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ADVOCATES & SOLICITORS

Vol. III, Issue XI
November 2019

S&A PHARMA NEWSLETTER

EDITORIAL

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The regulatory body of any country should be the strongest body as it is responsible for taking necessary actions in its jurisdiction to maintain the quality of drugs during research, manufacturing and distribution. It plays an important role in running the health care system of the country. Any amendments made in acts and regulatory guidelines should be placed on the public domain to make access of such amendments and guidelines easy for public and various stakeholders dealing with drug manufacturing.

We are pleased to present this Vol. III Issue XI of S&A – Pharma Newsletter. Through this newsletter, we aim to share recent information allied to regulatory reforms and updates from pharmaceutical sector in India as well as from foreign jurisdictions, based on information collated through research and appraisal of applicable statutory provisions.

In the present issue, we start with the proposal of CDSCO to notify certain medical devices under Medical Device Rule, 2017. The current issue also throws some light on DCGI notifying manufacturers to furnish declaration of not marketing drugs having similar brand name, issues which could lead serious medication errors. Going ahead the issue discusses the collaboration of the Health Ministry with Bill & Melinda Gates Foundation to strengthen primary health care and innovation in country. Further, the volume also discusses the disapproval by Indian Pharmaceutical association on the schedule K amendment in the Drugs and Cosmetics Act..

Going ahead we elaborate the decision of the NPPA to exempt price capping for ready to use infusion bag by Sun Pharma. The article clearly states that the exemption decision for price control of 'Ready to use Infusion bag' by NPPA is probably the first decision implementing *DPCO (amendment), 2019* taken after an application of exemption was made by the Sun Pharmaceuticals Industries Limited.

The volume also discusses the recent healthcare updates from India presented as a separate section under '*India Healthcare Highlights November 2019'*.

From the international arena, a separate section which discusses on recent regulatory updates from US FDA and WHO are also discussed under the heading '*US FDA Pharma Updates November 2019'* and '*WHO updates November 2019'* respectively.

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Trust you enjoy reading this issue as well. Please feel free to send your valuable inputs / comments at newsletter@singhassociates.in

Thank you.

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S&A Pharma Newsletter
Volume III, Issue XI
November 2019

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Published by
Singh & Associates
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Contents

WHO Pharma Highlights November 2019

This segment of the newsletter focuses on recent regulatory reforms and updates in Healthcare and Pharmaceutical domain from World Health Organization (WHO). This segment collates information periodically by conducting research and review of pharmaceutical updates from the WHO. Below are the highlights for the month of November 2019:

1. WHO launches first-ever insulin prequalification programme for diabetes treatment[1]

On November 13, 2019, the World Health Organization (WHO) announced the launch of a pilot programme to increase the treatment of diabetes in low- and middle-income countries. The programme aims to boost access to treatment by facilitating easy access to quality products on the international market, providing countries with greater choice and patients with lower prices.

2. Mosquito sterilization technique - a new way to prevent chikungunya, dengue, and Zika[2]

WHO has announced testing of mosquito sterilization technique as part of global health efforts to control diseases such as chikungunya, dengue, and Zika. The sterilization process involves rearing sterilized male mosquitos in defined environment and then releasing them to mate with females in the wild. As they do not produce any offspring, the insect population is expected to decline over time.

3. WHO prequalified Ebola vaccine for the first time in countries most at risk of Ebola outbreaks[3]

On November 12, 2019, WHO has for the first time prequalified Ebola vaccine which will increase the licensing process across countrys most at risk of Ebola outbreaks. Prequalification is the process in which vaccines meet WHO standards for quality, safety and efficacy.

4. Global leader adds their commitment to vaccinate 450 million children against polio each year.[4]

WHO has announced the start of a pilot programme to prequalify human insulin with an aim to augment treatment for diabetes in low- and middle-income countries. The decision, announced ahead of the World Diabetes Day (14 November), is a part of a series of steps WHO has taken to address the growing diabetes burden in all regions. About 65 million people with type 2 diabetes need insulin, but only half of them are able to access it, largely due to high prices. All patients with type 1 diabetes need insulin to survive.

