



Drug Information Bulletin

Drug Information Centre (DIC)

Indian Pharmaceutical Association

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Editorial

The recent notification by Govt. of India directing all Pharmacy, Chemist and Druggist dispensing anti-tubercular medicines, shall notify respective tuberculosis patients along with details of medicines to local Public Health Authority, namely, District Health Officer or Chief Medical Officer of a District and Municipal Health Officer of urban local bodies in whatever way they are known; or their designated District Tuberculosis Officers.

Pharmacy, Chemist and Druggist, failing to notify may attract the provisions of sections 269 and 270 of the Indian Penal Code (45 of 1860), as the case may be, which are reproduced below: "269. Negligent act likely to spread infection of disease dangerous to life. - Whoever unlawfully or negligently does any act which is, and which he knows or has reason to believe to be, likely to spread the infection of any disease dangerous to life, shall be punished with imprisonment of either description for a term which may extend to six months, or with fine, or with both. 270. Malignant act likely to spread infection of disease dangerous to life. - Whoever maliciously does any act which is, and which he knows or has reason to believe to be, likely to spread the infection of any disease dangerous to life, shall be punished with imprisonment of either description for a term which may extend to two years, or with fine, or with both." This is an appropriate step to ensure proper tuberculosis diagnosis and its management in patients and their contacts and to reduce tuberculosis transmission and further to address the problems of emergence and spread of Drug Resistant-Tuberculosis, it is essential to collect complete information of all tuberculosis patients.

This direction is also applicable for Medical Practitioners and Medical Laboratories as notified vide F.No. Z-28015/2/2012-TB dtd. 16th March 2018 (available at: <http://www.cdsc.nic.in/writereaddata/management%20in%20patients.pdf>).

This is a golden opportunity for the pharmacists engaged in community pharmacy to establish them as one of the important health care provider.

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Schedule K of the Drug and Cosmetics Rule amended for improving access to ORS

As per the Drugs and Cosmetics Act drugs included need not require any licence for selling the same.

Oral Rehydration Salts: Composition of the formulation in terms of the amount in g, to be dissolved in sufficient water to produce 1000ml.

Composition-

Sodium Chloride	2.6
Dextrose (anhydrous) or	13.5
Dextrose mono-hydrate	14.85
Potassium Chloride	1.5
Sodium Citrate	2.9

This shall come into force on the 1st day of November 2018.

Clozapine Risk of agranulocytosis

Health Canada has requested that manufacturers of clozapine (Clozaril®) submit a report, in two years, of all data collected in relation to agranulocytosis with use of clozapine. Clozapine is indicated to treat symptoms of schizophrenia in adults when other drugs have not helped. Agranulocytosis is a known adverse drug reaction that can occur in association with clozapine use. For this reason, white blood cell levels are monitored periodically in patients treated with clozapine to make sure that they do not become too low. During routine safety review activities, concerns were raised about whether or not processes to monitor agranulocytosis were effective. Health Canada reviewed all of the available evidence related to the effectiveness of the white blood cell monitoring measures currently in place for clozapine. From 1991 to the time of the review, Health Canada has received 92 Canadian reports of low numbers of white blood cells in patients using clozapine. A review of these reports found that 11 of them were possibly linked to clozapine use. The review concluded that monitoring measures that are in place to detect low numbers of white blood cells are acceptable, however this risk should still be monitored. Therefore, Health Canada has asked that the manufacturers of clozapine submit a report, in two years, of all the data related to the risk of agranulocytosis with clozapine use.

Reference: Summary Safety Review, Health Canada, 9 March 2018 (www.hc-sc.gc.ca)

Ulipristal acetate Potential risk of liver injury

EMA's PRAC is currently reviewing the benefits and risks with ulipristal acetate (Esmya®), following reports of serious liver injury, including liver failure leading to transplantation. Ulipristal was authorized in the EU in 2012 for the treatment of moderate to severe symptoms of uterine fibroids. As a temporary measure while the review is ongoing, the PRAC has recommended regular liver monitoring for women taking ulipristal for uterine fibroids. All women taking ulipristal should have a liver function test at least once a month during treatment. If the test is abnormal (liver enzyme levels more than two times the upper limit of normal), the healthcare professional should stop treatment and closely monitor the patient. Liver tests should be repeated two to four weeks after stopping treatment.

