



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

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Content

- Editorial
- New Drug: Sofosbuvir
- Gottlieb tells Senate committee that opioid crisis would be main priority
- Fast-track status granted for Duchenne muscular dystrophy drug
- Govt. of India notified BCS classification for conducting Bio Equivalence study for approval of new drug
- Reader Speak.....
- Pics. of lecture by Prof. Amitava Nandy on “Prevention and Control of Vector borne diseases” on 08.04.2017 at IPA Bengal Branch Auditorium

Editorial

It is indeed a proud moment to script the first issue of the 11th year's Drug Information Bulletin. Thank you very much for your kind words and suggestions conveyed to our team, which will encourage us to work hard for its betterment.

A number of issues have emerged since the last issue was published. The first one is the draft notification vide no. G.S.R. 319(E) dated 31.03.2017 (available at www.cdsco.nic.in), through which it is proposed to conduct every inspection at the manufacturing premises jointly by State Drug Control Inspectors and the Central Drugs control Inspectors. There is another proposal to fix the late fees on a percentage basis, which may lead to loss of exchequer. Large sectors of the stakeholders are of the opinion that “this step is unbecoming and against the basic principle of our constitution and usurpation of the power of the state”. Another section feels that it will bring uniformity in implementation of Drugs and Cosmetics Act in the country. Hope that the final notification will be made with due consideration of the opinion from the stake holders

The other important notification vide G.S.R. (E) dated 3rd April 2017(available at www.cdsco.nic.in), including concept of “biopharmaceutical classification system” to classify drugs on the basis of solubility and permeability, classified as category I- high solubility and high permeability, category II- low solubility and high permeability, category III- high solubility and low permeability, and category IV- low solubility and low permeability.”; The applicant require to submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.” This is an welcoming step in the process of approving solid dosage form.



Smandal

Dr. Subhash C. Mandal
Editor

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

New Drug: Sofosbuvir

Approved indication: hepatitis C

Sovaldi (Gilead)

400 mg tablets

Australian Medicines Handbook section 5.4

There are six major types of hepatitis C – genotypes 1–6. In Australia, about half of cases are caused by genotype 1, a third by genotype 3 and 5% by genotype 2. Until recently, standard treatment for chronic hepatitis C infection was with peginterferon and ribavirin. Protease inhibitors boceprevir ([Aust Prescr 2012;35:102-3](#)) and telaprevir ([Aust Prescr 2012;35:128-35](#)) were approved in 2012. Adding either of these to peginterferon and ribavirin seems to improve the response rates in people with genotype 1 disease.

Sofosbuvir is another antiviral drug that can be added to combination treatment for chronic hepatitis C. It is a direct-acting nucleotide polymerase inhibitor. The prodrug is converted to a nucleotide analogue in hepatocytes. This active analogue then binds to RNA polymerase which terminates RNA synthesis and inhibits viral replication.

Sofosbuvir 400 mg/day has been investigated in four pivotal phase III hepatitis C trials.^{1,2} One trial enrolled people with genotypes 1, 4, 5 or 6 and the others enrolled those with genotypes 2 or 3. Some patients in the trials had evidence of liver cirrhosis (15–35%). The primary outcome was the proportion of patients who had achieved a sustained virologic response, defined as undetectable viral RNA 12 weeks after the end of treatment. The highest rate of response to treatment was seen when sofosbuvir was added to peginterferon and ribavirin (90%) in previously untreated patients with genotypes 1, 4, 5 or 6. Response rates were high with all genotypes although there were only seven people with serotypes 5 or 6.¹ When sofosbuvir was added to ribavirin in patients with genotypes 2 or 3, response rates in genotype 3 infections were considerably lower than those in genotype 2 infections.^{1,2} Liver cirrhosis was also associated with lower

response rates, particularly in those with genotype 3 disease ([see Table](#)).

Another trial found that extending sofosbuvir plus ribavirin treatment from 12 to 24 weeks improved response rates in people with genotype 3 infection from 27% (3/11) to 85% (213/250).³ However, as the trial design was changed during the study, there was no hypothesis testing or statistical comparisons and results were only descriptive. Other trials have found that patients co-infected with HIV⁴ and those with hepatocellular carcinoma awaiting liver transplant benefit from treatment with sofosbuvir added to ribavirin.

