Drug Information Bulletin

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Regulatory Affairs Division (RAD), IPA

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Content

Editorial

Regulatory Sciences and the profession of Regulatory Affairs is emerging as one of the most important discipline in the Pharmaceutical Profession.

A Pharmacy Graduate or Post Graduate in pharmacy may opt for different specializations like-Research, Manufacturing, Quality Control, Quality Assurance, Marketing etc. Generally they get exposure in the selected field only. A manufacturing Pharmacist generally gets opportunity to manufacture a single category, if not so fortunate to get exposure to all types of manufacturing. Similarly a QC Pharmacist gets hardly any exposure in other areas like -manufacturing, sales etc. But a Pharmacist opting for Regulatory Affairs requires handling of Manufacturing, Quality Control, Product Development, Clinical Trial, and Quality Assurance of medicines. He needs to handle not only Allopathic medicines, but also other systems like -Ayurvedic including Siddha, Unani and Homoeopathy also. A regulatory Pharmacist requires to be an expert on Blood Banks, Medical Devices, Cosmetics etc. as these are integral part of functioning under FDA. Being a regulatory personnel, a pharmacist needs to handle Import and export matters and thus must be an expert in this matter –requiring to be conversant with the regulatory mechanisms like-ICH, USFDA, EDQM, MCA, TGA, WHO certification etc. Regulatory personnel not only deal with Drugs and Cosmetics Acts, but also deal with other related laws like- IPR, Patenting, Copy Rights and Trade Marks, DPCO etc.. This is very important in case of introduction of a new product and even introduction of Generics in other countries. Therefore, RA covers a vast area in the pharmaceutical profession, providing immense opportunity of work. Additionally, there is tremendous scope for Regulatory personnel in Pharma Industry throughout the Globe.

Dr. Subhash C. Mandal
Editor

New Drug: Dienogest

Approved indication: endometriosis
Visanne (Bayer) 2 mg tablets Australian Medicines Handbook section 17.4
Endometriosis is a common condition, affecting up to 10% of women. It occurs when endometrial cells proliferate outside the uterus, for example on the ovaries or in the peritoneum. It is associated with symptoms such as chronic pelvic pain, and pain during menstruation and sexual intercourse. Drug treatments for endometriosis aim to suppress ovarian function and include androgens (e.g. danazol), gonadotropin-releasing hormone agonists (e.g. goserelin) and progestogens. Dienogest is a progestogen-only hormone preparation for the treatment of endometriosis. It works by suppressing oestradiol production and preventing the growth of the endometrium. Dienogest is already available in Australia in combination with an oestradiol in some oral contraceptive pills (Aust Prescr 2007;30:50-5, Aust Prescr 2015:38;6-11). In an open-label, dose-finding trial of 68 women, daily dienogest 2 mg or 4 mg significantly reduced the severity of endometriosis, scored by laproscopic examination at baseline and 24 weeks later. It also decreased rates of pain during sexual intercourse from 52% to around 6%. Rates of premenstrual pain, dysmenorrhoea and diffuse pelvic pain were also reduced. The trial concluded that dienogest 2 mg once a day was the lowest effective dose.1 (A 1 mg dose of dienogest was also included in the trial, but randomisation was stopped prematurely due to irregular bleeding in all four patients receiving this dose.) In a 12-week placebo-controlled trial involving 198 women, daily dienogest 2 mg significantly reduced pelvic pain compared with placebo on a 100-mm visual analogue scale (by 27.4 mm vs 15.1 mm).2 The clinical significance of this difference was unclear. In a 52-week open-label extension of this study, 87 women continued dienogest and 81 who had taken placebo started the drug. Treatment continued for up to 52 weeks. The mean pain score declined from 27.89 mm to 9.72 mm in previously treated patients, and from 40.73 mm to 13.49 mm in those who switched from placebo. At the end of treatment the mean score for all patients was 11.52 mm.3 However, approximately a quarter of the women still used analgesia for their symptoms. A group of 34 women were followed up for 24 weeks after treatment finished. Their mean pain score increased slightly to 14.56 mm.3 Dienogest has been compared to the gonadotropinreleasing hormone agonist leuprolide (leuprorelide) in an open-label non-inferiority study of 252 women. After 24 weeks of treatment, pelvic pain – assessed by a 100-mm visual analogue score – had reduced from 60.2 mm to 12.7 mm with daily dienogest 2 mg and from 57.9 mm to 11.9 mm with leuprorelide (3.75 mg by depot intramuscular injection every four weeks). The trial concluded that dienogest was non-inferior to leuprorelide.4 (A non-inferiority margin of 15 mm was pre-specified on a 100-mm visual analogue scale.) Similarly dienogest was found to be as effective as buserelin (given intranasally), another gonadotropinreleasing hormone agonist. However, dienogest was associated with more vaginal bleeding than the comparator.5 In a safety cohort of 727 women, the most frequently reported adverse effects with dienogest were headache (9%), acne (5.1%), nausea (4.2%), weight gain (3.6%), breast tenderness (3.3%), depressed mood (3.0%) and flatulence (3.0%). As severe depression has been reported with dienogest,4 patients with a history of

