Newsletter of the Drug Control Authority, Malaysia

BERITA UBAT-UBATAN

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EVENT

1) *WHO NATIONAL REGULATORY AUTHORITY (NRA) ASSESSMENT ON VACCINES*

National Regulatory System: Assessment on the Status of Vaccines Indicators

The National Pharmaceutical Control Bureau (NPCB) was successfully assessed by the WHO on the 25th - 27th February 2014. The assessment was conducted by seven assessors headed by Mr. Lahourai Belgharbi from the WHO Headquarters.

The objectives of the assessment were:

- to assess the systems and functions of the NRA Malaysia using WHO NRA tool;
- to review the NRA documents including their laws, decrees, administrative orders, guidelines, etc;
- to validate and finalise institutional development plan (IDP); and
- to provide necessary recommendations to the NRA and Ministry of Health Malaysia.

The NPCB plans to begin implementation of Lot Release for Vaccines and the requirement for monitoring of cold chain for importation of vaccines at entry points or distributors warehouses by 1st July 2014 and subsequently, its full implementation by 1st January 2015.

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NEW DIRECTIVES

The following directives have been issued under Regulation 29 of the Control of Drugs and Cosmetics Regulations 1984 (Revised 2006) by the Senior Director of Pharmaceutical Services, YBhg. Dato' Eisah A. Rahman:

1. ***Directive 01/14 [Ruj: (7) dlm. BPFK/PPP/07/25]: Extending the Scope of Regulatory Control of Active Pharmaceutical Ingredients (APIs) for Generic Products that Contain Scheduled Poison (Phase II)***

Following the decision made by the Drug Control Authority (DCA) in its 271st Meeting on 16th December 2013, the directive was issued to extend the scope of mandatory control of APIs of generic products that contain Scheduled Poison starting with products in parenteral dosage forms. The regulatory control will commence in phases as listed below:

New application of generic products with Scheduled Poison:

Products in parenteral dosage forms	:	1st July 2014
Products in oral dosage forms	:	1st July 2016
Products in other dosage forms	:	1st July 2018

Registered products that contain Scheduled Poison:

Products in parenteral dosage forms with registration expiring	:	1st July 2015
Products in oral dosage forms with registration expiring	:	1st July 2017
Products in other dosage forms with registration expiring	:	1st July 2019

The procedure for control of APIs established by the NPCB is described in the Guideline on Regulatory Control of Active Pharmaceutical Ingredients (API) which can be obtained from NPCB's web portal www.bpfk.gov.my.

This directive will take effect from **10th January 2014.**

2. ***Directive 02/14 [Ruj: (90) dlm. BPFK/30/12/05/1 Bhg 3]: Requirement of Full Time Registered Pharmacist to Lead Production Unit of Manufacturing Premise that Involves Pharmaceutical, Radiopharmaceutical and Veterinary Products Registered with the Drug Control Authority (DCA)***

In accordance to the Pharmaceutical Inspection Co-operation Scheme (PIC/S) Guideline that has been used since 2002, the PIC/S Guideline PE 009-10, January 2013 states that persons responsible for production including the Head of Production Unit should be qualified and have suitable experience.

The Pharmacy Curriculum accredited by the Malaysian Qualifications Agency (MQA) and Pharmacy Board Malaysia does not differ much from the European Curriculum for Qualified Persons (QP) who are responsible to ensure that products manufactured for release meet the stipulated requirements and

specifications. The pharmacists' knowledge in formulation, pharmaceutical technology, drug interaction and side effects of drugs manufactured should be used in order to avoid risk of contamination during the manufacturing process and to ensure its safety, efficacy and quality.

This directive is to be implemented by manufacturers (including primary repackaging) of pharmaceutical products, radiopharmaceuticals and veterinary (Scheduled Poison) products registered with the Drug Control Authority (DCA) and will take effect from **1st July 2014.**

3. *Directive 03/14 [Ruj: (19) dlm. BPFK/PPP/07/25]: Restriction on Indication of all Oral Ketoconazole and Restriction on the Usage at Hospitals Only due to Risk of Hepatotoxicity Adverse Reaction*

A directive was issued following the decision made by the Drug Control Authority (DCA) in its 273rd meeting on 27th February 2014 in line with the suggestion of the Malaysian Adverse Drug Reactions Advisory Committee (MADRAC) in their 136th meeting (12th December 2013) to impose regulatory actions in accordance to other regulatory agencies in other countries.

This directive was issued in order to further restrict the usage of oral ketoconazole **to be used only in hospitals starting the effective date.**

Restriction of Indication on Package Insert of All Oral Ketoconazole Products Using the Information below:

[Brand Name] (ketoconazole) Tablets should be used only when other effective antifungal therapy is not available or tolerated and the potential benefits are considered to outweigh the potential risks.

