ANDEXXA (coagulation factor Xa (recombinant), inactivated-zhzo) is a recombinant modified human factor Xa (FXa) protein indicated for patients treated with rivaroxaban or 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 that demonstrate an improvement in hemostasis in patients.

Limitations 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 or rivaroxaban.

Please see additional Important Safety Information on reverse side and accompanying full Prescribing Information including Boxed Warning on thromboembolic risks, ischemic risks, cardiac arrest, and sudden death.

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

Presented by
[Name], [Degree]
>Title
[Affiliation]

Hosted by
[Alexion Representative Name]
[Alexion Rep Mobile Number]
[Alexion Rep Email]

Program Details
Date:
Time:
Location:

Please register by going to www.hlxregister.com
Please reference program code:

ANDEXXA Promotional Program Overview

• Burden of life-threatening bleeds related to FXa inhibitors
• Review the indication, mechanism of action, efficacy, and safety of ANDEXXA for the reversal of FXa inhibitors apixaban or rivaroxaban in patients with life-threatening bleeds

Please see additional Important Safety Information on reverse side and accompanying full Prescribing Information including Boxed Warning on thromboembolic risks, ischemic risks, cardiac arrest, and sudden death.

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 a recombinant modified human factor Xa (FXa) protein indicated for patients treated with rivaroxaban or 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 that demonstrate an improvement in hemostasis in patients.

Limitations 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 or rivaroxaban.

Please see additional Important Safety Information on reverse side and accompanying full Prescribing Information including Boxed Warning on thromboembolic risks, ischemic risks, cardiac arrest, and sudden death.

Alexion is committed to complying with all applicable laws and regulations and adhering to the highest standards in its interactions with healthcare professionals. Certain states and federal agencies have defined the maximum fair market value allowable for modest meals given to healthcare professionals or prohibited the receipt of meals at company-sponsored events. You are accountable for understanding such restrictions and complying with them. Alexion may restrict your participation in this program. Please note, per industry guidelines, we are unable to accommodate spouses or guests at this event. The invitation is nontransferable and is for relevant healthcare professionals only. In order to ensure accurate transparency reporting of meals, Alexion requires program attendees to sign in upon arrival. Subject to all applicable federal and/or state regulations, Alexion will disclose information related to meals provided to you. In most cases, this information will be made public. Attendees may opt out of the meal by indicating on their RSVP. Healthcare providers and professionals regularly practicing in Vermont, and District of Columbia Medication Advisory Committee members will not receive a meal.
Thromboembolic and Ischemic Risks

The thromboembolic and ischemic risks were assessed in 352 bleeding subjects who received ANDEXXA. Of the 63 subjects who experienced a thrombotic event, the median time to first event was 7 days, and 21 subjects experienced the event within the first three days. A total of 63 (18%) experienced 88 thromboembolic or ischemic events. Of the 352 subjects who received ANDEXXA, 223 received at least one anticoagulation dose within 30 days after treatment. Of these 223, 18 subjects (8%) had a thrombotic event and/or ischemic event after resumption.

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. The anti-FXa activity returned to the placebo levels approximately two hours after completion of a bolus or continuous infusion. Subsequently, the anti-FXa activity decreased at a rate similar to the clearance of the FXa inhibitors.

Seventy-one subjects were anticoagulated with apixaban and had baseline levels of anti-FXa activity > 150 ng/mL. Nineteen subjects who were anticoagulated with rivaroxaban had elevated baseline anti-FXa activity levels > 300 ng/mL. Forty-eight of the 71 apixaban-treated subjects (68%) experienced a > 90% decrease from baseline anti-FXa activity after administration of ANDEXXA. Ten of the 19 rivaroxaban subjects (53%) experienced a > 90% decrease from baseline anti-FXa activity after administration of ANDEXXA.

