EMA reviews diabetes medicine canagliflozin following data on toe amputations in ongoing study

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Information on Canagliflozin

- Canagliflozin is an SGLT2 inhibitor which works by blocking a protein in the kidneys called sodium glucose co-transporter 2 (SGLT2). SGLT2 absorbs glucose back into the bloodstream as the blood is filtered in the kidneys.
- By blocking the action of SGLT2, canagliflozin causes more glucose to be removed via the urine, thereby reducing glucose in the blood. The other SGLT2 inhibitors are dapagliflozin and empagliflozin.
- Canagliflozin is the active substance in two centrally authorised diabetes medicines, Invokana and Vokanamet (which also contains metformin) which were approved in the EU in 2013 and 2014 respectively.

Invokana is available in Malta through the centralized procedure.

Information on the review of the diabetes medicine canagliflozin after an increase in amputations was observed.

The European Medicines Agency (EMA) has started a review of the diabetes medicine canagliflozin after an increase in amputations, mostly affecting toes, was observed in an ongoing clinical trial called CANVAS.

- Cases of lower limb amputation occurred in both the canagliflozin and placebo groups in the trial and the possibility that canagliflozin increases lower limb amputations is currently not confirmed.
- The Pharmacovigilance Risk Assessment Committee (PRAC) has requested more information from the company to assess whether canagliflozin causes an increase in lower limb amputations and whether any changes are needed in the way this medicine is used in the EU.
- Patients with diabetes (especially those with poorly controlled diabetes and pre-existing problems with the heart and blood vessels) are at increased risk of infection and ulceration which can result in lower limb amputations.
- No increase in such amputations was seen in 12 other completed clinical trials with canagliflozin however a small, non-statistically significant increase in the number of amputations occurred in another ongoing study called CANVAS-R. Both CANVAS and CANVAS-R involve patients at high risk of problems with the heart and blood vessels.

The PRAC will also ask for data on other SGLT2 inhibitors namely dapagliflozin and empagliflozin and may decide to extend the scope of the review to cover these medicines also.

The PRAC will issue its recommendations following this review, which will be forwarded to the Committee for Medicinal Products for Human Use (CHMP), which will then adopt an opinion

In Malta

For Healthcare Professionals and Patients

While the review on canagliflozin is ongoing;

- Healthcare professionals will receive a letter reminding them about the importance of routine foot care to avoid cuts or sores of the feet, and to treat them promptly should they occur to prevent infection and ulceration.
- Patients at increased risk of amputation (such as those who have had a previous amputation) should be carefully monitored.
- As a precautionary measure, doctors may consider stopping treatment with canagliflozin in patients who develop significant foot complications.

Patients who have any questions should speak to their doctor or pharmacist. It is important that patients with diabetes continue to take their prescribed treatment and do not stop treatment without first consulting a healthcare professional

For more information on this review and the CANVAS studies, please see the **press release** issued by the European Medicines Agency.

Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on canagliflozin. Suspected Adverse Drug Reactions (side effects) or medication errors may be reported using the Medicines Authority ADR reporting form or online at http://www.medicinesauthority.gov.mt/adrportal or to the marketing authorisation holder or their local representatives.

Prof. John J Borg PhD (Bristol)

Post-licensing Director

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

The Medicines Authority thanks you for your 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

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