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1 https://www.who.int/news-room/detail/13-11-2019-who-launches-first-ever-insulin-prequalification-programme-to-expand-access-to-life-saving-treatment-for-diabetes

2 https://www.who.int/news-room/detail/14-11-2019-mosquito-sterilization-offers-new-opportunity-to-control-chikungunya-dengue-and-zika

3 https://www.who.int/news-room/detail/12-11-2019-who-prequalifies-ebola-vaccine-paving-the-way-for-its-use-in-high-risk-countries

4 https://www.who.int/news-room/detail/19-11-2019-global-leaders-pledge-us-2.6-billion-to-eradicate-polio-at-the-reaching-the-last-mile-forum-in-abu-dhabi

CDSCO brings some home-use medical devices under regulations as per the Medical Device (MD) Rules, 2017

The Central Drug Standard Control Organization has issued a notice on its site on bringing devices like digital thermometer and blood pressure monitors under regulation from January 01, 2020, as per the new Medical Device (MD) Rules, 2017.[1]

Background

According to various clinical studies seventy per cent of digital blood pressure monitors for home use show inaccurate results. For people who rely on these results, serious health issues can arise if they self-medicate and from the side effects associated with the drugs. As per studies, certain group of patients were asked to monitor their blood pressure through the device at home and report the results accordingly according to the result of the

According to the data from the India Heart Study (IHS) 42 per cent Indians are at risk due to misdiagnosis of hypertension. The study also highlights high prevalence of **masked hypertension and white-coat** hypertension in Indians on first clinic visit. The investigators examined the blood pressure of 18,918 participants (male and female) through 1,233 doctors across 15 states over a period of nine months. The participants' blood pressure was monitored at home four times in a day for 7 consecutive days. The study also revealed that Mumbai fares a tad better at 38.2 per cent with 15.4 per cent masked and 22.8 per cent white-coat hypertensives.

The data supports the fact that strict regulations need to be imposed to have some measure on medical devices used by individuals for monitoring the parameters. In response to this need, devices like digital thermometers and blood pressure monitoring devices will be considered under new regulations with effect from January 01, 2020.

However, the machines which are not categorized under machines meant for composite purpose and not for the individual monitoring are not considered under these regulations at this stage.

Note: Masked hypertension is defined as normal blood pressure (BP) in the clinic or office but an elevated BP out of the clinic (ambulatory daytime BP or home BP), while white coat hypertension is a syndrome whereby a patient›s feeling of anxiety in a medical environment results in an abnormally high reading on measurement of blood pressure.

Conclusion

Due to recent cases of the misinterpretation of results in patients using various medical devices at home, the central government has come up with the notice where such medical devices should be placed under the regulations of the Medical Device Rule to make manufacturers follow the guidelines during the making of such products.

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1 https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=NTIyOQ==

DCGI introduces an undertaking from manufacturers to furnish declaration of not marketing drugs having similar brand names

The Drugs Controller General of India (DCGI), on November 06, 2019, has issued Drugs and Cosmetics (Thirteenth Amendment) Rules, 2019. The amendment is followed after consultation with the Drugs Technical Advisory Board (DTAB), which directed all manufacturers to furnish an undertaking in Form 51 to the licensing authority, declaring that respective company is not marketing any drug with similar brand names in the country to avoid brand names related confusion in the market[1].

Drugs and Cosmetic (Thirteenth amendment) Rule, 2019

The Drugs and Cosmetic (Thirteenth amendment) Rule, 2019, has introduced a detailed format of the undertaking declaring brand name or trade name by manufacturers in *Form 51*. The manufacturer has to submit the form 51 (undertaking) to the licensing authority for marketing a drug under a brand name or trade name clearly mentioning name of the drug, dosage form and composition to avoid any confusion or deception among doctors, chemists and patients in the market.

