Drug Information Bulletin

Drug Information Centre (DIC)

Indian Pharmaceutical Association

Bengal Branch

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Volume: 08 ***Number: 08*** ***20th July 2014***

Content

Editorial

Dietary supplements (DS) showed an upsurge during last few years throughout the globe including India. It was felt that production and marketing is not properly regulated in India leaving ample scope of compromising the safety of the consumers of DS. A study has been undertaken to find out the status of the dietary supplements in the Indian market and suggest regulatory measures, at least, for manufacturing, labeling, safety and quality aspects so as to safeguard the interest of the common people. The study was conducted in 50 wholesale and 100 retail medicine outlets spread over Malda district in West Bengal between June 2008 and May 2010. Change of life style of the populace via-a-vis high profile marketing through print and electronic media are believed to be the main reason behind such upsurge. A serious trend has been revealed concerning shifting of a drug to Dietary Supplement category made possible due to existing lenient regulation on Dietary Supplements in India. Manufacturing of DS does not require maintaining GMP or GLP and other regulatory requirements favoring it's low cost of production and more profit. Further less legislation on DS in comparison to drugs helps its easy access to market. Less regulation on production and less vigilance in the market may compromise the safety of the people who will be using such DS. Thus it is high time that some legislation is brought in or PFA Act amended to differentiate a DS clearly from a drug and it is produced properly.

Though the Food Safety and Standards Act 2006 was published in 2006, the Food Safety and Standard Rules was framed in 2011 and finally the Food Safety and Standards (Prohibition and Restrictions on Sales) Regulations, 2011was enacted in 2011 and all are effective since 5th August 2011, no much improvement was noticed because of weak enforcement mechanism.

Dr. Subhash C. Mandal
Editor

Press Information Bureau
Government of India
Ministry of Health and Family Welfare
18-July-2014 16:04 IST

Banned/Unapproved Drugs

Certain cases of sale of banned drugs were detected during the raids conducted by Central Drugs Standard Control Organization in 2011 in and around Delhi and in Mumbai to check the withdrawal of Gatifloxacin, Tegaserod and Rosiglitazone after their prohibition for marketing and sale in the country. These drugs were being sold in 29 shops after issue of notification of ban, 27 cases in Delhi and 2 cases in Rajasthan. The concerned State Licensing Authorities were asked to take action as per the provision of Drugs and Cosmetics Act, 1940. Further, 23 cases of new Fixed Dose Combinations (FDCs), considered as new drugs, and were also found to be licensed by State Licensing Authorities (SLAs) without approval of the Drugs Controller General (India) [DCG (I). In all such cases, the office of DCG (I) took up the matter with respective State Licensing Authorities for necessary action. State and year-wise details of these 23 cases are given below:-

Name of the State	**No. of FDC for which licenses were granted by SLAs without prior approval of DCG(I)**
Puducherry	8
Goa	1
Madhya Pradesh	2
Uttarakhand	5
Maharashtra	2
Daman & Diu	1
Himachal Pradesh	2
Haryana	1
Tamilnadu	1
Total	**23**

Year wise details

Year	**No. of Cases**
2011	11
2012	12

Apart from these, following the statutory direction issued by the Central Government to all the State / UT Governments on 1.10.2012 under Section 33P of the Drugs & Cosmetics Act, 1940 not to grant licenses for manufacture for sale or for distribution or for export of such new drugs, except in accordance with the procedure laid down under the said rules i.e. without prior approval of the DCG(I), the manufacturers of all FDC licensed before 1.10.2012 without the approval of DCG(I) have been asked to prove the safety and efficacy of such FDCs before the CDSCO within a period of 18 months failing which such FDCs will be considered for being prohibited for manufacture and marketing in the country. About 7000 applications in respect of such FDCs have been received by the CDSCO.

The State Drug Controllers have also been requested in the Drugs Consultative Committee meetings to ensure that New Drugs and FDCs are not permitted without approval from the office of DCG (I) and the drugs prohibited by the Central Government are withdrawn from the market with immediate effect. States have also been advised to strengthen the infrastructure for better enforcement and develop vigilance mechanism over the drugs moving in the market.

The Government regularly monitors shortages and availability of drugs on the basis of monthly reports received from State Drugs Control Administration and also complaints, if any, received from NGOs, individuals etc. On receipt of any report on shortage for a particular drug, the Government immediately takes up the matter with the concerned manufacturer and advises them to rush the stock in the affected area. The Government has not received any report regarding shortage of abortion drug in the country.

The Health Minister stated this in a written reply in the Lok Sabha here today.

New Drug: Riociguat

Approved indication: Pulmonary hypertension
Adempas (Bayer)
0.5 mg, 1 mg, 1.5 mg, 2 mg and 2.5 mg film-coated tablets
Australian Medicines Handbook section 6.6

There are several causes of hypertension in the pulmonary circulation. They include pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension. In pulmonary hypertension there is an imbalance between vasodilators such as nitric oxide and vasoconstrictors such as endothelin-1. Nitric oxide activates guanylate cyclase which leads to relaxation of smooth muscle. Riociguat is a drug which acts synergistically with nitric oxide and also independently stimulates guanylate cyclase.