Treatment discontinuation because of an adverse event occurred in 2% or less of patients taking sofosbuvir-containing regimens. The most common adverse events with sofosbuvir added to ribavirin were fatigue (30–38%), headache (24–30%), nausea (13–22%) and insomnia (15–16%). These events occurred more frequently in patients who were also receiving peginterferon. This was also the case for anaemia and neutropenia.

Absorption is rapid after an oral dose of sofosbuvir with peak plasma concentrations reached after 0.5–2 hours. After metabolism in the liver, most of the dose is excreted in the urine (80%) and faeces (14%). The mean terminal half-life of the main metabolite is 27 hours.

Sofosbuvir is a substrate of P glycoprotein so potent inducers of this transporter, such as rifampicin and St John's wort, should be avoided as they may decrease sofosbuvir's therapeutic effect. Other drugs that may reduce sofosbuvir exposure and are not recommended include modafinil, carbamazepine, phenytoin, phenobarbitone and tipranavir in combination with ritonavir. Sofosbuvir should always be used in a combination regimen. As ribavirin is teratogenic, adequate contraception must be used during and for six months after treatment in men and women.

Sofosbuvir is effective and well tolerated when added to current therapy for people

with chronic hepatitis C. The main predictors of response are viral genotype and liver cirrhosis. Response rates in people with genotype 3 infection are lower than with other genotypes and these people may need to take treatment for longer. Sofosbuvir also provides an alternative for people who have relapsed, cannot tolerate or do not want to take interferon-containing regimens.

References

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4. Sulkowski MS, Naggie S, Lalezari J, Fessel WJ, Mounzer K, Shuhart M, et al. Sofosbuvir and ribavirin for hepatitis C in patients with HIV coinfection. *JAMA* 2014;312:353-61.

Status in India: Sofosbuvir 400 mg film coated Tablet have been approved by the Central Drug Standard Control organization on 16.02.2017 with indication "In combination with other medicinal products for the treatment of Chronic Hepatitis C (CHC) in adults With the condition: to be sold by retail on the prescription of Hepatologistonly"

Gottlieb tells Senate committee that opioid crisis would be main priority

Dr. Scott Gottlieb, President Donald Trump's nominee to head the FDA, told a Senate health committee Wednesday that addressing the country's opioid crisis would be his main priority and that impartial science would continue to guide the agency's decisions under his leadership. Critics have cited consulting and other fees Gottlieb has

received from pharmaceutical companies, but he said in an ethics document filed last week that he would recuse himself from decisions related to approximately 20 companies for a year if confirmed.

Other issues raised Wednesday:

—Gottlieb made clear that he disagreed with President Donald Trump's contention that vaccines may be linked to autism. Gottlieb said that has been "one of the most exhaustively studied questions in scientific history" and it was time to accept the conclusions of those studies that "there is no causal link."

—Gottlieb said he was committed to tobacco control, saying, "I am not going to countenance a rise in adolescent smoking rates in this country under my watch." Pressed on e-cigarettes that increasingly come with kid-friendly flavors like gummy bears, Gottlieb said vaping has a role in helping established smokers quit but that with the flavorings, "I recognize there is a line here somewhere and I don't know where that line gets drawn."

—On drug pricing, Gottlieb said it was time to adjust FDA policies that make it difficult to quickly approve lower-cost generic versions of certain treatments, particularly drug-and-device combinations.

—As for FDA's food side, Gottlieb deferred questions about advice on seafood consumption during pregnancy, genetically engineered salmon and new nutrition labels set for next year, saying he needed to hear from FDA's scientists and staff.

Source: *The Associated Post*

Fast-track status granted for Duchenne muscular dystrophy drug

The FDA has granted fast-track status to vamorolone, or VBP15, from ReveraGen BioPharma, an investigative once-daily oral medication for Duchenne muscular dystrophy. The drug maker is enrolling boys with DMD from six countries in clinical trials.

