



Drug Information Bulletin

Drug Information Centre (DIC)

Indian Pharmaceutical Association

Bengal Branch

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Editorial

The Nobel Prize in Physiology or Medicine for this year is awarded to three US scientists- Jeffrey C. Hall, Michael Rosbash and Michael W. Young for their discoveries of molecular mechanisms that control circadian rhythms. Circadian rhythms are driven by an internal biological clock that anticipates day/night cycles to optimize the physiology and behavior of organisms. Several scientists worked on this subject for proper explanation. But joint research by Jeffrey, Hall and Rosbash revealed a series of interlocked transcription-translation feedback loops, together with a complex network of reactions. These involve regulated protein phosphorylation and degradation of Transcription Translation Feedback Loop (TTFL) components, protein complex assembly, nuclear translocation and other post-translational modifications, generating oscillations round the clock. Circadian oscillators within individual cells respond differently to entraining signals and control various physiological processes, such as sleep patterns, body temperature, hormone release, blood pressure, and metabolism. The pioneering discoveries by Hall, Rosbash and Young have revealed a crucial physiological mechanism explaining circadian adaptation, with important implications for human health and disease. Since the pioneering discoveries by the three scientists, elucidating a fundamental physiological mechanism, circadian biology has developed into a vast and highly dynamic field of research, with important implications for human health and wellbeing.



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Editor

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Latest circular from DCGI on procedure to be followed for subsequent applicants in respect of FDCs declared as rational by Kokate Committee

File No. 4-01/2013-DC (Misc. 13-PSC)
Directorate General of Health Services
Office of Drugs Controller General (India)
(FDC Division)

FDA Bhawan, Kotla Road
New Delhi-110002

Dated: 05 OCT 2017

NOTICE

Subject: Procedure to be followed for subsequent applicants in respect of FDCs declared as rational by Kokate Committee and approved by DCGI-regarding.

References: 1. This Directorate's letter no. 4-01/2013-DC (Misc. 13-PSC) dated 15.01.2013. 2. This Directorate's notice no. 4-01/2013-DC (Misc. 13-PSC) dated 16.03.2017. 3. This Directorate's notice no. 4-01/2013-DC (Misc. 13-PSC) dated 05.06.2017.

This is in continuation to this Directorate notice of even number dated 05.06.2017 whereby pathway for clearance of cases with respect to subsequent applicants in respect of FDCs declared as rational by Prof. Kokate Committee and approved by DCGI was clarified.

It was also requested that all the manufacturers who are already holding licence from State Licensing Authority for such FDCs and did not obtain NOC from DCGI are required to submit their applications to this Directorate at the earliest but not later than 4 months, failing which their applications will not be considered and their licenses will be considered as without legal validity.

In view of above, it is again requested that such manufacturers who are yet to submit their applications shall submit the same to this Directorate within 2 months as per the procedure laid down under this Directorate's notice of even number dated 05.06.2017.

Yours faithfully,


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

To:-
All State/UT Drugs Controllers/All Zonal/Sub Zonal offices of CDSCO.

Copy to:-
1. PS to JS(R), Ministry of Health and Family Welfare, Nirman Bhawan, New Delhi.
2. Drug Manufacturing Associations: IDMA/OPPI/IPA/CIP/FOPE etc.

Domperidone Risk minimisation of cardiovascular effects

The HSA has reassessed whether additional measures to further mitigate the cardiovascular (CV) risk associated with the use of domperidone are necessary. The HSA has updated package inserts for products containing domperidone to strengthen cardiovascular warnings and include recommendations on new dosing regimens and treatment durations. Domperidone is a pro-kinetic and anti-emetic drug used for the treatment of dyspepsia, nausea and vomiting. Risk factors that increase the risk of cardiotoxicity include: advanced age (>60 years old), underlying CV conditions, high domperidone dose (>30 mg/day) and concomitant use with QT prolongation drugs and CYP3A4 inhibitors. The HSA has received two cases of QT prolongation associated with domperidone (from 2006 to 2016). Considering that domperidone has been used in local clinical settings for a long period of time, and that there is a relatively low incidence of locally reported cardiac-related adverse events, the HSA concluded that the benefit-risk profile of domperidone remains favourable when used appropriately. Additional measures were recommended to mitigate the risk of cardiotoxicity, which included restricting its use in high risk patients.