The PRAC is also recommending that no new patients should be started on ulipristal and no patients who

have completed a course of treatment should start another one for the time being. A link between ulipristal and cases of serious liver injury is under review. An EU-wide review of ulipristal started in December 2017

following reports of serious liver injury in women using the medicine. The review is ongoing; however, temporary safety measures were considered necessary following receipt of the fifth case of Safety of Medicines hepatic failure (the fourth that required liver transplantation).

Reference: EMA, 9 February 2018 (www.ema.europa.eu)

Artemisia annua extract in grape seed oil Potential risk of harm to the liver

The Medicines and Medical Devices Safety Authority (Medsafe) has advised health-care professionals to consider liver toxicity as a possible adverse effect of Artemisia annua (Arthrem®). Artemisia annua is a natural dietary supplement used for maintaining and supporting joint health and mobility. The Centre for Adverse Reactions Monitoring (CARM) received 14 reports

of liver toxicity associated with the use of artemisia annua. Many of the reports included jaundice as a reaction. All of the patients stopped taking artemisia annua, and at the time of reporting most had already recovered or were improving.

Medsafe advises health-care professionals to advise patients/consumers experiencing liver problems and taking artemisia annua or other natural health products, to stop taking the product and contact their general practitioners.

Reference: Safety Information, Medsafe, 15 February 2018 (www.medsafe.govt.nz/)

USFDA allowed Fast Track review to ACE-083 for one type of muscular dystrophy

The FDA designates Acceleron Pharma's (XLRN - 0.2%) ACE-083 for Fast Track review for the treatment of facioscapulohumeral muscular dystrophy, a form of muscular dystrophy that affects the muscles of the face, scapula and upper arms. Fast Track status shortens the review clock to six months from the standard 10 months. Phase 2-stage ACE-083, based on a naturally occurring protein called follistatin, binds to (inhibits) certain proteins that negatively regulate muscle growth (activins and myostatin). It is claimed by the company representative that untreated muscles or other organs are unaffected thereby reducing the risk of unwanted systemic side effects.

For details:
<https://seekingalpha.com/news/3350828-accelerons-aceminus-083-fast-trackd-type-muscular-dystrophy>

South Korean pharma firms target rare diseases to enter US market

South Korean pharma companies are targeting the U.S. market with rare diseases. In 2017, six locally developed drugs received Orphan Drug Designation (ODD) by the FDA, while two more drugs – Oraxol and HM15136 -- received orphan drug designation this year.

Hanmi Pharmaceutical's Oraxol, a novel oral formulation commonly used during chemotherapy treatment, received ODD status for angiosarcoma on April 20.

The drug is an anticancer treatment that transformed injectable anticancer medicines into oral medications. Hanmi Pharmaceutical had licensed out the cure to Athenex, a U.S. biopharmaceutical company, in 2011. The company had also received ODD status for HM15136, a congenital hyperinsulinemia drug, in February.

Hanmi plans to enter phase 1 clinical trials for the HM15136, a drug that used Hanmi's Lapscovery technology, in the first half of this year. It is also developing Poziotinib, a drug candidate technology transferred to Spectrum, a U.S. biopharmaceutical firm, to treat non-small cell lung cancer, which is a rare disease.

Youngjin Pharmaceutical also received ODD status from the FDA recently for KL1333, a drug the company recently transferred technology to Neurovive, a Swedish pharmaceutical company.

Youngjin recently transferred exclusive rights for KL1333, a treatment for a mitochondrial genetic disease, to Neurovive except for Korea and Japan.

