andexxa among patients with intracerebral hemorrhage following treatment with rivaroxaban or apixaban. On January 31, 2024, the Applicant submitted a supplemental Biologics Licensing Application (sBLA) for Andexxa with the results of the ANNEXA-I trial to fulfill this requirement. The FDA convened a meeting of the Cellular, Tissue, and Gene Therapies Advisory Committee (AC) on November 21, 2024[1], to discuss the results of the ANNEXA-I trial. The major safety findings discussed at the AC meeting included a doubling of the rate of thromboses and thrombosis-related deaths at Day 30 in the Andexxa arm compared with usual care (UC):

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- Increased risk of thrombosis: ANNEXA-I demonstrated an increased incidence of thrombosis (14.6% versus 6.9%) and thrombosis-related deaths at Day 30 (2.5% versus 0.9%) in the Andexxa arm compared with the UC arm, respectively.
- Death related to thrombotic events through 30 days occurred in 6 patients (2.5%) in the Andexxa arm compared with 2 patients (0.9%) in the usual care control arm.

The FDA will continue working with AstraZeneca to keep providers and the public informed as AstraZeneca prepares to end sale of Andexxa.

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