

## **U.S. Centers for Medicare and Medicaid Services (CMS) Grants New Technology Add-On Payment for Portola Pharmaceuticals' Andexxa**

**– Add-on payment to support patient access by providing additional Medicare reimbursement in the hospital setting –**

SOUTH SAN FRANCISCO, Calif. , Aug. 03, 2018 (GLOBE NEWSWIRE) -- Portola Pharmaceuticals, Inc.<sup>®</sup> (Nasdaq: PTLA) today announced that the U.S. Centers for Medicare and Medicaid Services (CMS) has granted a New Technology Add-on Payment (NTAP) for Andexxa<sup>®</sup> [coagulation factor Xa (recombinant), inactivated-zhzo], the first and only antidote approved by the U.S. Food and Drug Administration (FDA) for patients treated with rivaroxaban and apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding.

In the final rule concerning the Hospital Inpatient Prospective Payment System and CMS Fiscal Year 2019 (scheduled for publication in the Federal Register on August 17, 2018), CMS states that Andexxa meets all criteria for approval for new technology add-on payments. Additional information on the CMS final rule and its discussion of NTAP and Andexxa can be found on pages 783-806 of the pre-publication on the [Federal Register](#).

<https://www.federalregister.gov/documents/2018/08/17/2018-16766/medicare-program-hospital-inpatient-prospective-payment-systems-for-acute-care-hospitals-and-the>

“We are pleased that CMS has recognized the breakthrough innovation of Andexxa and the substantial clinical value of rapidly reversing the anticoagulating effects of the Factor Xa inhibitors. rivaroxaban and apixaban, in the event of life-threatening or uncontrolled bleeding,” said John T. Curnutte, M.D., Ph.D., interim co-president of Portola and head of research and development. “The establishment of a NTAP for Andexxa is an important decision for a very vulnerable patient population, as it both broadens Medicare beneficiary access to Andexxa, and supports the hospitals who are incorporating this important therapy into their treatment protocols.”

Introduced in 2001, the CMS NTAP program was created by Congress to support timely access to innovative therapies used to treat Medicare beneficiaries in the hospital inpatient setting. For a new technology to qualify for an add-on payment, it must meet the NTAP definition of “new,” demonstrate a substantial clinical improvement and meet specific cost thresholds.

Effective for the Fiscal Year 2019 starting October 1, 2018, the maximum NTAP for a case involving the use of Andexxa is \$14,062.50, or 50 percent of the wholesale acquisition cost of the standard dose. NTAP is expected to remain in effect for a period of two to three years until the cost of Andexxa is included in the recalibration of the DRG payment rates.

### **About Factor Xa Inhibitor-Related Bleeding**

The use of Factor Xa inhibitors is growing rapidly because of their efficacy and safety profile compared to enoxaparin and warfarin in preventing and treating thromboembolic conditions such as stroke, pulmonary embolism and venous thromboembolism (VTE). This growth has come with a related increase in the incidence of hospital admissions and deaths related to bleeding, the major complication of anticoagulation. In 2016, there were approximately 117,000 hospital admissions attributable to Factor Xa inhibitor-related bleeding and nearly 2,000 bleeding-related deaths per month in the U.S.

### **About Andexxa**

Andexxa is a recombinant protein specifically designed to bind to Factor Xa inhibitors and rapidly reverse their anticoagulant effect. Andexxa was approved by the FDA in May 2018 as the first and only antidote indicated for patients treated with rivaroxaban and apixaban, when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding. Andexxa received both U.S. Orphan Drug and FDA Breakthrough Therapy designations and was approved under the FDA's Accelerated Approval pathway based on the change from baseline in anti-Factor Xa activity in healthy volunteers.

For additional Important Safety Information and Andexxa's full Prescribing Information, please visit <http://www.Andexxa.com>.

### **IMPORTANT INFORMATION FOR ANDEXXA [coagulation factor Xa (recombinant), inactivated-zhzo]**

#### **BOXED 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-Factor Xa

(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 in patients.

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.

## **SELECT IMPORTANT SAFETY INFORMATION**

### **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 six days. Of the 86 patients who were re-anticoagulated prior to a thrombotic event, 11 (12.7%) patients experienced a thromboembolic event, 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.

No thromboembolic events were observed in 223 healthy volunteers who received Factor Xa inhibitors and were treated 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 four 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 apixaban 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 ( $\geq 5\%$ ) in patients receiving Andexxa were urinary tract infections and pneumonia.

The most common adverse reactions ( $\geq 3\%$ ) 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).

## **About Portola Pharmaceuticals, Inc.**

Portola Pharmaceuticals is a commercial-stage biopharmaceutical company focused on the discovery, development and commercialization of novel therapeutics that could significantly advance the fields of thrombosis and other hematologic diseases. The Company's two FDA-approved medicines are Bevyxxa<sup>®</sup> (betrixaban), the first and only oral, once-daily Factor Xa inhibitor for the prevention of VTE in adult patients hospitalized for an acute medical illness, and Andexxa<sup>®</sup> [coagulation factor Xa (recombinant), inactivated-zhzo], the first and only antidote for the Factor Xa inhibitors rivaroxaban and apixaban. The company also is advancing cerdulatinib, a Syk/JAK inhibitor for the treatment of hematologic cancers.

## **Forward-Looking Statements**

This announcement contains forward-looking statements, including statements relating to Portola Pharmaceuticals' expectations regarding the potential commercial and medical impact of receiving the NTAP for Andexxa. These statements are subject to significant risks and uncertainties, and actual results could differ materially from those projected. Portola Pharmaceuticals cautions investors not to place undue reliance on the forward-looking statements contained in this release. These risks and uncertainties include, without limitation, risks and uncertainties that physicians may not see the benefits of utilizing Andexxa for the indications which it is approved; the ability of Portola to continue to manufacture Andexxa and to expand approved manufacturing facilities; the possibility of unfavorable results from additional clinical trials involving Andexxa; the amount of time that the NTAP is available; the risk that the EMA may not approve Andexxa in the currently anticipated timelines or at all, and that any marketing approvals may have significant limitations on its use; the risk that Portola may not obtain additional regulatory approvals necessary to expand approved indications for Andexxa; and other general business risks which could have a material adverse impact on Portola's business, including risks associated with the launch of Portola's first product Bevyxxa<sup>®</sup>; regulatory actions or delays or government regulation generally; Portola's ability to

obtain or maintain proprietary intellectual property protection; the particular prescribing preferences of physicians and patients; global trends toward health care cost containment, including government, payor and general public pricing and reimbursement pressures; general economic and industry conditions, including the effects of the persistently weak economic and financial environment in many countries; safety, quality or manufacturing issues. Risks and uncertainties relating to Portola Pharmaceuticals and its business can be found in the “Risk Factors” section of Portola Pharmaceuticals’ Annual Report on Form 10-K for 2017, which was filed with the SEC on March 1, 2018, as updated by subsequent periodic reports filed by Portola with the SEC, including Quarterly Reports on Form 10-Q and Current Reports on Form 8-K which are deemed “filed” with the SEC. Portola Pharmaceuticals undertakes no duty or obligation to update any forward-looking statements contained in this release as a result of new information, future events or changes in Portola Pharmaceuticals’ expectations.

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<https://investors.portola.com/2018-08-03-U-S-Centers-for-Medicare-and-Medicaid-Services-CMS-Grants-New-Technology-Add-On-Payment-for-Portola-Pharmaceuticals-Andexxa>