Use of Heparin Following Administration of ANDEXXA

ANDEXXA may interfere with the anticoagulant effect of heparin. Use of ANDEXXA as an antidote for heparin has not been established. Avoid use of ANDEXXA for the reversal of direct FXa inhibitors (apixaban and rivaroxaban) prior to heparinization as ANDEXXA may cause unresponsiveness to heparin. If anticoagulation is needed, use an alternative anticoagulant to heparin.

Immunogenicity

As with all therapeutic proteins, there is the potential for immunogenicity. Using an electrochemiluminescence (ECL)-based assay, 145 ANDEXXA-treated healthy subjects were tested for antibodies to ANDEXXA as well as antibodies cross-reacting with Factor X (FX) and FXa. Low titer 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 ongoing ANNEXA-4 study has been similar to that observed in healthy volunteers. Of the 236 subjects with available samples, 6.8% (16/236) had antibodies against ANDEXXA. None of these anti-ANDEXXA antibodies were neutralizing. No neutralizing antibodies cross-reacting with FX or FXa were detected in healthy subjects (0/145) or in bleeding patients (0/209) to date.

To report SUSPECTED ADVERSE REACTIONS, call 1-866-777-5947 or contact the FDA by visiting www.fda.gov/medwatch, or calling 1-800-FDA-1088.

Please see additional Important Safety Information on reverse side and accompanying full Prescribing Information including Boxed Warning on thromboembolic risks, ischemic risks, cardiac arrest, and sudden death.

Andexxa and Alexion are registered trademarks of Alexion Pharmaceuticals, Inc. Other brands noted herein are the property of their respective owners.
**ANDEXXA**

**Coagulation Factor Xa (recombinant), lyophilized powder for solution for injection**

**INDICATIONS AND USAGE**

ANDEXXA is indicated for patients treated with rivaroxaban or apixaban who require urgent medical attention due to life-threatening or uncontrolled bleeding. ANDEXXA is recommended for patients treated with rivaroxaban or apixaban who require urgent medical attention due to life-threatening or uncontrolled bleeding. ANDEXXA is recommended for patients treated with rivaroxaban or apixaban who require urgent medical attention due to life-threatening or uncontrolled bleeding.

**CONTRAINDICATIONS**

ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA is not recommended for patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA is not recommended for patients with a known hypersensitivity to ANDEXXA components or lyophilized powders.

**WARNINGS AND PRECAUTIONS**

ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders.

**ADVERSE REACTIONS**

ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders.

**DOSE AND ADMINISTRATION**

ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders.

**Pharmacokinetics**

ANDEXXA is a recombinant modified human factor Xa (FXa) protein indicated for the treatment of bleeding related to any FXa inhibitors. ANDEXXA is a recombinant modified human factor Xa (FXa) protein indicated for the treatment of bleeding related to any FXa inhibitors. ANDEXXA is a recombinant modified human factor Xa (FXa) protein indicated for the treatment of bleeding related to any FXa inhibitors.

**CLINICAL PHARMACOLOGY**

ANDEXXA is a recombinant modified human factor Xa (FXa) protein indicated for the treatment of bleeding related to any FXa inhibitors. ANDEXXA is a recombinant modified human factor Xa (FXa) protein indicated for the treatment of bleeding related to any FXa inhibitors. ANDEXXA is a recombinant modified human factor Xa (FXa) protein indicated for the treatment of bleeding related to any FXa inhibitors.

**INDICATIONS AND USAGE**

ANDEXXA is indicated for patients treated with rivaroxaban or apixaban who require urgent medical attention due to life-threatening or uncontrolled bleeding. ANDEXXA is indicated for patients treated with rivaroxaban or apixaban who require urgent medical attention due to life-threatening or uncontrolled bleeding. ANDEXXA is indicated for patients treated with rivaroxaban or apixaban who require urgent medical attention due to life-threatening or uncontrolled bleeding.

**CONTRAINDICATIONS**

ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders.

**WARNINGS AND PRECAUTIONS**

ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders.

**ADVERSE REACTIONS**

ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders.

