Drug Information Bulletin

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Regulatory Affairs Division (RAD), IPA

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Content

Editorial

It is my proud privilege to pen an editorial in the successive ninth year of this bulletin. It has been possible due to whole hearted cooperation and encouragement from our readers. The Drug Information Bulletin has stepped into its ninth year without failing to bring up a single issue during the last eight years.

This bulletin had started its journey eight years back from the Drug Information Centre of IPA Bengal Branch and now it is published jointly with Regulatory Affairs Division of Indian Pharmaceutical Association. This e-bulletin was the first one to be published by any of the branches of IPA. Recently one more Division i.e. Community Pharmacists Division and one more branch i.e. Assam Branch have started publishing its own e-bulletin. Both of the bulletins are making good contribution to the profession in addition to this bulletin.

I, on behalf of Drug Information Bulletin request your kind feedback for enriching this publication to make it more useful to the readers. Please feel free to mail your suggestions, topic of interest and any other variety of information that you would like to see in this bulletin.

Thanking you once again for your kind support!

Dr. Subhash C. Mandal
Editor

New Drug: Empagliflozin

Approved indication: type 2 diabetes
Jardiance (Boehringer Ingelheim)
10 mg and 25 mg film-coated tablets
Australian Medicines Handbook section 10.1.5

Empagliflozin is the third inhibitor of the sodium-glucose co-transporter 2 (see Aust Prescr 2014;37:14-16 and 2014;37:17-20) to be approved for the treatment of adults with type 2 diabetes. Canagliflozin and dapagliflozin are already available in Australia. By inhibiting renal reabsorption of glucose, the drugs increase glucose excretion thereby decreasing blood glucose.

Empagliflozin is rapidly absorbed and there is an immediate increase in the excretion of glucose which continues for at least 24 hours. The elimination half-life is approximately 12 hours with excretion in urine and faeces. There is some metabolism, but this does not involve the cytochrome P450 system. Empagliflozin is a substrate for the P-glycoprotein transporter, but it is unlikely that it will cause interactions with other substrates. Renal and hepatic impairment will increase plasma concentrations of empagliflozin, but no dose adjustment is recommended. However, empagliflozin is contraindicated if the eGFR is 45 mL/min/1.73 m2 or less.

A phase III placebo-controlled trial randomised 899 previously untreated patients to take once-daily empagliflozin 10 mg or 25 mg or sitagliptin 100 mg. These patients had a mean HbA1c of 63 mmol/mol (7.88%). After 24 weeks this had been significantly reduced by the active treatments. The proportion of patients achieving a concentration below 53 mmol/mol (7%) was 12% with placebo, 35% with empagliflozin 10 mg, 44% with 25 mg and 38% with sitagliptin. Patients taking empagliflozin 10 mg lost 2.26 kg in weight and those taking 25 mg lost 2.48 kg while there was no significant weight loss with placebo or sitagliptin.1

Like other sodium-glucose co-transporter 2 inhibitors, empagliflozin has also been studied in combination with other drugs for diabetes (see Table 1). It is most likely to be used in this way, unless the patient has an intolerance of metformin.

Effect of once-daily empagliflozin on glycated haemoglobin (HbA1c)

Empagliflozin was added to the treatment of patients who had a mean HbA1c of at least 53 mmol/mol (7%) despite treatment with metformin. A placebo was given to 207 patients, while 217 added empagliflozin 10 mg and 213 added empagliflozin 25 mg. After 24 weeks the mean HbA1c fell by 1.4 mmol/mol with placebo, 7.7 mmol/mol with empagliflozin 10 mg and by 8.4 mmol/mol with 25 mg. In percentage units, the difference from placebo was 0.57% with empagliflozin 10 mg and 0.64% with empagliflozin 25 mg.2

In another study of patients with diabetes that was not completely controlled by metformin, 495 were randomised to add either empagliflozin 1 mg, 5 mg, 10 mg, 25 mg or 50 mg, or a placebo or open-label sitagliptin 100 mg daily. Apart from the 1 mg dose, all the active treatments produced a significant reduction in HbA1c by 12 weeks. Adding empagliflozin 10 mg reduced the mean HbA1c from 63 mmol/mol (7.9%) to approximately 57 mmol/mol (7.34%). The proportion of patients achieving an HbA1c of 53 mmol/mol (7%) or less was 15.5% with placebo, 38% with empagliflozin 10 mg and 33.8% with sitagliptin. Body weight reduced by 1.2 kg in the control group and by 2.7 kg with 10 mg empagliflozin.3

Another study compared empagliflozin with glimepiride in patients with diabetes that was inadequately controlled by diet, exercise and metformin. The mean HbA1c at baseline was 63 mmol/mol (7.92%) in the 769 patients randomised to add empagliflozin and in the 780 randomised to add glimepiride. After 104 weeks the mean reduction in HbA1c was 0.66% with empagliflozin and 0.55% with glimepiride. This showed that the effect of empagliflozin was statistically superior to glimepiride. Empagliflozin also reduced weight and blood pressure.4

