Drug Information Bulletin

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Content

Editorial

Pharmacovigilance Programme of India (PvPi) has put Bedaquiline under strict vigilance to protect this new member of anti TB drug. Considering its importance six Adverse Drug Monitoring Centers (AMCs) have given the responsibility of Active Surveillance (Cohort Event Monitoring). Bedaquiline Tablet 100 mg have been approved by CDSCO on 14.01.2015 with an indication " In adults higher than 18 years, as part of combination therapy of pulmonary tuberculosis due to multi-drug resistant Mycobacterium tuberculosis when an effective regimen cannot otherwise be provided". Subsequently, DCG (I) instructed on 18th April 2015 that only Revised National Tuberculosis Control Programme (RNTCP) centers are allowed to prescribe Bedaquiline.

Earlier World Health Organization (WHO) has issued interim guidance on the use of Bedaquiline on 13th June 2013, the first new drug to treat tuberculosis in more than 40 years after Rifampicin, acknowledging the growing crisis of multidrug-resistant TB (MDR-TB) and the urgent need for improved drugs with better efficacy and safety profiles. This step of WHO to make interim recommendations about a drug based on phase IIb clinical trial data is considered as an unprecedented. Bedaquiline received accelerated approval by the US Food and Drug Administration (USFDA) on 31 December 2012. Bedaquiline affects the proton pump for ATP synthase. Let all health care professionals protect this drug through judicious use.

Dr. Subhash C. Mandal
Editor

New Drug: Linagliptin

Approved indication: type 2 diabetes

Trajenta (Boehringer Ingelheim)

5 mg tablets

Patients with diabetes produce less of the peptide hormones known as incretins. Their concentration can be increased by inhibiting the enzyme (dipeptidyl peptidase 4) which metabolises them. This increases insulin secretion and lowers glucose concentrations. Saxagliptin, sitagliptin, vildagliptin and now linagliptin are all inhibitors of the enzyme (see:Incretin mimetics and enhancers, Aust Prescr 2008;31:104-8).

Linagliptin is taken once a day. Its bioavailability is only 30% and this can be reduced by drugs, such as rifampicin, which induce the P-glycoprotein transporter. The metabolism of the drug involves cytochrome P450 3A4, but this may not be clinically important. Most of the dose is excreted unchanged in the faeces. The terminal half-life of the drug exceeds 100 hours.

Several thousand patients have been involved in trials of linagliptin. These studies included combinations with other treatments for type 2 diabetes as well as monotherapy. In 503 patients with inadequately controlled diabetes, 24 weeks of monotherapy had a significantly greater effect than placebo. From a baseline mean of 8%, the mean glycated haemoglobin (HbA1c) reduced by 0.44% with linagliptin 5mg, but increased by 0.25% with placebo.1 In Australia however, linagliptin is only approved in combination with metformin, a sulfonylurea or both.

Another 24-week trial randomised 701 patients whose diabetes was not controlled by metformin. A group of 523 patients took linagliptin and 177 took placebo. From a baseline of 8.09%, the HbA1c reduced by 0.49% with linagliptin 5 mg and increased by 0.15%, from 8.02%, with placebo. A target HbA1c of 7% or less was achieved by 26% of the linagliptin group and 9% of the placebo group.2

In a similar group of 333 patients, another placebo-controlled trial studied three different doses (1 mg, 5 mg and 10 mg) of linagliptin and also included a glimepiride arm. All the patients continued to take metformin during the trial. After 12 weeks the active treatments had significantly reduced HbA1c from similar baseline values 3 A longer term comparison found that after a year linagliptin 5 mg reduced HbA1c by 0.38% and glimepiride reduced it by 0.6%.

An 18-week trial studied linagliptin in combination with a sulfonylurea. Compared with placebo, the mean treatment difference was 0.47%.

Linagliptin has also been studied, in 1058 patients, as an addition to treatment with metformin and a sulfonylurea. While adding a placebo reduced the mean HbA1c by 0.1% after 24 weeks, linagliptin reduced it by 0.72%.4

Adding a drug which increases insulin secretion to the treatment of patients with diabetes increases the risk of hypoglycaemia. In patients taking metformin and a sulfonylurea, hypoglycaemia was reported in 22.7% when linagliptin was added and in 14.8% when a placebo was added.4

During monotherapy the adverse events in patients taking linagliptin included musculoskeletal problems, hypertension and headache.1 Some patients may have increases in triglycerides and uric acid concentrations. Rare adverse events include hypersensitivity reactions and pancreatitis. A meta-analysis of cardiovascular events found no increased risk associated with linagliptin.

Animal studies have shown that linagliptin crosses the placenta and is excreted in breast milk.