Further, the amendment has clarified that the concerned manufacturers have to follow the prescribed sub-rule inserted in *Drugs and Cosmetic (D&C) Rules 71(9), 71A (5), 71B (v), 76(11) 76A (v),* which says*:*

> *"In case the applicant intends to market the drug under a brand name or trade name, the applicant shall furnish an undertaking in Form 51 to the licensing authority to the effect that to the best of his knowledge based on search in trademarks registry, central data base for brand name or trade name of drugs maintained by Central Drugs Standard Control Organization, literature and reference books on details of drug formulations in India, and internet, such or similar brand name or trade name is not already in existence with respect to any drug in the country and the proposed brand name or trade name shall not lead to any confusion or deception in the market."*

Background

The 81st meeting of DTAB has deliberated this matter that the brand name/trade name of pharmaceuticals is neither controlled by the Drug Licensing Authority under the Drugs and Cosmetic Act 1940 & Rules 1945, nor the Trademarks office, which creates confusion around having similartrade names for different drugs manufactured and sold in the country. It can cause a risky situation possibly fatally detrimental to patient safety. Therefore, the DTAB recommended amendments in Drugs and Cosmetic Rules 1945, to include the provisions for regulating brand names/ trade names of pharmaceutical products by the Central and State Licensing Authorities[2].

Further, DCGI in May 2019, issued a circular notifying all the state drug controllers (DCs) not to allow companies to market drug formulations in which the composition (active pharmaceutical agents) has been changed while retaining the old brand name, which is not only misleading the consumers but also not in the interest of patient safety. The DCGI notification resulted after a long discussions conducted by Drugs Consultative Committee (DCC) meetings held during the period of December 10, 2008 to February 15, 2011.

1 http://www.egazette.nic.in/WriteReadData/2019/213740.pdf

2 https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/common_download.jsp?num_id_pk=NTY2

Note – This is not the first time when DCGI has reported this matter. Apart from DCGI, the National Pharmaceuticals Pricing Authority (NPPA) and various state drug controllers and advisory committees have earlier reported about this unethical practice of drug manufacturers to Health Ministry. Moreover, some state Drugs Controller have suggested that changing the composition of any drug formulation but retaining the same brand name should require permission from drug regulatory authorities, where manufacturers need to apply a fresh application for grant of license to manufacture that particular drug formulation.

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Health Ministry collaborates with Bill & Melinda Gates Foundation to strengthen primary health care and innovation in country

On November 18, 2019, the Ministry of Health and Family Welfare (MoHFW) signed a memorandum of cooperation (MoC) with Bill & Melinda Gates Foundation (BMGF). As per the MoC, the Gates Foundation will offer technical, management and program design support to government via its grantees and other partners. The MoC will specially focus on innovation, enhancing performance management and strengthening the primary health aspects such as reducing maternal and child mortality, improving nutrition services and increasing the immunization reach[1].

The Foundation will support other healthcare programs like increase in access to family planning measures amongst younger women and reduction in the burden of select infectious diseases such as Tuberculosis, Visceral Leishmaniasis and Lymphatic Filariasis. The work will also include strengthening of supply chains and monitoring systems while focusing on budget utilization, management and skills of human resources for health, ultimately bolstering the entire health system.

About Bill and Gates Foundation

The Bill & Melinda Gates Foundation works to help all people lead healthy, productive lives. In developing countries, it focuses on improving people's health, giving them a chance to lift themselves out of hunger and extreme poverty. In the United States, it seeks to ensure that all people especially those with the fewest resources have access to the opportunities they need to succeed in school and life[2].

Note – The MoC with Gates Foundation will bring in more innovative approaches in Indian healthcare system which will not only strengthen the existing health programs and initiative but also help in achieving sustainable development goals for the country.

