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Media and Public Relations

Press release

First antidote for reversal of anticoagulation with factor Xa inhibitors apixaban and rivaroxaban

EMA's human medicines committee (CHMP) has recommended granting a conditional marketing authorisation in the European Union for Ondexxya (andexanet alfa). This medicine is to be used as an antidote for adult patients taking the anticoagulant (clot-preventing) medicines apixaban or rivaroxaban, when reversal of their action is needed due to life-threatening or uncontrolled bleeding.

Anticoagulants are used to treat blood clots and reduce the risk of them forming in the arteries and veins, which can lead to pulmonary embolism, stroke or other organ damage. Apixaban and rivaroxaban belong to a newer class of anticoagulants called factor Xa (FXa) inhibitors, which work by blocking the action of activated factor X, a substance in the blood that has a key role in making it clot.

However, because anticoagulants stop the blood from clotting normally, patients taking them can be at risk of serious and uncontrolled bleeding, especially in emergency situations. Until now, there has been no specific antidote that could prevent the anticoagulant effect of apixaban or rivaroxaban once they have been given.

Andexanet alfa, the active substance of Ondexxya, is a recombinant protein that acts as a decoy for the direct oral FXa inhibitors apixaban and rivaroxaban in the blood. As a result, andexanet alfa neutralises the anticoagulant effect of these inhibitors.

The effects of the therapy with Ondexxya were studied in 352 patients for safety and 167 patients for efficacy. Clinical efficacy is based upon reversal of anti-fXa-activity in healthy volunteers and interim results of study in patients with life-threatening bleeding. Ondexxya enabled the reversal of the apixaban and rivaroxaban anticoagulant effect within 2 minutes of its administration.

The CHMP recommended a conditional approval for this therapy. This is one of EU's regulatory mechanisms to facilitate early access to medicines that fulfil an unmet medical need. Conditional approval allows the Agency to recommend a medicine for marketing authorisation in the interest of public health where the benefit of its immediate availability to patients outweighs the risk inherent in the fact that all the data are still not available. For example, andexanet alfa has not been investigated when direct oral fXa inhibitors are administered before surgery or other invasive procedures; there are insufficient clinical data to support its use in patients with severe bleedings related to direct-oral anticoagulants other than apixaban and rivaroxaban; formation of blood clots has been reported

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following treatment with Ondexxya; and a confirmation of the recommended dosage is yet to be expected. In light of this, the company is required to complete a number of post-authorisation studies to further investigate the efficacy and safety of the medicine within specified timeframes.

The opinion adopted by the CHMP at its February 2019 meeting is an intermediary step on Ondexxya's path to patient access. The CHMP opinion will now be sent to the European Commission for the adoption of a decision on an EU-wide marketing authorisation. Once a marketing authorisation has been granted, decisions about price and reimbursement will take place at the level of each Member State, taking into account the potential role/use of this medicine in the context of the national health system of that country.

Notes

1. The applicant for Ondexxya is Portola Netherlands B.V.
2. Apixaban is licensed in the EU as Eliquis and rivaroxaban as Xarelto.
3. More information on the work of the European Medicines Agency can be found on its website: www.ema.europa.eu

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