**DOSE AND ADMINISTRATION**

ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders. ANDEXXA should not be used in patients with a known hypersensitivity to ANDEXXA components or lyophilized powders.

**Pharmacokinetics**

ANDEXXA is a recombinant modified human factor Xa (FXa) protein indicated for the treatment of bleeding related to any FXa inhibitors. ANDEXXA is a recombinant modified human factor Xa (FXa) protein indicated for the treatment of bleeding related to any FXa inhibitors. ANDEXXA is a recombinant modified human factor Xa (FXa) protein indicated for the treatment of bleeding related to any FXa inhibitors.

**CLINICAL PHARMACOLOGY**

ANDEXXA is a recombinant modified human factor Xa (FXa) protein indicated for the treatment of bleeding related to any FXa inhibitors. ANDEXXA is a recombinant modified human factor Xa (FXa) protein indicated for the treatment of bleeding related to any FXa inhibitors. ANDEXXA is a recombinant modified human factor Xa (FXa) protein indicated for the treatment of bleeding related to any FXa inhibitors.
8.5 Geriatric Use

The safety and efficacy of ANDEXXA in Study 3 ANNEXA-4 study of ANDEXXA, 314 were 65 years of age or older, and 227 were 75 years of age or older. Based on the review of all clinical data, no overall differences in safety or efficacy were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses in between elderly and younger patients; however, greater sensitivity of some older individuals cannot be ruled out.

11 DESCRIPTION

ANDEXXA is a recombinant, human coagulation factor Xa (FXa) antagonist. ANDEXXA is manufactured from genetically engineered human cells. ANDEXXA is supplied as a white to off-white lyophilized cake or powder provided as a 200 mg/vial reconstituted dose. Reconstitution is accomplished by adding 5 mL sterile water for injection (SWFI) and administering as a 200 mg IV push over 2 minutes. After reconstitution ANDEXXA is a clear to slightly opalescent, colorless solution.

12.3 Pharmacokinetics

The safety and efficacy of ANDEXXA were evaluated in an ongoing, prospective, single-arm, open-label study (Study 3 ANNEXA-4) in 314 healthy adults. Patients received ANDEXXA 200 mg IV bolus followed by a 400 mg IV continuous infusion for 120 minutes (total 480 mg).

Table 3: Summary of PK Parameters in Healthy Volunteers

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ANDEXXA</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cmax (µg/mL)</td>
<td>76.6 (17.5)</td>
<td>19.4 (12.5)</td>
</tr>
<tr>
<td>Tmax (h)</td>
<td>0.5 (0.1)</td>
<td>0.5 (0.1)</td>
</tr>
<tr>
<td>AUC0-∞ (µg*h/mL)</td>
<td>572.9 (16.0)</td>
<td>27.9 (10.1)</td>
</tr>
<tr>
<td>Vss (L)</td>
<td>4.4 (17.6)</td>
<td>0.2 (0.1)</td>
</tr>
<tr>
<td>Mean residence time (h)</td>
<td>9.7 (0.6)</td>
<td>4.5 (0.4)</td>
</tr>
</tbody>
</table>

The pharmacokinetics of ANDEXXA in elderly (≥ 65 years) subjects was determined in 22 subjects (≥ 65 years) subjects were not different compared to younger (18-45 years) subjects.

12.1 Mechanism of Action

ANDEXXA on carcinogenesis, mutagenesis, or impairment of fertility.

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

ANDEXXA was not shown to be effective for bleeding related to any FXa inhibitors other than apixaban or rivaroxaban.

10 ADVERSE REACTIONS

ANDEXXA is supplied as a white to off-white lyophilized cake or powder provided as a 200 mg/vial reconstituted dose. Reconstitution is accomplished by adding 5 mL sterile water for injection (SWFI) and administering as a 200 mg IV push over 2 minutes. After reconstitution ANDEXXA is a clear to slightly opalescent, colorless solution.