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1 https://pib.gov.in/newsite/PrintRelease.aspx?relid=109852

2 https://www.gatesfoundation.org/Who-We-Are/General-Information/Foundation-Factsheet

India Healthcare Highlights November 2019

This segment of the newsletter shares recent information related to regulatory reforms from Healthcare and Pharmaceutical sectors in India. This segment collates information on monthly basis via conducting research and appraisal of applicable statutory provisions. Below are the highlights for November 2019.

1. Cabinet approves healthcare MoUs with Germany and Brazil

The Union Cabinet has approved the Memorandum of Understanding (MoUs) between India and Germany for collaboration in the field of Occupational Diseases, Re-habilitation and vocational training of Insured Persons with disabilities; and the MoU between India and Brazil in the field of Health and Medicine. The MoUs with Germany will broadly help in 1) Exchanging information and promoting activities in the area of rehabilitation related to medical, occupational and social re-habilitation of Insured Persons with disabilities; and Prevention, detection and treatment of occupational diseases 2) Exchange of information and collaboration will enable capacity building and social re-habilitation of Insured Persons with disabilities, besides prevention, detection and treatment of occupational diseases.

The bilateral MoU between India and Brazil will strengthen bilateral ties and encourage cooperation in technology development in the health sector and development of research in the health sector. It will also aim to facilitate the improve public health status of both the countries[1].

2. CDSCO to regulate adhesive for fixing wig, scalp cleansing products and artificial nail system under cosmetics category

Central Drugs Standard Control Organization (CDSCO) is planning to regulate adhesive for fixing wig, scalp cleansing products and artificial nail system under definition of cosmetics under Drugs and Cosmetics Act, 1940. In view of the above, the government invites the stakeholder's comments within 30 days from the date of publication of the notice. The apex body of CDSCO deliberated the matter in light of the document submitted by various applicants and recommended that above mentioned products should be regulated under cosmetics of D&C Act. Further, in case of artificial nail system regulation, the Bureau of Indian Standard (BIS) IS 4707 will be applicable[2].

3. NPPA has fixed/ revised retail/ceiling prices of 75 formulation under DPCO

NPPA has fixed/revised the retail and ceiling prices of 75 drug formulations, which include drugs from various categories of antibiotics, anti-hypertensives, painkillers, anti-diabetic, drugs to treat AIDS/HIV etc. The drugs prices capped are exclusive of goods and services tax, if any, in relation to the formulation specified in the notification with the strength, unit and name of manufacturer & marketing company. Therefore, all manufacturers of scheduled formulations, selling branded or generic version or both of scheduled formulations at a price higher than the ceiling price (plus goods and services tax as applicable) so fixed and notified by the government, shall revise the prices of all such formulations downward not exceeding the ceiling price as notified by the government[3].

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1 https://www.biospectrumindia.com/news/22/15066/cabinet-approves-healthcare-mous-with-brazil-and-germany.html

2 https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=NTE5Nw==

3 http://www.nppaindia.nic.in/en/whats-new/

IPA opposed recent amendment of Drugs and Cosmetics Rules

The Indian Pharmaceutical Association has opposed the amendment in Schedule K of Drugs & Cosmetics (D&C) Rules by health ministry.

Background

Recently the Health Ministry made the amendment in schedule K of the Drugs and Cosmetics act which states that:

"Drugs supplied by Health Functionaries including Community Health Officers, Nurses, Auxiliary Nurse Midwives and Lady Health Visitors attached to Primary Health Centres/ Sub-Centres/ Health & Wellness Centres in rural and urban areas, Community Health Volunteers such as Accredited Social Health Activists (ASHAs) under the National Health Mission, and (iii) Anganwadi Workers."[1]

