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

Indian market is flooded with Fixed Dose Combinations (FDCs). Several sources quoted different numbers ranging from 60,000 – 100000. Though there is handful of FDCs having advantage over single ingredient products, there is hardly any benefit of most of the FDCs. As per the experts this situation becomes more complicated due to unregulated approval of FDCs by some state licensing authorities. Sometimes back DCGI published a list of FDCs as irrational, but those are still available in the market as a result of some litigation. Again DCGI has given a direction to submit Safety and Efficacy data of the FDCs available in the market without approval from the DCGI with a deadline on 30th August 2013. After 2013 there were several exercise by the DCGI and ultimately they have banned about 344 irrational combination vide SO 705 (E) to 1048(E) dated 10.03.2016. Mainly FDCs of NSAIDs and FDCs of antibiotics are banned besides other therapeutic categories. This is a unique occasion that a huge number of drugs have been banned by the Indian regulators. Sources revealed that this move make pharmaceutical manufacturers are not in a comfortable position. However the Health activists who are fighting to eradicate irrational drugs/combinations since last few decades are quite satisfied, but some of them expressed that they will continue their fight till all irrational drugs are withdrawn from the market. Some experts are hopeful that the way Pharmacovigilance Programme of India (PvPI) is working only evidenced based medicines will be available in the market in near future.

Dr. Subhash C. Mandal
Editor

Off-label use of Bevacizumab Injection in opthalmological condition are allowed by DCGI with some conditions

F. No.12-52/2004-DC(Part I)
Directorate General of Health Services
Office of Drugs Controller General (India)
(Biological Division)

FDA Bhawan, Kotla Road,
New Delhi 110002

Dated: 09.03.2016
11-03-16

Notice

This is in continuation to alert notice issued vide letter no. 12-52/2004-DC (Part-I) dated 21.01.2016 regarding use of Bevacizumab Injection in Ophthalmologic condition. The matter has been examined by the Ministry of Health and Family Welfare based on recommendation of Expert Committee meeting held on 08.02.2016 on this subject.

The Committee examined and deliberated on the use of Bevacizumab Injection in Ophthalmologic conditions as an off-label indication and following observations were made by the Committee:-

1. Bevacizumab Injection is not approved by global regulatory Authorities for intravitreal use due to non-application by the Innovator for this purpose. However, WHO (April 2015) has recommended Bevacizumab Injection by including in the list of essential medicines prepared as anti-vascular endothelial growth factor in ophthalmic section based on recommendation of International Council of Ophthalmology (ICO). Further, regulatory agencies of France and Italy have allowed its off-label use as a Temporary Recommended Use (TRU).
2. The safety and efficacy of Bevacizumab injection in intravitreal use is stated to be proven by various independent studies (over 2500 studies published) conducted globally. It was discussed that rate of endophthalmitis is significantly lower after the injection of Bevacizumab Injection as compared to standard cataract surgery.
3. The Bevacizumab Injection is 40 times cheaper than other available drug (Ranibizumab Injection) for same use and equally effective in India. This would put less financial burden on patients and prevent blindness of many.

Based on the above facts, following recommendations were made by the Committee:

The office of DCG(I) was requested to take necessary measures to withdraw the Alert Notice issued on 21.01.2016 which was primarily issued as a precautionary measure in the light of the incidences of blindness reported in Gujarat. Further, it was proposed that All India Ophthalmological Society (AIOS) and Vitreo Retinal Society of India (VRSI) will formulate guidelines for safe and effective use of Bevacizumab Injection for Ophthalmic purpose based on the written-informed consent as practiced globally for off-label use under appropriate environmental conditions by skilled ophthalmic surgeons based on risk-benefit analysis. They will further ensure that appropriate training and awareness may be imparted to its members.

The Ministry of Health and Family Welfare, Government of India has accepted recommendations of the Committee. Accordingly, this notice is issued.