Riociguat is taken three times a day. It is converted by the cytochrome P450 system to an active metabolite. There are many potential interactions and co-administration with drugs such as ketoconazole and ritonavir is not recommended. The use of nitrates and phosphodiesterase inhibitors, such as sildenafil, is contraindicated. Riociguat and its metabolites are eliminated in bile and urine. It is not recommended for patients with severe hepatic or renal impairment. As smoking reduces plasma concentrations of riociguat, the doses may need to be adjusted in patients who stop or start smoking during treatment.

The effect of riociguat on exercise tolerance was studied in a phase III placebo-controlled trial of 443 patients. These patients had pulmonary arterial hypertension that was mainly idiopathic or associated with connective tissue disease or congenital heart disease. In one group of patients the dose of riociguat was adjusted up to a maximum of 2.5 mg three times daily while another group was limited to a maximum of 1.5 mg three times daily. After 12 weeks the patients in the 2.5 mg group could walk an extra 30 metres and those in the 1.5 mg group could walk an extra 31 metres. In the placebo group the patients walked on average six metres less than they did at the start of the study. Riociguat also improved cardiac output and mean pulmonary artery pressure. The benefits of treatment were seen irrespective of whether the patients were already taking prostanoids or endothelin-receptor antagonists.1

Riociguat has also been studied in 261 patients with chronic thromboembolic pulmonary hypertension. The 173 patients who took riociguat started at a dose of 1 mg three times a day which was adjusted up to a maximum of 2.5 mg three times a day. After 16 weeks their mean six-minute walking distance had increased from 342 metres to 381 metres. This increase of 39 metres was significantly better than the six metre decrease in the placebo group. Cardiac output and pulmonary artery pressure also improved.2

Systemic hypotension is a predictable adverse effect of riociguat. Relaxation of smooth muscle could also contribute to complaints of headache, dizziness and dyspepsia. Nausea, vomiting and diarrhoea are also more frequent with riociguat than with placebo. Approximately 3% of the patients taking riociguat withdrew from the trials because of adverse events.1,2

Riociguat increases the risk of bleeding and anaemia. In the clinical trials serious bleeding affected 2.4% of patients, but

none of the placebo group. There was serious haemoptysis in 1% of the patients taking riociguat and one case was fatal.1

In animal studies, riociguat was teratogenic so it is contraindicated in pregnancy. It is also contraindicated in lactation.

Extensions of the main clinical trials showed that the increase in walking distance was at least maintained, but the long-term clinical efficacy and safety of riociguat is unknown. Thromboembolic pulmonary hypertension can be treated by pulmonary endarterectomy. Riociguat may be an option for patients who cannot have surgery or who do not improve after surgery. In pulmonary arterial hypertension only 21% of patients have an improvement in their functional class.1 Although riociguat has a dual mechanism of action it is unclear if this gives it any clinical advantage over the phosphodiesterase inhibitors. A phase II trial involving 201 patients with pulmonary hypertension due to left ventricular dysfunction found that after 16 weeks the effect of riociguat on mean pulmonary artery pressure was not statistically different from placebo.3

References:

1. Ghofrani HA, Galiè N, Grimminger F, Grünig E, Humbert M, Jing ZC, et al. Riociguat for the treatment of pulmonary arterial hypertension. N Engl J Med 2013;369:330-40.
2. Ghofrani HA, D'Armini AM, Grimminger F, Hoeper MM, Jansa P, Kim NH, et al; CHEST-1 Study Group. Riociguat for the treatment of chronic thromboembolic pulmonary hypertension. N Engl J Med 2013;369:319-29.
3. Bonderman D, Ghio S, Felix SB, Ghofrani HA, Michelakis E, Mitrovic V, et al. Riociguat for patients with pulmonary hypertension caused by systolic left ventricular dysfunction: a phase IIb double-blind, randomized, placebo-controlled, dose-ranging hemodynamic study. Circulation 2013;128:502-11.

Ref. Australian Prescriber

Global antibiotics use rises 36%, study finds

A study in The Lancet Infectious Diseases found a 36% increase in the world's antibiotics use driven by economic growth in Brazil, China, India, Russia and South Africa. Consumption of broad-spectrum antibiotics increased sharply. Researchers called for global guidelines and a reporting system for antibiotic use.

Reference: Los Angeles Times

Forthcoming Event:

IPA Convention 2014

(IPAs Platinum Jubilee Celebration Launch Programme)

8th August 2014

Venue: NIMHANS Convention Centre, Bangalore

Registration:

Non Member: Rs.1500
Member: Rs. 1000
Student Member:Rs. 750

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