However, the officials of Indian Pharmaceutical Association stated that no other professional other than the registered pharmacists can compound prepare, mix or dispense any medicine on the prescription of a medical practitioner according to section 42 of the Drugs and Cosmetics Act. A person who is found guilty shall be punishable with imprisonment for a term which may extend to six months or with fine or with both. As per IPA, Schedule K exempts only the provisions of Chapter IV of the Act and Rules thereunder, which required them to be covered by a sale license. It means only requirement of obtaining a sale license is exempted, but the requirement of a Registered Pharmacist is nowhere exempted. This amendment will not only violate Drugs and Cosmetics Act and Pharmacy Act but will also violate Article 16, Article 21 and Article 47 of the Indian Constitution. National Health Policy 2017 has suggested inclusion of pharmacists also for developing mid-level practitioners for rural areas i.e. Community Health Officers. Health Ministry issued necessary orders for nurses and Aayush doctors only, despite the fact that pharmacists are more competent than other categories as mentioned in National Health Policy, 2017. However, despite such regulations Government is again not considering the noble profession of the pharmacists and their right to practice their profession for earning their livelihood.

As per the resource information medicines contains toxic components and if these products are handled by non-professionals, it could lead to misuse of drugs. Various pharmaceutical associations and pharmacists have opposed this decision because it allows the unqualified to supersede the qualified and will render lakhs of Qualified Registered Pharmacists jobless in the country.

Conclusion

Recent amendment in schedule K of the Drugs and Cosmetics Act has raised concern for officials of Indian Pharmaceutical Association since such amendment can lead to compounding of medicines in the hands of the nonprofessionals which can become a major contributor of drugs misuse.

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1 https://cdsco.gov.in/opencms/opencms/system/modules/CDSCO.WEB/elements/download_file_division.jsp?num_id=NTE5OA==

NPPA exempts price capping for Sun Pharma's anti-cancer drug

The National Pharmaceutical Pricing Authority (NPPA), an executive body of government, has been formed to fix prices and notify changes in prices of bulk drugs and formulations, monitor the prices of non-scheduled drugs and formulations and supervise the implementation of the provisions of the Drugs (Price Control) Order (DPCO). The NPPA, on November 08, 2019, exempted 'ready to use infusion bags of anticancer drug Gemcitabine Hydrochloride Injection 10mg/ml (ready to use infusion bags 1200mg/120ml, 1400mg/140ml & 1600mg/160ml)' from price capping for a period of five years from the date of the commencement of its commercial production in the country as prescribed under the provisions of para 32(ii) of DPCO, 2019[1].

Para 32(ii) of DPCO, 2013 says that, *a manufacturer producing a new drug in the country by a new process developed through indigenous Research and Development and patented under the Indian Patent Act, 1970 (39 of 1970) (process patent) shall be exempted for price capping for a period of five years from the date of the commencement of its commercial production in the country.*

The ready to use infusion bag has been developed and manufactured by Sun Pharmaceuticals Industries Limited, which was duly approved by the office of Central Drugs Standard Control Organization (CDSCO), the drug regulatory authority of India, as 'new drug' under Rule 122(E) of the Drugs and Cosmetics Act and Rules thereunder, and patented (Patent No. 296771) in year 2018 by the Indian Patent office (IPO) under the Patents Act, 1970.

The DPCO (amendment), 2019[2] brings all the new drugs under exemption from price control for five years from their commercial marketing in India, whether the said new drug is being developed and produced by a manufacturer indigenously or outside India, and which are patented under the Indian Patent Act, 1970. Before this amendment only those new drugs were exempted from price capping which were patented in India (product patent) and were developed through indigenous research & development. Moreover, the amendment has also kept orphan drugs (drugs for treating orphan/rare diseases) outside the price control for the first time.

Note – The exemption from price control decision for 'Gemcitabine Ready to use Infusion bag' by NPPA is probably the first decision to implement *DPCO (amendment), 2019* taken after an application of exemption was made by the Sun Pharmaceuticals Industries Limited.