(Dr. G. N. Singh)
Drugs Controller General (India)

To

All State/UT Drugs Controller

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i. **PPS to DGHS**
ii. **PS to JS(R)**

Drug makers, governments scramble to develop Zika virus vaccine

Researchers with the National Institute of Allergy and Infectious Diseases, Bharat Biotech, Sanofi, Inovio Pharmaceuticals, NewLink Genetics, Scripps Research Institute and Chembio Diagnostics are among those working to develop vaccines and diagnostic tests for Zika virus infection, but clinical trials will not scale up for at least 18 months, says Marie-Paule Kieny, World Health Organization assistant director-general for health systems and innovation. Many are building on prior research on other vaccines. "I think we're going to see a very robust field of vaccines coming forward," said NIAID Director Anthony Fauci. Ref.: The Wall Street Journal

Human rights group protests excise taxes on drugs in India

The imposition of excise taxes on some medicines, including chemotherapy, Parkinson's disease and bone disease treatments, triggered a protest from the National Human Rights Commission against the Indian Union Ministries of Finance and Health. "At a time when the health care system in the country as a whole is plagued with various ills, any action that pushes up the cost of medicines is bound to adversely affect people's right to health care," said the commission, which called for reports within four weeks.
Ref.: The Economic Times (India)

Maharashtra FDA issues prosecution orders in 90 cases of NSQ drugs

Maharashtra Food and Drug Administration (FDA) has issued prosecution orders in 90 cases of Not- of-Standard-Quality (NSQ) drugs across the state after testing 3413 drug samples between April 2015 and January 2016 as per Section 18 of Drugs and Cosmetics Act.
FDA action will ensure that consumers are not at risk as prosecution orders will help ensure circulation of quality drugs in the market. According to sources, it has been observed that not-of-standard drugs remain in the market for 62 days on an average before it is consumed by the patient.
As effective drug recall is the major objective of drug testing, the state regulator is also in the process of establishing three new drug testing laboratories at Nagpur, Nashik and Pune to test the quality standards of the drugs manufactured in the state.
Currently, FDA has only two drug testing laboratories one at Mumbai and another at Aurangabad. The drug testing laboratory located at Mumbai is accredited by the National Accreditation Board for Testing and Calibration Laboratories (NABL).
Drawing samples, analysing them for safety and drug recall will get a boost with the upgradation of drug testing infrastructure across the state. There would be considerable reduction in downtime with the upgradation of drug testing labs and samples would be tested in five to 15 days time.
Meanwhile, the spurious drugs study data of 47,000 samples collected as part of mammoth pan-India drugs survey involving around 1000 drug inspectors have reached its last leg and most likely to be submitted to the Union health ministry and the Parliament in a couple of months time for its final release.
The survey is significant as all studies till date have been done only for spurious drugs and no 100 per cent testing for NSQ drugs has been done till date. This is for the first time that complete testing of NSQ drugs would be done as per Indian pharmacopoeia and other pharmacopoeias. Only 10 per cent of the

samples were tested during the pan-India study in 2009.

High Incidence of Anti-Microbial Resistance: The Health Minister, Shri J P Nadda stated this in a written reply in the Rajya Sabha

It is generally believed that availability of antibiotics over the counter and lack of awareness about using antibiotic drugs only as prescribed by doctors results in inappropriate use of antibiotics.

As per a recent report (2015) released by Global Antimicrobial Resistance Partnership (GARP), it is reported that resistance among common pathogens is increasing worldwide though regional patterns of resistance vary.

Common bacterial pathogens becoming resistant to antimicrobials are Staphylococcus aureus, Enterococus, S. pneumoniae, N. gonorrhoeae, N. meningititidis, E.coli, Klebsiella pneumoniae, Typhoidal Salmonella, Shigella species, Vibrio cholerae, Mycobacterium tuberculosis and in other diseases such as Malaria, Kala azar, HIV etc.

It is estimated that the prevalence of Multi-Drug-Resistant Tuberculosis (MDR-TB) in India is 2-3% among notified new pulmonary TB patients and around 15% for re-treatment pulmonary TB patients.

While separate data on disease burden of the Indian population caused by infectious diseases is not available, it is estimated that over-all communicable disease contribute to 37% of the entire disease burden.

