Drug Information Bulletin

Drug Information Centre (DIC)

Indian Pharmaceutical Association

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Regulatory Affairs Division (RAD), IPA

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Editorial

Access to health care information especially in resource poor countries is a major impediment to reach quality health care to the people. There are isolated initiatives to reach the health care information to the health care providers and the general people, but there is a huge gap. Dr. Neil Pakenham-Walsh- Coordinator, HIFA2015 – Co-Director, Global Healthcare Information Network has said in an interview that- "It is tragic that so many children continue to die unnecessarily for want of simple, low-cost interventions that are often locally available. It is even more tragic that many of these children would have been saved if only their mothers, fathers, family caregivers and, indeed, health workers, had basic healthcare knowledge to recognize serious illness requiring urgent, appropriate, life-saving action."

Recently WHO has modified its Essential Medicine Information Portal. Through this portal Non-WHO publications are being included in the database – these can include journal articles, reports from other organizations and other books where permitted by copyright. Essential medicines documents are now combined with those on other health technologies. WHO partner organizations like - MSH, USAID, World Bank and UNICEF are also making available with their data base.

Now it is possible to find reports of MSF, articles from BMJ, meeting reports of ICDRA, required information from 'Managing Drug Supply" and so on as per available sources.

More such initiative will improve access to health care information and improve the quality of health care system.

As a recognition of continuous transmission of health care information by Drug Information Centre (DIC) run by IPA, Bengal Branch & publication of Drug Information Bulletin (DIB) HIFA invited DIC to join as supporting organization and now DIC is one of the supporting organizations of HIFA 2015, having its HQ at UK.

Dr. Subhash C. Mandal
Editor

New Drug: Alogliptin

(Alogliptin Tablet 6.25/12.5/25 mg approved by CDSCO for glycemic control in combination with other glucose lowering medicinal products including insulin when these together with diet and exercise, do not provide adequate glycemic control or as monotherapy as adjunct to diet and exercise to improve glycemic control in adults aged 18 years or older with type II Diabetic mellitus.)

Approved indication: type 2 diabetes

Nesina (Takeda)

6.25 mg, 12.5 mg and 25 mg tablets

Australian Medicines Handbook section 10.1.3

Alogliptin is the fifth dipeptidyl peptidase 4 (DPP4) inhibitor to be approved for diabetes in Australia, along with linagliptin (Aust Prescr 2012;35:70-1), saxagliptin (Aust Prescr 2011;34:89-91), vildagliptin (Aust Prescr 2010;33:89-95) and sitagliptin (Aust Prescr 2008;31:49-55).

DPP4 enzymes inactivate incretin hormones which are produced after a meal. These hormones promote insulin release and lower glucagon production which leads to lower serum glucose concentrations. By inhibiting DPP4 enzymes, the 'gliptins' prolong the effects of incretins and improve glycaemic control (Aust Prescr 2008; 31:102-4 and 104-8).

Alogliptin's bioavailability is 100%. Following oral administration, peak plasma concentrations are reached after 1–2 hours. The drug is not extensively metabolised and clinically relevant pharmacokinetic drug interactions are not expected. Alogliptin has a terminal half-life of 21 hours and the majority of the dose (60–71%) is eliminated unchanged in the urine.

Alogliptin has been investigated in numerous randomised controlled trials in patients whose type 2 diabetes is not adequately managed with diet and exercise or other antidiabetic drugs.

Once-daily alogliptin was found to significantly reduce glycated haemoglobin (HbA1c) – a surrogate marker for glycaemic control – when added to stable doses of metformin1, glibenclamide2, pioglitazone3 or insulin (with or without metformin)4. HbA1c reductions were also seen when it was added to dual therapy with metformin and pioglitazone5(see Table).

As initial therapy, alogliptin was significantly better than placebo at lowering HbA1c.6 It also showed benefit as initial therapy in combination with pioglitazone7 (see Table).

During trials, the most common adverse event with alogliptin was pruritus. Headache, diarrhoea, myalgia, rash, musculoskeletal pain, abdominal pain, nausea and infections (influenza, nasopharyngitis, upper respiratory tract infection) were also common (1–10% of patients).

Severe hypersensitivity reactions (e.g. angioedema, Stevens-Johnson syndrome), hepatic failure and pancreatitis have been reported in postmarketing surveillance. Alogliptin is not recommended in patients with severe hepatic impairment.

Hypoglycaemia can occur when alogliptin is added to insulin or a sulfonylurea so these drugs may need to be given at lower doses during combination therapy.

Alogliptin is a category B3 pregnancy drug. There are no data in humans so it is best avoided during pregnancy. Alogliptin was excreted in breast milk in animal studies so there is a risk of exposure to a breastfeeding infant.

Renal function should be assessed before patients start alogliptin. Dose reduction is recommended in patients with moderate (creatinine clearance 30 to 50 mL/min) or severe renal impairment (creatinine clearance <30 mL/min) and those with

end-stage renal disease requiring dialysis. Experience in patients with severe renal disease is limited and caution is urged.