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1 http://www.nppaindia.nic.in/wp-content/uploads/2019/11/5-Exemption.pdf

2 https://pharmaceuticals.gov.in/sites/default/files/Gazette%20Notification_DPCO.pdf

USFDA Pharma Highlights November 2019

This segment discusses the recent drug approvals from the United State Food and Drug Administration (USFDA). The write-ups cover approval of a new drug for the treatment of serious conditions such as rare blood disorders, drugs to treat heart conditions etc. and the recall of substandard drugs. The USFDA is one of the strict regulatory bodies globally which takes care of health of the public by assuring the safety and effectiveness of human drugs, medical devices and other products used and approved in United States.

1. FDA approves first therapy to treat patients with rare blood disorder

On November 08, 2019, the USFDA granted approval to Reblozyl (luspatercept–aamt) for the treatment of anemia (lack of red blood cells) in adult patients with beta thalassemia who require regular red blood cell (RBC) transfusions. Beta thalassemia, also known as "Cooley's anemia," is an inherited blood disorder that reduces the hemoglobin production, which carries oxygen to cells throughout the body. The management of this condition requires supportive treatment like lifelong regimens of chronic blood transfusions, but which has the risk of iron overload resulting in increased risk of developing abnormal blood clots. The approval of Reblozyl was supported by the results of efficacy trial conducted on 336 patients with beta thalassemia who required RBC transfusions, of which 112 received a placebo. Twenty-one percent of the patients who received Reblozyl achieved at least a 33% reduction in transfusions compared to 4.5% of the patients who received a placebo. The FDA granted approval of Reblozyl to Celegene Corporation. Reblozyl also received Fast Track designation and Orphan Drug designation from USFDA[1].

2. FDA approves new Antibiotic drug to treat complicated urinary tract infections (cUTI)

On November 14, 2019, the USFDA approved Fetroja (cefiderocol), an antibacterial drug for treatment of patients 18 years of age or older with complicated urinary tract infections (cUTI), including kidney infections caused by susceptible Gram-negative microorganisms, who have limited or no alternative treatment options. The approval of Fetroja is followed by safety and efficacy trial conducted on 448 patients with cUTIs. Of the patients who were administered Fetroja, 72.6% had resolution of symptoms and eradication of the bacteria approximately seven days after completing treatment, compared with 54.6% in patients who received an alternative antibiotic. The FDA granted the approval of Fetroja to Shionogi & Co. Ltd. Earlier, Fetroja has also received Qualified Infectious Disease Product (QIDP) designation given to the antibacterial and antifungal drug products intended to treat serious or life-threatening infections and it had also received priority review from USFDA[2].

3. FDA authorizes marketing of first next-generation sequencing test for detecting HIV-1 drug resistance mutations

On November 05, 2019, the USFDA authorized marketing of a test to detect human immunodeficiency virus (HIV) Type-1 drug resistance mutations using next generation sequencing (NGS) technology. The Sentosa SQ HIV Genotyping Assay is the first HIV drug resistance assay that uses NGS technology that the FDA has authorized for marketing in the U.S. When untreated, HIV infection can lead to acquired immunodeficiency syndrome (AIDS). It is transmitted through direct contact with HIV-infected bodily fluids such as blood, and the majority of HIV infections in the U.S. are from HIV-1. According to the CDC, there were more than 1 million Americans living with HIV in 2016. The current standard of care for patients with HIV-1 is antiretroviral therapy, also known as ART, the daily use of a combination of drugs to treat HIV by suppressing the virus. According to the National Institute of Health, it is a lifesaving treatment that can let patients with HIV lead long and healthy lives but it is not a cure[3].

1 https://www.fda.gov/news-events/press-announcements/fda-approves-first-therapy-treat-patients-rare-blood-disorder

2 https://www.fda.gov/news-events/press-announcements/fda-approves-new-antibacterial-drug-treat-complicated-urinary-tract-infections-part-on going-efforts

3 https://www.fda.gov/news-events/press-announcements/fda-authorizes-marketing-first-next-generation-sequencing-test-detecting-hiv-1-drug-resistance