You are cordially invited to attend a peer-to-peer presentation

Andexxa®
(coagulation factor Xa (recombinant), inactivated-zhzo)

Presented by: **JOHN CORNELL, MD**
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REGISTER TODAY!

Please register by going to: **www.hlxregister.com**

Please reference program code: **XT3J37**

Program Details

Date: **WEDNESDAY, SEPTEMBER 18, 2019**

Time: **6:00 PM**

Location: FOGO DE CHAO
525 SMITHFIELD STREET, PITSBURGH, PA 15222

Andexxa Promotional Program Overview

- Burden of life-threatening bleeds related to FXa inhibitors
- Review the indications, mechanism, efficacy and safety of Andexxa for the reversal of FXa inhibitors rivaroxaban and apixaban

Please see Important Safety Information, including Boxed Warning below, and full Prescribing Information at:
https://www.andexxa.com/prescribing-information/

INDICATION AND SELECT IMPORTANT SAFETY INFORMATION

WARNING: THROMBOEMBOLIC RISKS, ISCHEMIC RISKS, CARDIAC ARREST, AND SUDDEN DEATHS

See full prescribing information for complete boxed warning

Treatment with ANDEXXA has been associated with serious and life-threatening adverse events, including:

- **Arterial and venous thromboembolic events**
- **Ischemic events, including myocardial infarction and ischemic stroke**
- **Cardiac arrest**
- **Sudden deaths**

Monitor for thromboembolic events and initiate anticoagulation when medically appropriate. Monitor for symptoms and signs that precede cardiac arrest and provide treatment as needed.

INDICATION

ANDEXXA, coagulation factor Xa (recombinant), inactivated-zhzo is indicated for patients treated with rivaroxaban and apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding.

This indication is approved under accelerated approval based on the change from baseline in anti-FXa activity in healthy volunteers. An improvement in hemostasis has not been established. Continued approval for this indication may be contingent upon the results of studies to demonstrate an improvement in hemostasis.

Limitation of Use:
ANDEXXA has not been shown to be effective for, and is not indicated for, the treatment of bleeding related to any FXa inhibitors other than apixaban and rivaroxaban.

Important Safety Information continued on reverse side.

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SELECT IMPORTANT SAFETY INFORMATION (con't)

Thromboembolic Risk

Arterial and venous thromboembolic events, ischemic events, sudden deaths, or events where a thrombotic event could not be ruled out were observed within 30 days post-ANDEXXA administration in 33 of the 185 patients (17.8%) evaluable for safety in the ongoing ANNEXA-4 study. The median time to these events was 6 days. Of the 86 patients who were re-anticoagulated prior to a thrombotic event, 11 (12.7%) patients experienced a thromboembolic, ischemic event, cardiac event or death.

Monitor patients treated with ANDEXXA for signs and symptoms of arterial and venous thromboembolic events, ischemic events, and cardiac arrest. To reduce thromboembolic risk, resume anticoagulant therapy as soon as medically appropriate following treatment with ANDEXXA.

The safety of ANDEXXA has not been evaluated in patients who experienced thromboembolic events or disseminated intravascular coagulation within two weeks prior to the life-threatening bleeding event requiring treatment with ANDEXXA. Safety of ANDEXXA also has not been evaluated in patients who received prothrombin complex concentrates, recombinant factor VIIa, or whole blood products within seven days prior to the bleeding event.

Re-elevation or Incomplete Reversal of Anti-FXa Activity

The time course of anti-FXa activity following ANDEXXA administration was consistent among the healthy volunteer studies and the ANNEXA-4 study in bleeding patients. Compared to baseline, there was a rapid and substantial decrease in anti-FXa activity corresponding to the ANDEXXA bolus. This decrease was sustained through the end of the ANDEXXA continuous infusion. Following the infusion, there was an increase in anti-FXa activity, which peaked 4 hours after infusion in ANNEXA-4 subjects. After this peak, the anti-FXa activity decreased at a rate similar to the clearance of the FXa inhibitors.

Thirty-eight patients who were anticoagulated with apixiban had baseline levels of anti-FXa activity >150 ng/mL. Nineteen of these 38 (50%) patients experienced a > 93% decrease from baseline anti-FXa activity after administration of ANDEXXA. Eleven patients who were anticoagulated with rivaroxaban had baseline anti-FXa activity levels > 300 ng/mL. Five of the 11 patients experienced a >90% decrease from baseline anti-FXa activity after administration of ANDEXXA.

Adverse Reactions

The most common adverse reactions (≥ 5%) in patients receiving ANDEXXA were urinary tract infections and pneumonia.

The most common adverse reactions (≥ 3%) in healthy volunteers treated with ANDEXXA were infusion-related reactions.

Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. Low titers of anti-ANDEXXA antibodies were observed in 26/145 healthy subjects (17%); 6% (9/145) were first observed at Day 30 with 20 subjects (14%) still having titers at the last time point (days 44 to 48). To date, the pattern of antibody response in patients in the ANNEXA-4 study has been similar to that observed in healthy volunteers with 6% of the patients having antibodies against ANDEXXA (6/98 patients). None of these anti-ANDEXXA antibodies were neutralizing. No antibodies cross-reacting with FX or FXa were detected in healthy subjects (0/145) or in bleeding patients to date (0/98).

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