Drug Information Bulletin

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Regulatory Affairs Division (RAD), IPA

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Content

Editorial

Indian market is flooded with Fixed Dose Combinations (FDCs). Several sources quoted different numbers ranging from 60,000 – 100000. Though there is handful of FDCs having advantage over single ingredient products, there is hardly any benefit of most of the FDCs. As per the experts this situation becomes more complicated due to unregulated approval of FDCs by some state licensing authorities. Sometimes back DCGI published a list of FDCs as irrational, but those are still available in the market as a result of some litigation. Again DCGI has given a direction to submit Safety and Efficacy data of the FDCs available in the market without approval from the DCGI with a deadline on 30th August 2013. After 2013 there were several exercise by the DCGI and ultimately they have banned about 344 irrational combination vide SO 705 (E) to 1048(E) dated 10.03.2016. Mainly FDCs of NSAIDs and FDCs of antibiotics are banned besides other therapeutic categories. This is a unique occasion that a huge number of drugs have been banned by the Indian regulators. Sources revealed that these moves make some of the pharmaceutical manufacturers in an uncomfortable position and they went to the court of law. However the Health activists who are fighting to eradicate irrational drugs/combinations since last few decades are quite satisfied and some of them expressed that they will continue their fight till all irrational drugs are withdrawn from the market. Some experts are hopeful that the way Pharmacovigilance Programme of India (PvPI) is working only evidenced based medicines will be available in the market in near future.

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Carbamazepine Risk of Stevens Johnson's Syndrome

The Central Drugs Standard Control Organisation (CDSCO) and the Signal Review Panel of the Pharmacovigilance Programme of India-Indian Pharmacopoeia (SRP-PvPI-IPC) have requested that all manufacturers of carbamazepine should include Stevens Johnson's Syndrome as an adverse reaction in the package inserts and on the official websites. Carbamazepine is used as an anticonvulsant used in patients with epilepsy and in patients with trigeminal neuralgia. In India, there are 122 reports of life threatening or fatal skin reactions (Stevens Johnson's Syndrome, Toxic Epidermal Necrolysis) that may have been caused by the use of carbamazepine formulations. Although Stevens Johnson's Syndrome is a known adverse effect of carbamazepine and is already included in some package inserts, the Subject Expert Committee (SEC) have recommended that all manufacturers should include the same information on this adverse effect. The CDSCO/PvPI have decided that it was necessary to revise the package insert to include screening of HLA-B* 1502 prior to initiating the carbamazepine treatment, as HLA-B* 1502 is a known factor for carbamazepine-induced Stevens Johnson's Syndrome. (See WHO Pharmaceuticals Newsletters No.1, 2013: Potential risk of serious skin reactions associated with the HLA-A* 3101 allele in United Kingdom)

Reference: Central Drugs Standard Control Organisation, February 2016 (www.cdsco.nic.in)

Pseudoephedrine containing over-thecounter products Assessment of potential risk of inflammation and ischemic colitis

Health Canada published findings from a safety review which concluded that there is very limited evidence of ischemic colitis with the occasional use of pseudoephedrine at recommended doses and duration, in the absence of other risk factors. Pseudoephedrine is a medicinal ingredient in over-the-counter products that is used to treat the blockage of nasal passages due to excess fluid or mucus (nasal congestion). Ischemic colitis is an inflammation and injury of the large intestine (colon) due to reduced blood flow. The review was triggered following a serious case of ischemic colitis published in the scientific literature. At the time of the review, no Canadian cases of ischemic colitis were reported with the use of pseudoephedrine. A review of international data from the WHO Global ICSR Database, VigiBase® identified 24 cases of ischemic colitis, seven of which involved the use of pseudoephedrine as a single ingredient. These 24 cases could not be assessed due to limited information provided. In the scientific and medical literature, there were nine cases of ischaemic colitis associated with use of pseudoephedrine. Six cases contained other risk factors, two were not assessable due to limited information and in one case, ischemic colitis was assessed to be probably caused by pseudoephedrine.