[Brand Name] (ketoconazole) Tablets are indicated for the treatment of the following systemic fungi infections in patients who have failed or who are intolerant to other therapies: blastomycosis, coccidioidomycosis, histoplasmosis, chromomycosis and paracoccidioidomycosis.

[Brand Name] (ketoconazole) Tablets should not be used for fungal meningitis because it penetrates poorly into the cerebrospinal fluid.

The package insert update process must be done according to these dates:
New registration and products under evaluation: **Effective date**
Registered products: **Six (6) months from effective date**

The application for amendments of package inserts must be done through variation application.

This directive will take effect from **1st May 2014.**

4. *Directive 04/14 [Ref: (10) dlm. BPFK/PPP/07/25]: Restriction on Indication and Duration of Use for Products Containing Synthetic Salmon Calcitonin in the Form of Injections and IntraNasal Nasal Spray due to Risk of Cancer*

A directive was issued following the decision made by the Drug Control Authority (DCA) in its 273rd meeting on 27th February 2014 in line with the suggestion of the Malaysian Adverse Drug Reactions Advisory Committee (MADRAC) in their 137th meeting (20th February 2014) to impose regulatory actions

in accordance to other regulatory agencies in other countries. This is based on reports that found 0.7 - 2.4% risk of cancer due to prolonged usage (6 months - 5 years) of products containing synthetic salmon calcitonin which is statistically significant.

Therefore, the following instructions must be followed:

Restriction of Indication and Duration for Products Containing Synthetic Salmon Calcitonin

Injections

Prevention of acute bone loss due to sudden immobilisation such as in patients with recent osteoporotic fractures.
The duration of treatment should not be more than 4 weeks.

For the treatment of Paget's Disease, only in patients who do not respond to alternative treatments or for whom such treatments are not suitable, for example those with severe renal impairment.
The duration of treatment is limited to 3 months.

Treatment of hypercalcaemia of malignancy.

Nasal Spray

Prevention of osteoporosis: In acute bone loss due to sudden immobilisation such as in patients with recent osteoporotic fractures. Miacalcic® should be supplemented with adequate doses of calcium and Vitamin D, as needed by the individual patient, to prevent further bone loss.
The maximum duration of treatment is 3 months.

Paget's disease, only in patients who do not respond to alternative treatments or for whom such treatments are not suitable.
The duration of treatment is normally 3 months.

Algodystrophy or Sudeck's Disease (Neurodystrophic disorders) due to various causes and predisposing factors such as post-traumatic painful osteoporosis, reflex dystrophy, shoulder arm syndrome, causalgia and drug-induced neutrophic disorders.
The duration of treatment is up to 6 weeks.

The package insert should state on the **Dosage Information** that the duration of effective treatment must be optimised with the **lowest dose and at the shortest period.**

The package insert update process must be done according to these dates:
New registration and products under evaluation: **Effective date**
Registered products: **Six (6) months from effective date**

The application for amendments of package inserts must be done through variation application.

This directive will take effect from **1st May 2014.**

SUMMARY OF PRESS RELEASES

TRADITIONAL PRODUCTS / HEALTH SUPPLEMENTS

a) Caution on Using Unregistered Products Containing Scheduled Poison

i. Delima Raja Urat

The National Centre for Adverse Drug Reactions Monitoring, NPCB would like to remind the public not to buy or use the unregistered product sold as a Malay traditional medicine labelled as 'Delima Raja Urat'.

The product label claims that the product is to be used for muscle aches, joint aches, numbness, gout and lethargy. Sampling of the product was done after adverse reactions of urticaria, vasculitic rash and Addisonian crisis were reported and the results found that the product contains the scheduled poison, **dexamethasone.**

Dexamethasone is a potent corticosteroid and should only be used under medical supervision. Long term and unsupervised use of corticosteroids can cause serious adverse effects such as **Cushing Syndrome, increased blood glucose level, high blood pressure, glaucoma and bone disorders such as osteoporosis.**

The public is advised not to buy or consume products that are not registered with the DCA as their quality and safety are not known.

ii. Figure Up

The public is reminded not to use the unregistered product called 'Figure Up'. Following the press release by the Pharmaceutical Services Division on 8th November 2013, the National Centre for Adverse Drug Reactions Monitoring, NPCB still received adverse reaction reports due to this product. Among the reports received were serious adverse reactions of **seizures and duodenal ulcer bleeding** involving users aged 14 - 38 years old.

Sampling done by NPCB found that the product contains the scheduled poison, **sibutramine.** The use of scheduled poisons in health supplements is strictly prohibited. Sibutramine is used for the treatment of obesity. However, all products containing sibutramine have been recalled in Malaysia on 23rd December 2012 due to risk of adverse cardiovascular reaction. The adverse reactions included **increase in blood pressure and pulse rate, dryness of mouth and throat, vomiting, diarrhoea, dizziness, headache and sleep disturbances.**

Investigation revealed that the company named Biospecialty Food Trading is not a registered company with the Companies Commission of Malaysia (SSM) and the product is not registered with the DCA.