As with other DPP4 inhibitors, alogliptin is modestly effective at lowering HbA1c. It provides another option for monotherapy or as an add-on therapy when a patient's diabetes is not controlled by metformin, a sulfonylurea, a thiazolidinedione or insulin. It can also be added as a third option in patients already taking metformin and pioglitazone. Despite showing benefit in trials, alogliptin is currently not indicated for initial combination therapy in Australia.7

REFERENCES:

1. Nauck MA, Ellis GC, Fleck PR, Wilson CA, Mekki Q; Alogliptin Study 008 Group. Efficacy and safety of adding the dipeptidyl peptidase-4 inhibitor alogliptin to metformin therapy in patients with type 2 diabetes inadequately controlled with metformin monotherapy: a multicentre, randomised, double-blind, placebo-controlled study. Int J Clin Pract 2009;63:46-55.
2. Pratley RE, Kipnes MS, Fleck PR, Wilson C, Mekki Q; Alogliptin Study 007 Group. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor alogliptin in patients with type 2 diabetes inadequately controlled by glyburide monotherapy. Diabetes Obes Metab 2009;11:167-76.
3. Pratley RE, Reusch JE, Fleck PR, Wilson C, Mekki Q; Alogliptin Study 009 Group. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor alogliptin added to pioglitazone in patients with type 2 diabetes: a randomized, double-blind, placebo-controlled study. Curr Med Res Opin 2009;25:2361-71.
4. Rosenstock J, Rendell MS, Gross JL, Fleck PR, Wilson C, Mekki Q. Alogliptin added to insulin therapy in patients with type 2 diabetes reduces HbA1c without causing weight gain or increased hypoglycaemia. Diabetes Obes Metab 2009;11:1145-52.
5. Bosi E, Ellis GC, Wilson CA, Fleck PR. Alogliptin as a third oral antidiabetic drug in patients with type 2 diabetes and inadequate glycaemic control on metformin and pioglitazone: a 52 week, randomized, double-blind, active-controlled, parallel-group study. Diabetes Obes Metab 2011;13:1088-96.
6. DeFronzo RA, Fleck PR, Wilson CA, Mekki Q; Alogliptin Study 010 Group. Efficacy and safety of the dipeptidyl peptidase-4 inhibitor alogliptin in patients with type 2 diabetes and inadequate glycaemic control. Diabetes Care 2008;31:2315-7.
7. Rosenstock J, Inzucchi SE, Seufert J, Fleck PR, Wilson CA, Mekki Q. Initial combination therapy with alogliptin and pioglitazone in drug-naïve patients with type 2 diabetes. Diabetes Care 2010;33:2406-8.

Ref. *Aust Prescr 2014;37:28-35*

The proliferation of irrational metformin fixed-dose combinations in India

An article published in Lancet Diabetes & Endocrinology, Vol. 3, No. 2, P. 98-100, February 2015 reported that huge number of Metformin combinations is available in Indian markets, which are irrational.

For details:
http://www.thelancet.com/pdfs/journals/landia/PIIS2213-8587(14)70239-6.pdf

Hamburg resigning as FDA commissioner

Dr. Margaret Hamburg is resigning after nearly six years as FDA commissioner, according to officials. The FDA's chief scientist, Dr. Stephen Ostroff, will serve

temporarily as commissioner until a replacement for Hamburg is confirmed.
Ref. Reuters

Assay method looks at lipid bilayer to determine drug toxicity

A research team from Weill Cornell Medical College has developed a novel screen known as the Gramicidin-Based Fluorescence Assay to detect drug toxicity. The assay tracks changes in the gramicidin channel, a small protein, as a way of monitoring changes in the lipid bilayer of a cell that can indicate toxicity.
Ref. Genetic Engineering & Biotechnology News

India to get labs to test medical devices

India does not have a single nationally recognized medical device testing laboratory. That is set to change. In a first step towards recognizing medical devices as an industry separate from the pharmaceuticals industry and requiring different regulatory standards, the commerce ministry has decided to fund the setting up of three medical device testing laboratories in Noida (UP), Haryana and Gujarat, which already have device manufacturing clusters.

These laboratories are being set up to provide a boost to the domestic manufacturing sector by providing adequate infrastructure for device testing based on project proposals and technical support given by the National Health Systems Resource Centre (NHSRC), a technical support institution under the health ministry.

While the Haryana and Gujarat governments have promised to allot land for the labs, in Noida, HLL Lifecare Ltd, a PSU, will be providing its campus for setting up the laboratory.

Two reports released on Friday outlined the basic requirements, work flow, infrastructure and human resources required for establishing medical testing laboratories for testing of biomaterials and implants and for testing electrical and electronic medical devices. Released at a conference on patient safety and medical devices, the reports were prepared by the NHSRC in collaboration with the World Health Organization (WHO) country organization with inputs from Underwriter Laboratories (UL), a US-based international safety science company and technical support on implants from the Sri Chitra Tirunal Institute of Medical Sciences and Technology, Trivandrum.

Speaking at the conference, Rajiv Capoor, joint secretary in the ministry, said that though medical devices have a huge potential in India, 70-75% of the market continued to be import based. "To grow the industry and achieve the $25 billion target, we need to lay greater emphasis on developing standards and making regulatory amendments to the existing Drugs and Cosmetics Act," said Capoor.

He added that in keeping with government encouraging the medical devices sector in India and its 'Make in India' drive, the detailed report on setting up of these laboratories would be timely.
Ref. Times of India

Forthcoming Event:

National Workshop on Ensuring Quality through Good Laboratory Practice

Date: 8th March 2015 (Sunday)
Time: 9.30 am -5.00 pm
Venue: Flotel, Kolkata

Organized by:
Regulatory Affairs Division (RAD), IPA
Jointly with IPA, Bengal Branch

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