Reference: Summary Safety Review, Health Canada, 24 February 2016 (www.hc-sc.gc.ca)

Spironolactone and renin-angiotensin system drugs Risk of potentially fatal hyperkalaemia

The MHRA has reminded healthcare professionals that the concomitant use of spironolactone with angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blocker (ARB) is not recommended as routine treatment because of the risks of severe hyperkalaemia, particularly in patients with marked renal impairment.

Spironolactone is indicated for congestive heart failure. It is a competitive aldosterone antagonist that increases sodium excretion while Safety of Medicines reducing potassium loss at the distal renal tubule. Due to this mechanism of action hyperkalaemia can occur, particularly in patients with impaired renal function. ACEis are mainly indicated in patients with hypertension or heart failure. ARBs are also indicated in hypertension and some are also indicated in heart failure. Recognised adverse effects of ACEi and ARB include renal dysfunction and an increase in serum potassium. Risk factors for hyperkalaemia, such as renal insufficiency and diabetes mellitus, are more common in patients who require treatment with ACEi or ARB. Between January 1998 and December 2015, the MHRA has received 82 spontaneous reports of abnormal blood potassium in patients using spironolactone as well as an ACEi (n=63) or ARB (n=25), 70 of which describe hyperkalaemia. Three patients taking spironolactone and ACEi had a fatal outcome. The number of cases reported increased in the last two years. This could reflect an increase in co-administration of spironolactone and ACEi or ARB, or it could represent stimulated reporting due to increased awareness of the risks, following recommendations from an European review. The review concluded that combination use of ACEi and ARB (which both inhibit the reninangiotensin system) is not recommended because of an increased risk of hyperkalaemia, hypotension, and impaired renal function. Health-care professionals are reminded to:

- Use the lowest effective doses of spironolactone and ACEi or ARB if coadministration is considered essential
- Regularly monitor serum potassium levels and renal function
- Interrupt or discontinue treatment in the event of hyperkalaemia

Spironolactone should not be used in patients with severe renal impairment or preexisting hyperkalaemia. (See WHO Pharmaceuticals Newsletters No.2, 2014: New warnings regarding Aliskiren, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers in Canada)

Reference: Drug Safety Update, MHRA, Volume 9, issue 6: 2, February 2016 (www.gov.uk/mhra)

Vit.D3® (colecalciferol) Risk for patients with a peanut or soya allergy

Medsafe highlighted the safety concern of Vit.D3® and allergic reactions for patients with peanut or soya allergy. Vit.D3® is a prescription only colecalciferol containing product and now available in New Zealand. Colecalciferol is indicated for the prevention and treatment of vitamin D deficiency. Vit.D3® contains soya oil inside the capsule. Some people are allergic to soya oil and some people with peanut allergy also react to soya oil. This product should not be used by people who are allergic to peanut or soya.

Reference: Safety Information, Medsafe, 2 March 2016 (www.medsafe.govt.nz/)

Esomeprazole magnesium hydrate Risk of Rhabdomyolysis

The MHLW and PMDA have announced that the package insert for esomeprazole magnesium hydrate (Nexium®) will be revised to include risk of rhabdomyolysis as a clinically significant adverse reaction. Esomeprazole magnesium hydrate is used to treat: ulcers (gastric, duodenal , anastomotic); reflux esophagitis, and ZollingerEllison syndrome. It is also used to suppress the relapse of gastric or duodenal ulcers when prescribing non-steroid anti-inflammatory drugs (NSAIDs) or low-dose aspirin. In addition, it is indicated for the eradication of Helicobacter pylori, in combination with

antibiotics. The MHLW/PMDA stated that cases of rhabdomyolysis have been reported in patients treated with esomeprazole The package insert will be updated to include: Rhabdomyolysis: Rhabdomyolysis may occur. Patients should be carefully monitored. If symptoms including myalgia, feeling of weakness, increased creatinine kinase (creatine phosphokinase), or increased blood and urine myoglobin are observed, administration of this drug should be discontinued and appropriate measures should be adopted.