depression should be monitored closely. Changes in menstrual bleeding patterns were common in the trials, but did not usually lead to discontinuation. After 9–12 months, bleeding was normal in 22.8% of women but had stopped (28.2%), become infrequent (24.2%), frequent (2.7%), irregular (21.5%) or prolonged (4%) in others. Dienogest is contraindicated in undiagnosed vaginal bleeding and during pregnancy and lactation. Although ovulation is inhibited in most patients, dienogest is not a contraceptive and use of a nonhormonal method is recommended while taking dienogest. The menstrual cycle resumes within two months of stopping the drug. Dienogest should not be given to patients with an active thromboembolic disorder or a history of cardiovascular disease. The risk of cardiovascular events is associated with older age, hypertension and smoking. Diabetes and severe hepatic disease, a history of liver tumours or sex-hormone dependent malignancies are contraindications to dienogest. If cholestatic jaundice or pruritis develops, dienogest should be stopped. It was not clear from the trials if dienogest affects bone mineral density. If treatment is continued for longer than six months, consider monitoring bone mineral density. After oral administration, dienogest is rapidly absorbed with peak serum concentrations being reached after approximately 1.5 hours. It is completely metabolised, mainly by cytochrome P450 (CYP) 3A4, and metabolites are rapidly excreted in the urine and faeces. Inducers of CYP3A4, such as rifampicin or St John's wort, may decrease plasma concentrations of dienogest, whereas CYP3A4 inhibitors, such as fluoxetine, ketoconazole or erythromycin, may increase dienogest concentrations. Dienogest can be started on any day of the menstrual cycle. It should be taken every day without interruption. If a tablet is missed, the next one should be taken as soon as possible and dosing continued as normal the next day. As with the contraceptive pill, vomiting and diarrhoea can reduce the efficacy of dienogest. Dienogest reduces the pain associated with endometriosis and is comparable to gonadotropinreleasing hormone agonists. However, some women may still need analgesia for their pelvic pain.

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FDA approves 'female Viagra' with strong warning

The first drug to treat low sexual desire in women won approval from U.S. health regulators on Tuesday, but with a warning about potentially dangerous low blood pressure and fainting side effects, especially when taken with alcohol.

The U.S. Food and Drug Administration said the pink pill, to be sold under the brand name Addyi and made by privately held Sprout Pharmaceuticals, will only be available through certified and specially trained health care professionals and pharmacies due to its safety issues.

Addyi, whose chemical name is flibanserin, is designed for premenopausal women whose lack of sexual desire causes distress. The condition is formally known as hypoactive sexual desire disorder, or HSDD. The drug needs to be taken daily.

Addyi has been nicknamed the "female Viagra" even though it does not work like Pfizer Inc's blockbuster Viagra pill for men that in 1998 became the first approved drug for erectile dysfunction.

For Details:

http://www.reuters.com/article/2015/08/19/us-pink-viagra-fda-idUSKCN0QN2BH20150819

PCI urges Kerala govt to ensure implementation of Pharmacy Act in the state

Following the controversy over inspections at the retail medical shops by pharmacy inspectors in Kerala, the Pharmacy Council of India (PCI) has urged Kerala government lo look into the matter and ensure favorable situation for the State Pharmacy Council to perform its duties entrusted to it by the Pharmacy Act 1948.

Dr. B Suresh, president of the PCI informed Pharmabiz that the agitation by the All Kerala Chemists and Druggists Association (AKDCA) against the inspections of the pharmacy inspectors is quite disturbing and illegal. The traders should abstain from putting hindrance to the work of pharmacy inspectors who are doing legitimate duties. Dispensing of appropriate and genuine medicines by qualified and registered pharmacists is essential for the safety of patients and overall health of the people in the society. Pharmacy inspectors are appointed to ensure this safety through regulation of pharmacy practice, he said.

Referring to the inspections, the PCI president opined that the work done by the Kerala State Pharmacy Council in carrying out the inspection of pharmacies, medical stores, hospitals, clinics etc, and subsequent action for violation of the provisions of the Pharmacy Act, is appreciable and needs to be carried forward vigorously.

For details: Pharmabiz.com

Forthcoming Events:

75th FIP World Congress of Pharmacy and Pharmaceutical Sciences 2015

Düsseldorf, Germany • 29 September - 3 October 2015

Better practice – Science based, evidence driven

Registration for the FIP Congress in Düsseldorf

To register for the full congress click *here*.

To register for the Pharmacy Technicians Symposium only click *here*.

If you are entitled to the FIP member reduced fee you have already received an email with a personalised link to register.

67th Indian Pharmaceutical Association

Venue: JSS University, Mysuru

Dates: 19th -21st December 2015