Drug Information Bulletin

Drug Information Centre (DIC)
Indian Pharmaceutical Association
Bengal Branch
Tele fax: 033 24612776, E-mail: ipabengal.dic@gmail.com
Web Site: http://www.ipabengal.org
Contact: 09830136291
&
Regulatory Affairs Division (RAD), IPA

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Content

Editorial

Trivalent Oral Polio Vaccine (tOPV) is being replaced by bivalent Oral Polio Vaccine (bOPV) by April 2016. Currently, 145 countries use tOPV to vaccinate children against polio in their routine immunization programme. tOPV contains all three poliovirus serotypes (1, 2 and 3).The use of this vaccine has led to the eradication of wild poliovirus type 2 (WPV2), with the last case occurring in 1999. The last detected case of WPV3 was in 2012. Furthermore, four of the six WHO regions have been certified as polio-free. So it is wise to discontinue this type 2, because of its drawbacks like- causes more than 90% of vaccine-derived polio viruses (VDPVs), causes approximately 40% of vaccine-associated paralytic polio (VAPP) cases, interferes with the immune response to poliovirus types 1 and 3 in tOPV. Therefore, World Health Assembly (WHA) has adopted one resolution in May 2015 to switch over from tOPV to bOPV by April 2016 and set a goal to withdraw OPVs by 2020 after eradication of Polio from the Globe. Being a member country India is also a part of this exercise and adopted the strategies suggested by WHO and is going to switch over from tOPV to bOPV during the week beginning from 25th April 2016. This occasion has given an opportunity to the pharmacists working in Hospital, community Pharmacy, regulatory department, manufacturing to be associated in this important healthcare exercise.

Celebration of World Health Day 2016
7th April 2016
Lecture on "Beat diabetes" by Dr. Sujoy Majumdar
Venue: IPA Auditorium
Time: 6.30 pm

Dr. Subhash C. Mandal

Editor
E mail: subhash.mandaldr@gmail.com
Mob. 9830136291

New Drug: Lurasidone

Approved indication: schizophrenia

Latuda

20 mg, 40 mg and 80 mg tablets

Australian Medicines Handbook section 18.2

There are over 15 antipsychotics approved for schizophrenia in Australia. Lurasidone is the most recent addition to this drug class. As with other antipsychotics, lurasidone blocks dopaminergic transmission in the brain via the dopamine D_2 receptor. It also antagonises serotonin $5HT_7$ and $5HT_{2A}$ receptors and is a partial agonist of $5HT_{1A}$. Lurasidone does not appear to affect muscarinic and histamine receptors.

The efficacy of lurasidone for acute schizophrenia has been assessed in several short-term, placebo-controlled trials.1-5 After six weeks of treatment, once-daily doses of 40 mg, 80 mg, 120 mg and 160 mg significantly lowered signs and symptoms of schizophrenia, measured on psychiatric rating scales1-5 However, efficacy was not consistently shown for each dose and a dose–response relationship was not evident in the trials. For example, in a study of lurasidone 40 mg, 80 mg and 120 mg, only the 80 mg dose had a statistically significant effect over placebo.4 Discontinuation rates were very high in some of the trials (28–65%).1-5 Lack of efficacy and withdrawal of consent were the most common reasons for stopping treatment.

One of the placebo-controlled trials1 was extended to assess the long-term efficacy of lurasidone (40–160 mg/day) compared to quetiapine (200–800 mg/day) in 292 people.6 Flexible dosing was allowed. At 12 months, the estimated probability of relapse was 23.7% in people receiving lurasidone compared with 33.6% in those receiving quetiapine. Discontinuation rates were high (48% for lurasidone, 61% for quetiapine).6

Another longer term comparative study enrolled patients with stable schizophrenia. After 12 months, 20% of people (82/410) receiving lurasidone had relapsed compared with 16% (32/198) receiving risperidone.7

The most common adverse events in the short-term trials were somnolence (17% of patients), extrapyramidal symptoms (14%), akathisia (13%), insomnia (10%) and nausea (10%). Tachycardia, blurred vision, abdominal pain, diarrhoea, decreased appetite, rash, pruritus, hypertension and elevated creatine kinase also occurred in 1–10% of people. Prolactin elevations were more frequent with lurasidone than with placebo (2.8% vs 1%). QT prolongation did not seem to be a problem in the trials.

In the six-week trials, weight gain was modest with lurasidone compared with placebo (mean change of 0.43 kg vs –0.02 kg). In the longer term comparative studies, people taking lurasidone were less likely to have gained weight than those taking quetiapine6 and risperidone.7

As with other antipsychotics, lurasidone can cause neuroleptic malignant syndrome, tardive dyskinesia and orthostatic hypotension. It should be used with care in patients at risk of hypotension or seizures. Lurasidone should not be used in elderly patients with dementia-related psychosis because of an increased risk of death with antipsychotics.