Reference: Revision of Precautions, MHLW/PMDA, 16 February 2016 (www.pmda.go.jp/english/)

Fighting Chinese onslaught: Government plans to set up bulk drugs manufacturing hubs

The government is planning to set up bulk drugs manufacturing hubs as part of strategy to reduce the country's dependence on Chinese inputs for its exports-intensive pharmaceuticals industry.

India meets about 85% of its bulk drugs' requirement with imports from China. The landed price of bulk drugs from China is 15-20% lower than the cost of producing them locally, a factor that has fanned imports. A senior official told ET the government is considering establishing three or four pharma parks for manufacturing active pharmaceutical ingredients (API). "Due to the China factor we need to strengthen our self-dependence on essential medicines... correspondence with the PMO (Prime Minister's Office) is going on," the official said, requesting anonymity.

Each manufacturing park is estimated to cost about Rs 200 crore, he said, adding that Andhra Pradesh and Telangana are interested in offering land for the purpose.

The government had launched a similar scheme in 2007 — called Petroleum, Chemicals and Petrochemical Investment Regions — with the aim of developing dedicated integrated chemical clusters in coastal states. Although the scheme proved to be a nonstarter, this time efforts are being made with rigour as the PMO has been keeping a keen watch on the matter.

"API imports from China are sometimes of poor quality and spurious, due to which formulation quality gets affected. To ensure quality ingredients, we must have our own manufacturing," said another official.

India imported APIs worth $3.9 billion in 2014-15, of which drugs worth $3.3 billion came from China. In 2004-05, API imports stood at $800 million. "If China snaps supply of APIs, then our national healthcare programmes will suffer. Also, China's dominance in the market can lead to price increases of many essential drugs," said Ajay Sahai, director general of FIEO.

However, the plan to set up API parks faces one major hurdle — clearance from the environment ministry since APIs are highly polluting.

NPPA shifts onus of implementing revised prices of medicines to chemists

After dilly-dallying on the issue for several years, the National Pharmaceutical Pricing Authority (NPPA), in all practical purposes, has shifted the onus of implementing the revised prices of medicines to the chemists, putting at rest the hassles of recall, re-labelling and reshipment of old stocks to the chemists by thousands of manufacturers vide notification dated April 13th 2016.

For details:
http://www.drugscontrol.org/news.asp?id=14041

Forthcoming Event

26th FAPA Congress 2016

Bangkok, Thailand 9-13 November 2016

"Integrating Asian Pharmacy Wisdom for Better Global Health."

Venue:

Bangkok International Trade and Exhibition Centre
88th Bangna - Trad Road,
Bangna, Bangkok 10260, Thailand
Tel.+66 2 749 3939
www.bitec.co.th

Registration

	Before 31 July 2016	After 31 July2016
Participant	USD 350	USD 400
Accompanying persons	USD 150	USD 200
Student	USD 150	USD 200

สำหรับคนไทย	ก่อนวันที่ 31 ก.ค. 2558	หลังวันที่ 31 ก.ค. 2558
ผู้เข้าประชุม	4,500 บาท	5,000 บาท
ผู้ติดตาม	2,500 บาท	3,000 บาท
นิสิต/นักศึกษา	2,500 บาท	3,000 บาท

http://www.fapa2016.com/15616273/details-of-payment

Abstracts

Abstract submission time line
FAPA 2016 Bangkok, 9-13 November 2016

Activities	Period
- Open abstract submission	1 January 2016
- Last day for abstract submission	15 June 2016
- Acceptance of submitted abstract	15 July 2016
- Oral and poster present day	10-13 November 2016