Direct oral anticoagulants: no change in use

17.04.2020 | Circular Number P10.2020

Information on direct oral anticoagulants

- Direct oral anticoagulants (DOACs) are medicines used to prevent blood clotting in different situations, including in patients with non-valvular atrial fibrillation
- DOACs are used to treat deep vein thrombosis (a blood clot in a deep vein, usually in the leg) and pulmonary embolism (a clot in a blood vessel supplying the lungs), and to prevent these conditions from reoccurring
- The DOACs Eliquis (apixaban), Pradaxa (dabigatran etexilate) and Xarelto (rivaroxaban) are taken by mouth. These medicines act by directly blocking a single blocking factor in the body

In Malta Eliquis, Pradaxa and Xarelto are authorised through the centralised procedure

Information from the EMA about no change in use of direct oral anticoagulants

Following a study commissioned by EMA and using real world data on DOACs from Denmark, France, Germany, Spain, the Netherlands and the United Kingdom, no change to the conditions of use of DOACs is needed.

The study assessed the risk of serious bleeding with Eliquis (apixaban), Pradaxa (dabigatran etexilate) and Xarelto (rivaroxaban) when used to prevent blood clotting in patients with non-valvular atrial fibrillation (irregular rapid contractions of the heart) and compared this with other oral anticoagulants called vitamin K antagonists[1,2]. Results were also compared with data from other similar studies and published literature. From data collected, it was concluded that the pattern of serious bleeding associated with the use of Eliquis, Pradaxa and Xarelto was similar to the pattern seen in the clinical trials on which the marketing authorisation was based. The data were not sufficient to allow robust conclusions to be drawn on comparisons between the 3 medicines.

The study also evaluated if the use of DOACs in clinical practice was in line with the authorised uses, considering existing contraindications, warnings and advice on interactions with other medicines. No changes to the product information were warranted since data did not show a high level of non-adherence to the product information.

Further data on increased risk of bleeding in patients older than 75-yer-old were collected from the study. Companies marketing DOACs will be required to further explore the issue and to investigate whether changes to the recommended doses could be beneficial for these patients.

The Committee for Medicinal Products for Human Use (CHMP) has adopted the Agency's opinion.

In Malta

For Healthcare Professionals

- Risk of major bleeding associated with the use of DOACs compared to vitamin K antagonists (VKAs), in patients with non-valvular atrial fibrillation has been assessed in a retrospective, non-interventional study using European databases carried out in 6 countries. The study had been proposed following a workshop held by EMA in 20153 on the clinical use of DOACs
- New data confirmed that the bleeding pattern of DOACs is the one observed in clinical trials and described in the product information. For all the three DOACs investigated (apixaban, dabigatran, rivaroxaban) the risk benefit balance remains positive within the authorised indications. Comparable results were found in similar studies conducted in Canada and the US
- Adherence with sections 4.1, 4.3, 4.4, and 4.5 of the summary of product characteristics for the medicines was evaluated. Data analysed did not provide robust evidence of a high level of non-adherence to the authorised product information
- Increased risk of bleeding in patients older than 75-year-old was observed, but the data were not sufficient to recommend dose changes in this population. Further studies are needed to explore the issue and to determine whether there are differences in risk between individual DOACs
- Companies marketing these medicines will be asked to explore the issue and to carry out an analysis to determine whether modification of the dosing recommendations could be beneficial for older patients.

Advice for Patients

- A study on the use of the anticoagulant medicines Eliquis (apixaban), Pradaxa (dabigatran etexilate) and Xarelto (rivaroxaban) was carried out. These medicines prevent blood clots in different situations, including in patients with non-valvular atrial fibrillation. Blood clots can can cause serious problems when they occur in important organs such as the lungs and brain. However, because these medicines prevent clotting, bleeding in various parts of the body can be an unwanted side effect
- The study evaluated bleeding in patients with non-valvular atrial fibrillation (irregular rapid contractions of the heart) treated with one of the 3 medicines and compared with other anticoagulant medicines such as warfarin

- The EMA, after reviewing the results, concluded that risk of bleeding with these medicines was expected. The study did not show that there was a high level of incorrect use of the medicines
- EMA recommends that Eliquis, Pradaxa and Xarelto can continue to be used in the same way as they are now by patients and healthcare professionals and there is no need to change the current advice for these medicines
- Study results showed that patients older than 75-year-old are at higher risk of bleeding. For this reason, the EMA will ask companies marketing these medicines to explore the issue and investigate whether changes to the dosing recommendations for older patients could be beneficial for these patients
- If you have any questions about your medicines, talk to your doctor or pharmacist

For more information please see the European Medicines Agency's Direct oral anticoagulant's press release

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on direct anticoagulant medicinal products. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority Form and sending it to Sir Temi Żammit Buildings, Malta Life Sciences Park, San Ġwann SĠN 3000 or online to **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

Post-Licensing Directorate
Medicines Authority

Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.

Feedback Form

The Medicines Authority thanks you for the time taken to read this safety circular. The dissemination of safety circulars is an important process whereby Regulatory Authorities can communicate important issues with respect to the safety of medicines, in order to protect and enhance public health

The Medicines Authority kindly invites your anonymous feedback about the regulatory action being communicated. This may be returned by folding this formt (address side up), stapling the ends and then posting (no stamp required)

Feedback:

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Pharmacovigilance Section

Post-Licensing Directorate

Medicines Authority

Sir Temi Żammit Buildings

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