Linagliptin adds to the choice of drugs which can be considered when a patient's diabetes is not controlled by metformin and sulfonylureas. There seems little difference between the inhibitors of dipeptidyl peptidase, but linagliptin does not require a dose adjustment in patients with renal impairment.

REFERENCES:

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3. Forst T, Uhlig-Laske B, Ring A, Graefe-Mody U, Friedrich C, Herbach K, et al. Linagliptin (BI 1356), a potent and selective DPP-4 inhibitor, is safe and efficacious in combination with metformin in patients with inadequately controlled Type 2 diabetes. Diabet Med 2010; 27:1409-19 .
4. Owens DR, Swallow R, Dugi KA, Woerle HJ. Efficacy and safety of linagliptin in persons with type 2 diabetes inadequately controlled by a combination of metformin and sulphonylurea: a 24-week randomized study. Diabet Med 2011; 28:1352-61 .

(Linagliptin film coated Tablet 5mg was approved by CDSCO on 23.01.2012 as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus. Important limitations of use: 1. Should not be used in patients with type 1 diabetes or for the treatment of diabetic ketoacidosis. 2. Has not been studied in combination with insulin.)

Source: Aust Prescr 2012; 35:70-1

FAPA commitment to act signed by Dr. Rao, President, IPA

Off-label promotion presents high-stakes policy battle

Amarin recently won a court ruling allowing company representatives to promote a fish oil pill for uses unapproved by the FDA but supported by study data, and Pacira Pharmaceuticals filed a lawsuit against the FDA for the right to promote a pain drug for off-label uses. Some industry observers warn that allowing more off-label drug promotion endangers patients and will increase spending, but others do not expect radical changes. Source: The Boston Globe (tiered subscription model)/Stat

Draft IPR note to go through one more round of inter-ministerial scanning

The proposed new IPR policy will have to go through another round of inter-ministerial scrutiny before it is placed before the Cabinet for clearance, a move that could delay its finalisation further.

Comments would be sought again from other ministries and departments once the Department of Industrial Policy & Promotion (DIPP) incorporates changes suggested by many following the first round of consultations.
For details: The Hindu Businessline

DTAB sub-committee finds several nutraceuticals in market as drugs

Several controversial nutraceutical products, now being marketed as food supplements by some of the prominent pharma companies, will have to be withdrawn from the market and should be sold as drugs as the DTAB sub-committee, which analysed these products, has recommended that these products shall be classified as drugs.

Ferradol by Pfizer; Revital by Ranbaxy Laboratories; Beneficial capsules, CSN capsules and DSN capsules by Shreya Life Sciences, A to Z by Alkem Laboratories; Kidvit Z drops by Ceza Formulations; and Resource Diabetic and Resource Renal by Drytech Process are some of the products which have been examined by the sub-committee.

"Committee examined the ingredients present in the product. Committee noted that some ingredients present in the product fall under the range as prescribed under schedule-V of Drugs and Cosmetics Rules, 1945 either in prophylactic or in a therapeutic dose. The Committee recommended that the product shall be classified as drug," the sub-committee in its recommendation said.

News

Indian Pharmaceutical Association bags the Best Association Award

IPA bags the Best Association Award Indian Pharmaceutical Association (IPA) has been awarded the maiden Best Association Award during 5th India Association Congress on August 21, 2015 at Bangalore. IPA has been conferred with the Award in the first year of its inception. This is a significant recognition for IPA amongst all associations in India and the very first in pharmaceuticals sector. The award was received by Dr. Rao V.S.V. Vadlamudi, President - IPA, Mr. T.B. Nair and Mr. Kaushik Desai, Honorary General Secretary - IPA.

Forthcoming Event

Pharmacists Day Celebration-2015
by
IPA, Bengal Branch
Date: 25.09.2015

- *Pharmacist's badges will be worn by Pharmacists in all sectors at their work place throughout the state.*
- *Get well soon cards will be distributed amongst the patients in Hospitals (Govt. & Private), clinics & community pharmacies throughout the state.*

Seminars:

- **IPA Auditorium, Kolkata:**
  Seminar on "Impact of Pharmacy Practice Regulation-2015"
  Speaker: Dr. V. Ravichandiran, Director, National Institute of Pharmaceutical Education &Research (NIPER), Kolkata
  Time: 6.00 pm
- **Institute of Pharmacy, Kalyani:**
  "Impact of Pharmacy Practice Regulation-2015"
  Time: 1.30 pm
- **Coochbehar Municipality Hall:**
  Seminar on "Impact of Pharmacy Practice Regulation-2015"
  Seminar on "Impact of Pharmacy Practice Regulation-2015".
  (Jointly with PAWB)
  Time: 11.30 am