



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

EMA/439534/2014
EMA/H/C/002148

EPAR summary for the public

Eliquis

apixaban

This is a summary of the European public assessment report (EPAR) for Eliquis. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Eliquis.

What is Eliquis?

Eliquis is a medicine that contains the active substance apixaban. It is available as tablets (2.5 mg, 5 mg).

What is Eliquis used for?

Eliquis is used to prevent venous thromboembolism (blood clots in the veins) in adults following a hip or knee replacement operation. It is also used in adults to treat deep vein thrombosis (blood clot in a deep vein, usually in the leg) and pulmonary embolism (clot in a blood vessel supplying the lungs), and to prevent their reoccurrence.

Additionally, Eliquis is used to prevent stroke (caused by blood clots in the brain) and blood clots in other organs in adults with atrial fibrillation (irregular rapid contractions of the upper chambers of the heart). It is used in patients who have one or more risk factors, such as having had a previous stroke, having high blood pressure, diabetes, heart failure or being 75 years old or over.

The medicine can only be obtained with a prescription.

How is Eliquis used?

For patients who have had a hip or knee replacement, treatment with Eliquis should be started 12 to 24 hours after the operation. The recommended dose is one 2.5 mg tablet taken by mouth twice a day, usually for over one month (32 to 38 days) after a hip replacement or for 10 to 14 days after a knee



replacement. For patients with atrial fibrillation at risk of stroke or blood clots, the recommended dose is 5 mg taken twice a day.

For the treatment of deep vein thrombosis and pulmonary embolism, the recommended dose is 10 mg twice a day for the first week, followed by 5 mg twice a day for at least 3 months. To prevent deep vein thrombosis and pulmonary embolism from reoccurring, the recommended dose is 2.5 mg twice a day. For further information, see the package leaflet.

How does Eliquis work?

Patients undergoing hip or knee replacement surgery, who have had a recent trauma, or are confined to bed are at a high risk of blood clots forming in the veins, which can be dangerous and even fatal if they move to another part of the body such as the lungs. Similarly, patients with atrial fibrillation are at high risk of clots forming in the heart, which can reach the brain where they can cause a stroke.

The active substance in Eliquis, apixaban, is a 'factor Xa inhibitor'. This means that it blocks factor Xa, an enzyme that is involved in the production of thrombin. Thrombin is central to the process of blood clotting. By blocking factor Xa, it reduces the levels of thrombin in the blood, which reduces the risk of blood clots forming in the arteries and veins.

How has Eliquis been studied?

The effectiveness of Eliquis in preventing blood clots in veins following a hip or knee replacement has been investigated in two main studies involving a total of 8,464 patients. The first study was in 5,407 patients who had undergone a hip replacement. The second study was in 3,057 patients who had undergone a knee replacement. In both studies, Eliquis was compared with enoxaparin (another medicine used to prevent blood clots). The medicine's effectiveness was measured by looking at the number of patients who either had problems related to clotting in the veins or who died of any cause during the treatment period.

The effectiveness of Eliquis in preventing strokes and arterial blood clots in patients with atrial fibrillation has been investigated in two main studies: the first (in 18,201 patients) compared Eliquis with another medicine, warfarin, while the second (in 5,598 patients) compared Eliquis with aspirin. The main measures of effectiveness were based on the number of strokes or clotting events that occurred during treatment.

For the treatment of deep vein thrombosis and pulmonary embolism and the prevention of their reoccurrence, Eliquis has been investigated in two main studies: the treatment study included 5,395 patients, and the prevention study included 2,482 patients. In the first study, Eliquis was compared with enoxaparin followed by warfarin; the main measure of effectiveness was based on the number of patients who either had blood clots in the veins of the legs or lungs or died because of this during the treatment period. In the second study, Eliquis was compared with placebo (a dummy treatment) and its effectiveness was measured by looking at the number of patients who either had problems related to clotting in the veins or who died of any cause during treatment.

What benefit has Eliquis shown during the studies?

Eliquis was effective at preventing blood clots in the veins following a hip or knee replacement. In patients undergoing a hip replacement, 1.4% of the patients who completed treatment with Eliquis (27 out of 1,949) had a clotting event or died from any cause, compared with 3.9% (74 out of 1,917) of

the patients taking enoxaparin. In patients undergoing a knee replacement, the corresponding numbers were 15% (147 out of 976) for Eliquis compared with 24% (243 out of 997) for enoxaparin.

Eliquis was also shown to be effective in preventing strokes and arterial blood clots in patients with atrial fibrillation. In the study comparing Eliquis with warfarin, 1.3 % of the patients taking Eliquis had a stroke or clotting event every year compared with 1.6% of the patients taking warfarin. The yearly rates in the second study were 1.6% for patients taking Eliquis and 3.6% for patients taking aspirin.

Eliquis was also effective at treating deep vein thrombosis and pulmonary embolism and preventing their reoccurrence: in the treatment study, 2.3% of patients treated with Eliquis had a clotting event or died, compared with 2.7% of patients treated with enoxaparin plus warfarin, showing that Eliquis was as effective as the comparator treatment. In the prevention study, 2.3% of patients taking Eliquis (2.5 mg twice a day) experienced a clotting event or died, compared with 9.3% of patients taking placebo.

What is the risk associated with Eliquis?

The most frequent side effects with Eliquis (seen in between 1 and 10 patients in 100) are anaemia (low red blood cell counts), haemorrhage (bleeding), haematoma (a collection of blood under the skin), contusion (bruising) and nausea (feeling sick) when Eliquis is used for prevention of venous thromboembolism. When used for the prevention of stroke or systemic embolism the most common are epistaxis (nose bleeds), contusion (bruising), haematuria (blood in urine), haematoma and bleeding, in particular bleeding in the gut, eye, rectum and gums. When Eliquis is used for the treatment of deep vein thrombosis and pulmonary embolism and the prevention of their reoccurrence, the most common side effects are haemorrhage, haematoma, contusion, epistaxis, bleeding in the gut, rectum or gums, and haematuria (blood in the urine).

Eliquis must not be used in patients who are actively bleeding, or who have liver disease which leads to problems with blood clotting and an increased risk of bleeding. The medicine must also not be used in patients with conditions putting them at risk of major bleeding, such as an ulcer in the gut, or in patients being treated with other anticoagulant medicines except in specific circumstances (see summary of product characteristics).

For the full list of all side effects and restrictions with Eliquis, see the package leaflet.

Why has Eliquis been approved?

The CHMP decided that the benefits of Eliquis are greater than its risks and recommended that it be given marketing authorisation.

What measures are being taken to ensure the safe and effective use of Eliquis?

A risk management plan has been developed to ensure that Eliquis is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Eliquis, including the appropriate precautions to be followed by healthcare professionals and patients.

In addition, the company that markets Eliquis will provide educational material for healthcare professionals expected to prescribe Eliquis that addresses the risk of bleeding during treatment.

Other information about Eliquis

The European Commission granted a marketing authorisation valid throughout the European Union for Eliquis on 18 May 2011.

The full EPAR for Eliquis can be found on the Agency's website: ema.europa.eu/Find_medicine/Human_medicines/European_Public_Assessment_Reports. For more information about treatment with Eliquis, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 09-2014.