Lurasidone should be started at 40 mg once daily, taken with food. In the trials no additional benefit was seen with the 120 mg dose. The recommended starting dose in moderate to severe renal impairment is 20 mg. Lurasidone should not be used in people with severe hepatic impairment and the recommended starting dose is 20 mg in those with moderate impairment.

Peak concentrations are reached 1–3 hours after taking an oral dose and steady-state concentrations are reached

within seven days. The drug's elimination half-life is 18 hours and most of the dose is excreted in the faeces.

Concomitant use of strong cytochrome P450 (CYP) 3A4 inhibitors (ketoconazole, clarithromycin, ritonavir) and inducers (rifampicin, St John's wort, phenytoin) is contraindicated as lurasidone is metabolised by CYP3A4. The lurasidone dose should be halved in people taking moderate inhibitors (diltiazem). Patients should avoid grapefruit juice as it may increase lurasidone exposure.

Lurasidone is a category B1 drug in pregnancy. In animal studies, no fetal toxicities were observed. However, exposure during the third trimester in pregnant women increased the risk of extrapyramidal and withdrawal symptoms in newborns. Some babies had to be managed in the intensive care unit. Breastfeeding is not recommended with lurasidone as it has been found to be excreted in the milk of lactating rats.

In general, lurasidone was better than placebo in patients with acute schizophrenia. However, efficacy was not consistent at all doses and a dose–response relationship could not be shown. It is unclear how lurasidone will compare to other drugs in the class.

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Ref. Aust Prescr 2016; 39:25-6

WHO temporarily stops approval of Svizera's tuberculosis drugs

An investigation into production standards and quality management found problems at India-based Svizera Labs and prompted the World Health Organization to suspend authorization of the firm's

tuberculosis treatments produced at its Mumbai facility. The WHO suggested drugs already on the market be retested and possibly recalled.

Ref. Reuters

Discovery of $88M in black-market vaccines prompts crackdown promise in China

The discovery that resellers may be marketing about $88 million in illegal vaccines prompted a promise by the Chinese government to crack down on the country's black market for drugs. The vaccines for rabies, meningitis and other diseases were made by licensed producers but could be dangerous because they were not stored under proper conditions.

Ref. Reuters

Madras HC refuses to stay central govt ban on FDC drugs, disagrees with Delhi HC

The Madras high court has declined to stay a central government ban on sale and manufacture of 344 Fixed Dose Combination (FDC) drugs and made it clear that the notified drugs should not be sold. However, in a small consolation, the court said no coercive step should be taken against stockists.

The ruling is in 'disagreement' with an order of a single judge in the Delhi high court granting stay on the operation of the notification with an additional relief that no coercive action should be taken against stockists.

The first bench of Chief Justice Sanjay Kishan Kaul and Justice M M Sundresh, passing orders on the writ petition of Federation of South Indian Pharmaceutical Manufacturers Association, said: "We respectfully disagree with the view of the single judge of the Delhi high court and not inclined to pass an all-encompassing order. We are of the view that the mere fact of the sale of medicines for the last so many years ipso facto cannot call for the sale to continue when an expert body has gone into this issue."

"As to whether all procedural formalities have been followed or not, as also the provisions of the statute would be examined in the course of the proceedings. We are not dealing with a perishable commodity. There is a shelf life. Further, the larger public interest would weigh in favour of not staying the effect of the notification."

"We, however, are inclined to give limited protection to the extent that if no sales are made as per the notification, in the meantime, coercive steps be not initiated against the manufacturers, stockist/agents, in view of the stock which would have already been manufactured," the court said.

The matter relates to a notification issued by the Union ministry of health and family welfare dated March 10, under Section 26A of Drugs and Cosmetics Act 1940 and Drugs and Cosmetics Rules 1945, prohibiting manufacture, distribution and sale of the FDCs mentioned in schedule.

The notifications, issued in 'public interest' after it was found that the drugs had no 'therapeutic justification.' Noting that the entire pharmaceutical industry is adversely affected by the order, senior advocate Vijay Narayan argued that the notification overnight envisaged penal consequences.

The notification had been issued without notice to stakeholders which included manufacturers, stockists, agents, sellers and the general public, their petition said, adding that the entire expert committee proceedings were held in secrecy.

"The entire exercise has been carried out in a shroud of secrecy and in a clandestine manner, and the members of the petitioner-federation have been divested of their valuable fundamental rights without due process of law. The purported expert committee is not a committee constituted under the provisions of D&C Act, despite the Act providing for specific committees to advise the government," the petition read.

Ref. Drugs Control.org