ICMR is carrying out surveillance of drug resistance to antibiotics through its Antimicrobial Resistance Surveillance Research Network (AMRSN) in six pathogenic groups (i) Diarrhoeagenic bacterial organisms (ii) Enteric fever pathogens (iii) Enterobacteriaceae causing sepsis (iv) Gram negative Non-fermenters (v) Gram positives including MRSA (vi) Fungal infections. Four nodal centers for collection of data are CMC, Vellore, JIPMER, Puducherry, PGIMER Chandigarh and AIIMS, New Delhi. The significant findings from last 2 years indicate that Salmonella typhi multidrug resistance (MDR) to ampicillin, chloramphenicol and trimethoprim – sulfamethoxazole is showing a downward trend. However, more than 50% of bacterial isolates of Klebsiella spp. and E. coli were found to be resistant to the currently used 3rd generation cephalosporins, but they are sensitive to carbapenams and colistin.

To further regulate the sale of antibiotics, the Government of India, in the year 2013, amended the Drug and Cosmetics Rules, 1945 to incorporate a new Schedule H1 containing 46 drugs which also includes IIIrd and IVth Generation antibiotics and anti-TB drugs for a strict control over the sale of these drugs. The Drugs falling under Schedule H1 are required to be sold in the country with the following conditions:

(1) The supply of a drug specified in Schedule H1 shall be recorded in a separate register at the time of the supply giving the name and address of the prescriber, the name of the patient, the name of the drug and the quantity supplied and such records shall be maintained for three years and be open for inspection.

(2) The drug specified in Schedule H1 shall be labeled with the symbol Rx which shall be in red and conspicuously displayed on the left top corner of the label, and shall also be labeled with the following words in a box with a red border:

"Schedule H1 Drug-Warning:
-It is dangerous to take this preparation except in accordance with the medical advice.
-Not to be sold by retail without the prescription of a Registered Medical Practitioner."

An insertion has been made in the Drugs and Cosmetics Rules, 1945 to specify the withdrawal period of antibiotics in case of egg, milk, poultry and fish before these enter the human food chain. The Department of Animal Husbandry, Dairying and Fisheries has also issued Advisories in 2014 addressed to all States and Union Territories regarding judicious use of antibiotics to prevent AMR.

A National Programme for Containment of AMR has also been initiated in 12th Five Year Plan with the following objectives.

- To establish a laboratory based surveillance system by strengthening laboratories for AMR in the country and to generate quality data on antimicrobial resistance for pathogens of public health importance.

- To generate awareness among healthcare providers and in the community regarding rational use of antibiotics.

- To strengthen infection control guidelines and practices and promote rational use of antibiotics.

Safety: Allopurinol

Interaction with 6- mercaptopurine and azathioprine Australia. The TGA has issued a reminder to health professionals that concomitant use of allopurinol with 6- mercaptopurine or azathioprine should be avoided, due to increased risk of potentially fatal bone marrow toxicities and blood dyscrasias. Allopurinol is an anti-uricaemic agent used to treat gout, uric acid nephrolithiasis and hyperuricaemia, including the prevention of tumour-lysis syndrome. Azathioprine is used as an immunosuppressant and 6-mercapotpurine as a cytotoxic agent. Allopurinol reduces metabolism of 6-mercaptopurine and azathioprine, increasing the risk of bone marrow toxicities and blood dyscrasias, such as leukopenia, thrombocytopenia and pancytopenia. If co-administration of allopurinol with 6- mercaptopurine or azathioprine is necessary, the dose of 6-mercaptopurine or azathioprine should be reduced to one quarter of the normal dose and the patient's complete blood count should be closely monitored in accordance with the product information. The TGA recommends that, health professionals should check if patients are being treated with allopurinol when prescribing azathioprine or 6-mercaptopurine, and they should educate patients about this medicine interaction.

Reference: Medicines Safety Update, TGA, Vol. 6, No. 6, December 2015 (www.tga.gov.au)

Forthcoming Events

Celebration of World Health Day
Lecture on "Beat Diabetes"
7th April 2016

Venue: IPA Auditorium, 22 B Panchnontola Road, Kolkata-700029
Time: 6.30 pm