Reference: Product Safety Alerts, HSA, 26 May 2017 (<http://www.hsa.gov.sg/>) (See WHO Pharmaceuticals Newsletters No.2, 2015, No.3 and No.1, 2014 for related information)

Finasteride Potential risk of serious muscle-related adverse effects

Health Canada has recommended that manufacturers update the product information for finasteride containing products (Propecia®, Proscar® and generics) to include information about the potential risk of serious muscle-related adverse effects. Finasteride at a dose of 5mg is used to treat and control noncancerous enlargement of the prostate gland (benign prostatic hyperplasia) and for treatment of androgenic alopecia at a dose of 1mg. Health Canada reviewed the potential risk of serious muscle-related adverse events such as rhabdomyolysis, myopathy and muscle disorders such as pain, weakness, atrophy or stiffness. At the time of this review, Health Canada had received 11 Canadian reports of serious muscle-related adverse effects. Four cases were thought to be possibly linked to

finasteride use. In three of the four cases individuals recovered after stopping the use of finasteride (the outcome is unknown in the fourth case). There were not enough information to establish a link between finasteride and muscle-related adverse effects in the remaining seven reports. Three additional cases of serious muscle-related adverse effects with the use of finasteride were reported in the literature. Two cases reported either myalgia with an increase in muscle enzymes, or rhabdomyolysis following the use of finasteride to treat hair loss in men. These patients recovered after they stopped using finasteride. The WHO global database of Individual Case Safety Reports (ICSRs) contained 508 reports of serious muscle-related adverse effects suspected of being linked to the use of finasteride, mostly atrophy, weakness, myalgia and sudden, strong muscle tightening (spasms). There were not enough information in these reports to suggest a causal effect. Health Canada's review of the available information concluded that the risk of serious muscle-related adverse effects with the use of finasteride cannot be ruled out.

Reference: Summary Safety Review, Health Canada, 22 June 2017 (www.hc-sc.gc.ca)

Fluconazole and fosfluconazole Risk of drug-induced hypersensitivity syndrome

The MHLW and the PMDA have announced that the package inserts for fluconazole (Diflucan®) and fosfluconazole (Prodif®) have been updated to include the risk of drug-induced hypersensitivity syndrome (DIHS) as a clinically significant adverse reaction. Fluconazole and fosfluconazole (pro-drug of fluconazole) are antifungal medications used for fungal infections with Candida or Cryptococcus. A total of two cases associated with DIHS with fluconazole use have been reported in Japan. Of these, a causal relationship could not be excluded in one of the cases. For fosfluconazole, one case associated with DHIS has been reported. The company core datasheet (CCDS) for fluconazole has also been updated.

Reference: Revision of Precautions, MHLW/PMDA, 4 July 2017 (www.pmda.go.jp/english/)

Thalidomide, lenalidomide and pomalidomide Risk of hepatitis B reactivation, herpes zoster and pulmonary hypertension .

The NPRA has updated the package inserts for thalidomide, lenalidomide and pomalidomide to include information on the risk of hepatitis B reactivation, herpes zoster and pulmonary hypertension. Dear Health-care Professional Communication(DHPC) letters have also been issued. Thalidomide is indicated for both multiple myeloma and erythema nodosum leprosum (ENL), whereas lenalidomide and pomalidomide are only indicated for multiple myeloma. Cases of hepatitis B reactivation have been reported following treatment with thalidomide, lenalidomide and pomalidomide in patients who had a previous history of hepatitis B virus (HBV) infection. Some cases of HBV reactivation progressed to acute hepatic failure and resulted in death. In addition, reactivation of varicella-zoster virus and disseminated herpes zoster have been reported for both thalidomide, lenalidomide and pomalidomide use. In addition, thalidomide treatment has been linked to reports of fatal pulmonary hypertension cases. The NPRA has received 105 reports with the use of these products (thalidomide: 20 reports with 47 adverse events; lenalidomide: 84 reports with 136 adverse events; pomalidomide: one report with one adverse event) between 2006 and December 2016. At the time of the communication, there were no reports related to hepatitis B virus reactivation, herpes zoster and pulmonary hypertension received by the NPRA.

ASSOCIATION NEWS:



Health Camp at Paschim Medinipur organized by IPA Bengal Branch and IPA Bengal Pharma & Health Care Trust on 7th October 2017

Reference: Reaksi Drug Safety News, NPRA, No. 35, July 2017 (See WHO Pharmaceuticals Newsletters No.1, 2017, No.5 and No.3, 2016 for related information)

UK Biotech Company awarded up to \$1.25M to study drug-resistant bacteria

Biotechnology firm Centauri Therapeutics has been awarded up to \$1.25 million by Innovate UK to study treatments for drug-resistant infectious diseases. Centauri Therapeutics is working on a drug mechanism that places special molecules into patients that help their natural antibodies fight resistant bacteria.

Ref. [Kent Online \(U.K.\)](#)

Single Zika virus mutation may be cause of severe fetal microcephaly

Chinese researchers discovered that one genetic mutation, which may have occurred in 2013, could have triggered the Zika virus' capacity to induce severe fetal microcephaly. The findings, published in the journal Science, indicated that a lone serine to glutamin substitution in the virus' polyprotein increased virus infectivity considerably in the neural progenitor cells of humans and mice.

Ref. [Physician's Briefing/HealthDay News](#)



One of our SEC members Mr. Dibya Das has celebrated Pharmacists Day at a place 4928 m height at Nepal during his expedition on 25th September helping local people with some medicines.

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