# 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

Oxytocin-an essential drug is used widely for inducing labour. But unfortunately it is being misused in several means. Dairy farmers used it to extract milk from cows and buffaloes. Not only this drug makes cows barren sooner but also lowers the lifespan of the animal, thus causing economic loss to the owner in the long run. This hormone drug is also used by many farmers to plump up vegetables like-pumkin and bottle-gourd. Medical experts point out that sustained use of the drug can cause hormone imbalance in humans and harms the reproductive system of animals, reducing their life span. Similarly, it was reported that minor girls were given repeated and unregulated shots of oxytocin injection to speed up their sexual maturation.

Moreover, consuming this hormone unknowingly through Milk, vegetables, which causes several dysfunctions in human body. It is very harmful for humans who unwittingly are made to consume this hormone. Humans face all the harmful effects of this drug. Children are most susceptible to its effects and it is known to have caused imbalanced hearing and weak eyesight. Common symptoms are exhaustion and loss of energy. Expecting mothers should avoid milk that may have been adulterated with oxytocin because:

- Their children are born with deformities and low resistance levels are bound to have an adverse effect on the child.
- Oxytocin increase the risk of Post-partum hemorrhage
- Individual women may be hypersensitive to oxytocin and it can inhibit breastfeeding
- Oxytocin seriously affects the growth of hormones especially in females because of which minor girls attain early puberty.

Govt. of India has taken several steps to curb this menace, through a notification vide no. 29 E dated 17.01.2014 and a recent circular dated 22.10.2014

1. The manufacturers of bulk oxytocin drug shall supply the active pharmaceutical drug only to the manufacturers licensed under the Drug and Cosmetics Rules, 1945 for manufacture of formulations of the said drugs
2. The formulations meant for veterinary use shall be sold to the veterinary hospitals only

It is felt that apart from strict implementation of regulation the following measures may be adopted-

- Generation of awareness amongst the farmers through the concerned departments.
- Generation of awareness amongst the traders through trade associations.
- Generation of awareness amongst the general public through NGOs.

***Dr. Subhash C. Mandal,***
*Editor*

## New Drus: Ledipasvir with Sofosbuvir

Approved indication: hepatitis C
Harvoni

90 mg/400 mg tablets
Australian Medicines Handbook section 5.5

Sofosbuvir (Aust Prescr 2014;37:177-8) is a nucleotide analogue antiviral drug that is used in combination with other drugs to treat chronic hepatitis C. As the effectiveness of regimens containing interferon can be limited by adverse effects, there is interest in studying other drugs to use in combination with sofosbuvir.

Ledipasvir is an antiviral drug aimed at a protein (NS5A) in the hepatitis C virus. As this protein is involved in viral replication, ledipasvir will reduce the amount of virus in infected patients. Ledipasvir is rapidly absorbed. As the solubility of ledipasvir is pH-dependent, antacids, proton pump inhibitors and $H_2$-receptor antagonists can decrease absorption. Ledipasvir is minimally metabolised with most of the dose being excreted unchanged in the faeces. The median half-life is 47 hours. No dose adjustment is required in patients with hepatic impairment.

The fixed-dose combination of ledipasvir and sofosbuvir has mainly been studied in patients with genotype 1 infection. Its approval is based on open-label clinical trials which assessed the virological response. A sustained virological response was defined as a viral RNA in the patient's serum below 25 IU/mL 12 weeks after the end of treatment. However, the World Health Organization has previously considered a sustained response to be the absence of viral RNA six months after the end of treatment.

In ION-1, 865 previously untreated patients were randomised to take the combination, with or without ribavirin, in either 12- or 24-week regimens. There was a sustained viral response in 97–99% of the patients. This response was achieved by 94–100% of the patients who had cirrhosis (16% of the trial participants).1

The ION-2 trial used the same four treatment regimens as ION-1, but studied 440 patients who had not responded to other treatments for genotype 1 infections. Approximately 20% of these patients had cirrhosis. Twelve weeks after completing 12 weeks of treatment, there was a virological response of 94–96%. In patients who were treated for 24 weeks a viral RNA below 25 IU/mL was achieved in 99%. The response rate was significantly lower in patients with cirrhosis who were treated for 12 weeks compared with 24 weeks (82–86% vs 100%).2

The ION-3 trial assessed the efficacy of a shorter treatment regimen in previously untreated patients without cirrhosis. It randomised 647 patients to take the combination of ledipasvir and sofosbuvir, with or without ribavirin, for eight weeks, or the combination alone for 12 weeks. There was a sustained virological response in 94% of the patients who took the combination for eight weeks (93% with ribavirin) compared with 95% who took it for 12 weeks.3 An eight-week regimen can therefore be considered in previously untreated patients without cirrhosis who have pre-treatment viral RNA concentrations below 6 million IU/mL.