Source: [Rare Disease Report](#)

Govt. of India notified BCS classification for conducting Bio Equivalence study for approval of new drug

MINISTRY OF HEALTH AND FAMILY WELFARE

(Department of Health and Family Welfare)

NOTIFICATION

New Delhi, the 3rd April, 2017

G.S.R. 327(E).—Whereas the draft of certain rules further to amend the Drugs and Cosmetics Rules, 1945 was published as required by sections 12 and 33 of the Drugs and Cosmetics Act, 1940 (23 of 1940) in the Gazette of India, Extraordinary, Part II, Section 3, Sub-section (i), dated the 2nd February, 2017 vide notification of the Government of India in the Ministry of Health and Family Welfare, number G.S.R. 102(E), dated the 2nd February, 2017 for inviting objections and suggestions from all persons likely to be affected thereby before the expiry of a period of forty-five days from the date on which copies of the Official Gazette containing the said notification was made available to the public;

And whereas the copies of the said Gazette were made available to the public on 2nd February, 2017;

And, whereas, objections and suggestions received from the public on the said rules have been considered by the Central Government.

Now, therefore, in exercise of the powers conferred by sections 12 and 33 of the said Act, the Central Government, after consultation with the Drugs Technical Advisory Board, hereby makes the following rules further to amend the Drugs and Cosmetics Rules, 1945, namely:-

1. (1) These rules may be called Drugs and Cosmetics (Ninth Amendment) Rules, 2017.
- (2) They shall come into force on the date of their publication in the Official Gazette.

[भाग II—खण्ड 3(i)]

भारत का राजपत्र : असाधारण

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2. In the Drugs and Cosmetics Rules, 1945 (hereinafter referred to as the said rules), in rule 2, after clause (a), following shall be inserted, namely,-
 - (aa) “biopharmaceutical classification system” means a system used to classify drugs on the basis of solubility and permeability, classified as category I- high solubility and high permeability, category II- low solubility and high permeability, category III- high solubility and low permeability, and category IV- low solubility and low permeability.”;
3. In the said rules, in rule 74, after clause (p), the following clause shall inserted, namely.-

“(q) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.”.
4. In the said rules, in rule 74B, after clause (7), the following clause shall inserted, namely.-

“(8) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.”.
5. In the said rules, in rule 76, after clause (9), the following clause shall inserted, namely.-

“(10) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.”.
6. In the said rules, in rule 78, after clause (q), the following clause shall inserted, namely.-

“(r) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.”.
7. In the said rules, in rule 78A, after clause (8), the following clause shall inserted, namely.-

“(9) the applicant shall submit the result of bioequivalence study referred to in Schedule Y, along with the application for grant of a licence of oral dosage form of drugs specified under category II and category IV of the biopharmaceutical classification system.”.

[F. No. X.11014/12/2016-DRS]

K. L. SHARMA, Jt. Secy.

Foot note: Principal rules were published in the Official Gazette vide notification number F.28-10/45-H (1), dated the 21st December, 1945 and last amended vide notification number G.S.R. 303 (E) dated the 30th March, 2017.

Reader Speak.....

Dear Dr. Mandal,

Thank you so much your effort for sending the bulletin regularly without missing any one issue.

As a professional working in hospital I am always being updated about the new ADRS, New drugs and related information including the professional news.

Thank you so much again.

Sitesh

Sitesh C Bachar Ph. D

Professor and Chairman
Department of Pharmacy
Faculty of Pharmacy
University of Dhaka
Dhaka-1000, BANGLADESH

Pics. Of lecture by Prof. Amitava Nandy on "Prevention and Control of Vector borne diseases" on 08.04.2017 at IPA Bengal Branch Auditorium



TOPRA INDIA 2017
May 16-18, 2017, Bangalore

Theme:
Building Regulatory Excellence

Venue:
Bengaluru

Organized by:
The Organization for Professional in
Regulatory Affairs

Supported by:
Indian Pharmaceutical Association
&
Indian Society for Clinical Research

National Health Conclave 2017
May 25-27

Theme:
'Chronic care: Innovation
Opportunities and Challenges.'

Venue: New Delhi

Organizers:
Public Health Foundation of India
(PHFI) and Association of Healthcare
Providers India (AHPI)

Partners:
Several Govt. & Non Govt.
Organizations

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