Empagliflozin has also been studied in patients with diabetes that was not well controlled by metformin and a sulfonylurea. In one trial 669 patients were randomised to add empagliflozin 10 mg, 25 mg or a placebo to their regimen. After 24 weeks the HbA1c concentration had been significantly reduced by empagliflozin. Expressed as percentage units, the reductions

were 0.82% with 10 mg, 0.77% with 25 mg and 0.17% with placebo. At the start of the study the mean HbA1c was 65 mmol/mol (8.1%). While 9.3% of the patients in the placebo group achieved a concentration below 53 mmol/mol (7%), this was reached by 26.3% of the empagliflozin 10 mg group and 32.2% of the 25 mg group. There was a weight loss of 2.16 kg with empagliflozin 10 mg and 2.39 kg with 25 mg, compared with 0.39 kg in the placebo group.5

A study of empagliflozin as an add-on to basal insulin found significant reductions in HbA1c over 78 weeks. In the group of 169 patients who added 10 mg empagliflozin the HbA1c fell by 0.48% from a baseline of 8.26% (67 mmol/mol), while in the 170 patients who added a placebo it fell by 0.02% from a baseline of 8.1% (65 mmol/mol).6

There has been a systematic review of 10 studies of empagliflozin involving 6203 people. The results suggest that empagliflozin 25 mg has similar effects on HbA1c as metformin and sitagliptin. It also reduces weight and blood pressure.7

Meta-analysis of ten trials of empagliflozin for type 2 diabetes

Although empagliflozin increases the amount of glucose in the urine, the increase in urinary tract infections was not significantly different from placebo in the systematic review.7 However, a different pooled analysis did find a significant increase. There is also a significant increase in genital tract infections compared with placebo.7 The osmotic diuresis caused by glucose can lead to volume depletion and decreased renal function.

While the incidence of hypoglycaemia is no different from placebo with monotherapy it rises when empagliflozin is combined with other treatments.7 When combined with metformin and a sulfonylurea, the incidence of hypoglycaemia was 16.1% with empagliflozin 10 mg and 11.5% with 25 mg daily.5 In combination with insulin it was 19.5% with empagliflozin 10 mg and 28.4% with 25 mg daily.

Due to a lack of data, empagliflozin is not recommended for children or during pregnancy and lactation.

Prescribers now have a variety of drugs to consider when a patient's type 2 diabetes cannot be controlled by diet, exercise and metformin. If the prescriber adds a sodium-glucose co-transporter 2 inhibitor there is also a choice of drugs. All the members of the class reduce HbA1c and body weight, but increase the risk of genitourinary infection. There has been a concern about a possible higher risk of cancer in patients taking dapagliflozin, but it is too early to say if there will be a similar concern with empagliflozin. Although empagliflozin reduces the concentration of HbA1c, it is also too early to know the drug's effect on clinical outcomes.

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Pharmaceuticals official calls for making cheaper drugs

The pharmaceuticals secretary V.K. Subburaj called upon the pharma majors to reduce the cost of medicines to benefit more people. On an average, drugs worth about Rs 1 lakh crore are consumed every year and in addition, medicines are exported to about 200 countries, he said while inaugurating a one-day seminar on safe medicine.
For details:
http://www.drugscontrol.org/news.asp?id=11370

Maharashtra FDA raids Snapdeal office for selling prescription drugs

Recently Maharashtra's Food and Drug Administration (FDA) raided the corporate office of e-commerce giant Snapdeal for selling prescription drugs online. The agency got decoy customers to place orders on the portal and raided their office once most of the orders were delivered to respective addresses.

For details: The Times of India

Health ministry reconstitutes Drugs Technical Advisory Board

The Union health ministry has reconstituted the Drugs Technical Advisory Board (DTAB) which is the highest decision-making body under the Union health ministry on technical matters. Director General of Health Services (DGHS) is the ex-officio chairman of this statutory body which is constituted by the ministry under section 5 of the Drugs and Cosmetics Act.
Dr Jagdish Prasad, Director General of Health Services, is the chairman of the newly formed DTAB. Dr G N Singh, Drugs Controller General (India), is the member secretary of the Board.
Ref. Pharmabiz.com

Forthcoming Event:

IPA CONVENTION 2015
Venue: Hotel Trident, BKC, Mumbai
Date: 05-06 June 2015
Theme: Indian Pharma Inc.: Adapting to the Rapidly Evolving Global Challenges

Achievement:

Prof. Arup Mukherjee receiving "Biopolymer environmental remediation application National Award" instituted by the Ministry of Petroleum, Govt. of India