Medpacto, a subsidiary of Theregen ETEX, is undergoing phase 2 clinical trials for TEW-7197, an anticancer treatment with indications for myelodysplastic syndrome and liver cancer., after receiving ODD status.

Viomed has also received approval to conduct phase 2 clinical trials for VM202-ALS, a treatment for amyotrophic lateral sclerosis (Lou Gehrig's disease). Approximately 30,000 patients are suffering from the disease in America.

Winning an ODD status in the U.S. is noteworthy as it is also related to early market entry of a product.

The U.S. government is implementing the Orphan Drug Act and has expedited screening programs to encourage the development of rare disease treatments.

The ODD status provides specific benefits, including a seven-year period of market exclusivity after approval, as well as a tax reduction. Also, if the program receives ODD status, it minimizes the approval process for the drug and opens up possibilities for a huge licensing out agreement or even a merger and acquisition. "The U.S. gives ODD status much quicker than Korea. If a company manages to receive ODD status it has a high chance of also obtaining an orphan drug status in Korea," a domestic pharmaceutical official said. "Also, having

a new drug means that a company can get a big contract before long.”

Korean companies have stepped up efforts to receive ODD status over the years. FDA's designation of rare pharmaceuticals for domestic pharmaceutical companies was only one in 2006 but has since steadily increased to two in 2012, three in 2013, and six in 2017.

Ref.

<http://www.koreabiomed.com/news/articleView.html?idxno=3149>

India rejects U.S. request on price caps on medical devices: Sources

[India](#) has told the United States it won't abstain from capping prices for more [medical devices](#), regardless of pressure to rethink its stance after price controls on heart stents and knee implants spoiled the market for some U.S. firms, sources familiar with the matter said.

India's drug pricing authority is also pushing to bring three more devices used while treating heart ailments under the ambit of price controls as they are sometimes more expensive than the stent itself, showed a government letter reviewed by Reuters.

India's \$5 billion medical device market has provided rich fishing grounds for U.S.-based companies like Abbott Laboratories and Boston Scientific Corp, but the prospect of price caps being extended to more products sent shivers through their ranks.

During a meeting last month, Indian officials told USTR Assistant Trade Representative Mark Linscott that India had decided against making any such commitment, a trade ministry official told Reuters recently.

Price controls form part of Modi's broader agenda to improve India's dilapidated public health system and boost affordability of treatment.

Equating high trade margins on some medical devices with "illegal profiteering", the government last year capped prices of some high-end heart stents - small wire-mesh structures

compared to \$3,000 charged earlier.

During a visit to Britain last month, Modi himself extolled the price caps' success in making treatment much more affordable for Indians.

And India's National Pharmaceutical Pricing Authority (NPPA) has been pushing for more price controls.

The regulator wrote to the health ministry on Feb. 26, asking for three other devices used to treat heart ailments - cardiac balloons, catheters and guide-wire - to be added to a list of products eligible for price controls. In the letter, the NPPA described the prices charged for these products as "exorbitant", and said companies involved in bringing them to the market were enjoying high trade margins. "Because of these exorbitant prices of catheter and balloon, which are many times higher than the stent price itself, the objective of price capping of stents gets diluted," the NPPA said in its letter.

The NPPA also said intraocular lenses, which are used during eye surgery, should be brought under the list.

A senior health ministry official told Reuters that the NPPA's requests merited "consideration".

The medical device manufacturers argue that India's price control mechanism hurts innovation, profits and future investment, and the USTR described India's policy as "very troubling". Indian trade officials anticipate coming under more pressure from the United States. The USTR is currently reviewing India's eligibility under its Generalized System of Preferences (GSP), a programme that allows duty-free imports of certain goods. India was the largest GSP beneficiary at \$5.6 billion, the USTR said in April. Bilateral trade rose to \$115 billion in 2016, but the United States wants to reduce its \$31 billion deficit with India, and is pressing New Delhi to ease trade barriers.

Source:

<https://health.economictimes.indiatimes.com/news/medical-devices/india-rejects-u-s-request-on->

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