ION-4 was an open-labelled study involving 335 patients who were infected with hepatitis C virus and HIV. Using a 12-week regimen, a sustained response against hepatitis C was achieved by 96% of the patients. Results were similar irrespective of the treatments used for HIV in the trial, and whether or not the patients had cirrhosis.4

Less than 1% of the patients treated with ledipasvir and sofosbuvir had to stop treatment because of adverse effects. Without ribavirin, the most frequent adverse events with the combination were fatigue, headache, nausea and insomnia. There are

no human data in pregnancy and lactation, but the combination had no effect on fetal development in animal studies.

Drug interactions can occur with one or both components of the combination, so it is best to check the product information before prescribing. Its efficacy could be reduced by inducers of P-glycoprotein such as rifampicin and St John's wort. There is a potentially fatal interaction with amiodarone. Other interactions include digoxin, antiepileptic drugs, and statins particularly rosuvastatin. There is no known interaction with oral contraception.

Resistance to ledipasvir can develop during treatment. This should be considered in patients who do not have a sustained virological response.

A once-daily, interferon-free treatment, which in most cases only needs to be taken for 12 weeks, that has very high efficacy is an advance. While further research is needed for other genotypes, the combination of ledipasvir and sofosbuvir is probably the treatment of choice for genotype 1 hepatitis C infection in 2015. However, until similar antiviral drugs arrive, cure comes with a high cost.5 The Pharmaceutical Benefits Advisory Committee estimates that the cost of treatment in Australia will exceed $3 billion over five years.6

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Ref: Aust Prescr 2015;38:217-25

## PIL on State Drug Controller's Powers Dismissed

The High Court on Friday dismissed a petition challenging the withdrawal of power given to the State Drug Controller to certify the drugs to be exported. Justice Anand Byrareddy dismissed the petition filed by the Karnataka Drugs and Pharmaceutical Manufacturers' Association. The Association had contended that the guidelines of the World Health Organisation had declared State Drugs Controllers as the sole competent authority for Certification of Pharmaceutical Products.

The counsel for the Association argued that the withdrawal of the power has caused severe hardship and is causing delay in process of certification, resulting in financial loss to the drugs manufacturers.

The power was withdrawn by the Central Drugs Standard Control Organisation from 2009.

The contentions of the Union Government is that the World Health Organisation had authorised only the

Drugs Controller General of India as the competent authority for certification of pharmaceutical products and State Drugs Controllers were authorised to issue certificate based on the report of Central Drugs Inspector.
The Union Government also denied that there was delay in certification of drugs.

Ref. The New Indian Express

## WHO checklist targets major causes of maternal and newborn deaths in health facilities

Worldwide, the majority of maternal and newborn deaths occur around the time of birth, typically within the first 24 hours after childbirth. Most of these deaths are preventable.
WHO's new "Safe Childbirth Checklist and Implementation Guide" targets the major causes of maternal and newborn complications and deaths, including post-partum haemorrhage, infection, obstructed labour, preeclampsia and birth asphyxia.
Of the more than 130 million births occurring each year, an estimated 303 000 result in the mother's death, 2.6 million in stillbirth, and another 2.7 million in a newborn death within the first 28 days of birth. The majority of these deaths occur in low-resource settings, often lacking skilled birth attendants.
"Far too many women and children are still dying in childbirth from preventable causes often linked to poor quality of care," says Dr Marie-Paule Kieny, WHO Assistant Director-General, Health Systems and Innovation. "The WHO Safe Childbirth Checklist will help health care workers follow the essential care standards for every birth."
The checklist, developed and tested in partnership with Ariadne Labs, a joint centre of Brigham and Women's Hospital and the Harvard T.H. Chan School of Public Health and supported by the Bill & Melinda Gates Foundation, synthesizes existing evidence-based WHO guidelines and recommendations into a single and practical bedside tool targeted at improving adherence to best practices, including adequate communication around the time of delivery.
For details: http://www.who.int/mediacentre/news/releases/2015/maternal-newborn-deaths/en/

## Presage licenses cancer drug from India's Piramal to accelerate development using its microinjector

Seattle's Presage Biosciences has in-licensed Phase I oral cancer drug voruciclib from India's Piramal Enterprises to test its intratumoral microinjection platform, which the company says can accelerate drug development. Microdosing typically refers to systematic doses less than 1/100th the amount of the traditional dose, which means that side effects are limited. Presage's CIVO microinjector concentrates the dose at the site of the tumor, significantly enhancing the utility of the approach, the Fierce 15 company says.

Ref. FierceLifeSci

## Forthcoming Event:

### 67th Indian Pharmaceutical Congress
18-21 December 2015

**Organized by:**
Indian Pharmaceutical Congress Association
**Host:**
Indian Hospital Pharmacists' Association
**Venue & Local Host:**
JSS University, Mysuru
For details:

http://www.ipcmys.com/index.html