Drug Safety Update

Latest advice for medicines users

The monthly newsletter from the Medicines and Healthcare products Regulatory Agency and its independent advisor the Commission on Human Medicines

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Contents

The Medicines and Healthcare products Regulatory Agency is the government agency which is responsible for ensuring that medicines and medical devices work, and are acceptably safe.

The Commission on Human Medicines gives independent advice to ministers about the safety, quality, and efficacy of medicines. The Commission is supported in its work by Expert Advisory Groups that cover various therapeutic areas of medicine.

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This month we update readers on the risk of lower-limb amputation (mostly affecting the toes) with sodium-glucose co-transporter 2 (SGLT2) inhibitors following the completion of a European review. Although there is no evidence confirming the increased risk seen with canagliflozin with other SGLT2 inhibitors (dapagliflozin and empagliflozin), data available are limited and the risk may also apply to these medicines. Healthcare professionals are reminded that preventive foot care is important for all patients with diabetes, including those receiving SGLT2 inhibitors. For canagliflozin, patients who have risk factors for amputation should be carefully monitored; consider stopping canagliflozin treatment if patients develop foot complications. See page 2 for more information.

Also this month we are launching a pilot scheme for the reporting of suspected adverse reactions to new psychoactive substances (‘legal highs’). Healthcare professionals across the UK who come into contact with patients experiencing harms associated with the use of illicit drugs, particularly new psychoactive substances, will be able to use the Report Illicit Drug Reaction (RIDR) website over the next year. The 1-year pilot aims to better collect data on harms from illicit drug use to support provision of clinical guidance to professionals (see page 3).

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SGLT2 inhibitors: updated advice on increased risk of lower-limb amputation (mainly toes)

Canagliflozin may increase the risk of lower-limb amputation (mainly toes) in patients with type 2 diabetes. Evidence does not show an increased risk for dapagliflozin and empagliflozin, but the risk may be a class effect. Preventive foot care is important for all patients with diabetes.

Advice for healthcare professionals:

- carefully monitor patients receiving canagliflozin who have risk factors for amputation, such as poor control of diabetes and problems with the heart and blood vessels
- consider stopping canagliflozin if patients develop foot complications such as infection, skin ulcers, osteomyelitis, or gangrene
- advise patients receiving any sodium-glucose co-transporter 2 (SGLT2) inhibitor about the importance of routine preventive foot care and adequate hydration
- continue to follow standard treatment guidelines for routine preventive foot care for people with diabetes
- report any suspected side effect with SGLT2 inhibitors or any other medicine on a Yellow Card

Background

Sodium-glucose co-transporter 2 (SGLT2) inhibitors are indicated in adults with type 2 diabetes mellitus to improve glycaemic control when diet and exercise alone are inadequate for control.

SGLT2 inhibitors are given alone in patients for whom the use of metformin is considered inappropriate due to intolerance or contraindications. SGLT2 inhibitors can also be given with other glucose-lowering drugs, including insulin, when these drugs do not provide adequate glycaemic control.

The SGLT2 inhibitor-containing medicines marketed in the UK are Invokana▼ (canagliflozin), Vokanamet▼ (canagliflozin and metformin), Forxiga▼ (dapagliflozin), Xigduo▼ (dapagliflozin and metformin), Jardiance▼ (empagliflozin), and Synjardy▼ (empagliflozin and metformin).

Risk of amputation

In June 2016, we published a Drug Safety Update article about an increase in cases of lower-extremity amputation with canagliflozin, compared with placebo, in two clinical trials. A Direct Healthcare Professional Communication was also sent.

The trials, CANVAS and CANVAS-R, are ongoing and involve patients at high risk of cardiovascular disease. As of September 2016, the incidence of lower-limb amputation (mostly affecting the toes) in the CANVAS study was 7 in 1,000 patient-years with canagliflozin 100 mg daily and 5 in 1,000 patient-years with canagliflozin 300 mg daily, compared with 3 in 1,000 patient-years with placebo. The study enrolled around 4,300 patients.

A European review of the risk of lower-limb amputation with all approved SGLT2 inhibitors noted that 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 ulcers (sores), which can lead to amputations. The mechanism by which canagliflozin may increase the risk of amputation is still unclear.

An increased risk of amputation was not seen in studies of dapagliflozin and empagliflozin. However, data are limited and the risk could also apply to these other medicines. Further data are expected from ongoing trials with the approved SGLT2 inhibitors.

The product information for canagliflozin, dapagliflozin, and empagliflozin is being revised to include a warning on the potential increased risk of lower-limb amputation, mostly affecting the toes. For canagliflozin, the prescribing information will also list lower-limb amputation as an uncommon side effect (occurring in fewer than 10 patients in 1,000).

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Launch of pilot reporting scheme for harms associated with illicit drugs, particularly new psychoactive substances

We are launching a pilot scheme for healthcare professionals in the UK to report suspected adverse reactions to illicit drugs, particularly new psychoactive substances.

Background

New psychoactive substances (previously known as ‘legal highs’) pose potentially serious risks to public health. The number of new substances identified in recent years has increased rapidly, with greater availability over the internet.

Hospital admissions for poisoning by psychostimulants with abuse potential have increased by 44% in England and Wales from the period 2009–10 to 2014–15.[1] At present, evidence is lacking about the long-term harms to health associated with use of such illicit substances, and more monitoring in this area is needed.

1 Health and Social Care Information Centre. Hospital admissions for poisoning by illicit drugs up by more than 50 per cent in a decade, July 2016.

Use of these substances is commonly accompanied by use of licensed medicines. This project will enable us to collaborate more closely with Public Health England on safety issues that affect licensed medicines and illicit drugs.

Reporting of harm

A pilot reporting website, the Report Illicit Drug Reaction form, will be available for 1 year for healthcare professionals across the UK who come into contact with patients experiencing harm associated with use of illicit drugs, particularly new psychoactive substances. The pilot aims to better collect data on harms from illicit drug use, to support provision of clinical guidance to professionals.

The form is intended to be used by health professionals who work in emergency departments, general practice, drug treatment services, sexual health services, mental health services, and any other services who come into contact with people who have developed acute or chronic problems associated with use of new psychoactive substances.

The scheme is available for healthcare professionals throughout England, Scotland, Wales, and Northern Ireland.

The reporting site is modelled on our Yellow Card website, with the aim of offering a simple reporting process with which many Yellow Card reporters may be familiar. If you are a registered user of Yellow Card, you can even log in with these details to access all your incident reports in the same place.

Suspected adverse drug reactions to licensed medicines should continue to be reported through the Yellow Card website. Suspected interactions between licensed medicines and illicit drugs should also be reported via Yellow Card.

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