The public is reminded to immediately stop using this product and to beware of fake products that are sold on the internet. In addition, anyone who is in possession of this unregistered product is also advised to immediately stop selling, distributing or using it. The possession of this product is an offence under the Control of Drugs and Cosmetics Regulations 1984.

iii. 'Collagen Slim' and 'Beautiful Slim Body'

The NPCB has obtained information from the Therapeutic Goods Administration (TGA) which is the Regulatory Authority of Australia that the above mentioned products contain the scheduled poison, **sibutramine.** The content of sibutramine was also found to exceed the limit allowed. The products have been promoted and sold on the internet for beauty purposes and to reduce weight with the label claiming that it contains only natural contents.

Any person who is in possession of this product is advised to immediately cease selling, distributing or using it. The possession of this product is an offence under the Control of Drugs and Cosmetics Regulations 1984.

b) Cancellation of Registration of Traditional Products

i. Jingzhi Yinqiao Jiedu Tablet 260 mg

No.	Product Name (Registration Number)	Adulterant	Product Registration Holder	Manufacturer
1	Jingzhi Yinqiao Jiedu Tablet 260 mg (MAL06071213T)	Paracetamol	Bumari Sdn. Bhd., Pulau Pinang	Guang Dong Medi-health Pharmaceutical Co. Ltd., China.

The registration for the traditional product Jingzhi Yinqiao Jiedu Tablet 260 mg has been cancelled by the DCA following detection of the adulterant, **paracetamol** in the product.

Paracetamol was found in the traditional product registered with the indication to relieve fever, headache, sore throat, cough and cold.

Long term unsupervised and overdose usage of paracetamol can cause liver toxicity with symptoms such as nausea, vomiting, yellowish eyes and skin, dark coloured urine, stomach/abdominal pain and lethargy. Adverse reactions such as rashes, itchiness, dizziness, difficulty in breathing and swelling of face, lips, tongue and throat is also associated with persons allergic towards paracetamol.

Thus, those who are using these products are advised to stop using them immediately and to seek medical advice from healthcare professionals should they experience any discomfort or adverse effects.

COSMETICS

a) Caution on Using Cosmetic Products Containing Scheduled Poisons

The public is advised to avoid buying and using the following cosmetic products:

No	Name of Product	Notification Number	Heavy Metal Detected	Notification Holder	Manufacturer
1.	AS Beauty Night Cream	NOT101103172K	Mercury	ZMN Mahaka Enterprise	Penawar Industries Sdn. Bhd.
2.	AS Beauty Day Cream	NOT101103272K	Mercury	ZMN Mahaka Enterprise	Penawar Industries Sdn. Bhd.
3.	Golden Horse Herbal Milk Lotion – GH507	NOT120905457K	Mercury	Chee Sing (Labuan) Sdn. Bhd.	Chin San Chemical Works, Taiwan
4.	Golden Horse Bio Complex Cream – GH903-2	NOT120905465K	Mercury	Chee Sing (Labuan) Sdn. Bhd.	Chin San Chemical Works, Taiwan

The notification of the above cosmetics have been cancelled following the detection of the heavy metal, **mercury.**

Mercury is prohibited in cosmetic products due to its potential hazard on human health. Mercury compounds are readily absorbed through the skin on topical application and tend to accumulate in the body. Direct and prolonged exposure to mercury can cause damage to the brain, nervous system and kidneys. Usage of products containing mercury can also result in skin rashes, irritation and other changes to the skin.

Any person who is in possession of this product is advised to immediately cease selling, distributing or using it. The possession of this product is an offence under the Control of Drugs and Cosmetics Regulations 1984.

CONTACTS & MAP

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CENTRES	EXTENSION NO.
Centre for Product Registration – Deputy Director	5487
• New Drug Section	5522
• Generic Medicine Section	5490
• Biotechnology Section	8423
• Complementary Medicine Section	8415
• Active Pharmaceutical Ingredient Section	8424
• Veterinary Medicine Section	5500
• Regulatory Coordination Section	5502
Centre for Post-Registration of Products – Deputy Director	5538
• Surveillance and Product Complaints Section	5552
• Pharmacovigilance Section	5543
• Cosmetic Section	5532
Centre for Investigational New Product – Deputy Director	5581
Investigational Product Evaluation Section	8406
• Investigational Product Safety Monitoring Section	8408
• GCP Compliance Section	8401
• GLP Compliance Section	8404
Centre for Compliance and Licensing – Deputy Director	5564
• GMP Section	5566
• Quality, Certification, Licensing and GDP Section	5569
Centre for Organisational Development – Deputy Director	5553
• Information, Communication & Technology Section	5555
• Helpdesk	5561, 5562, 5563
Centre for Quality Control – Deputy Director	5429
• Bio-Pharmaceutical Testing Section	8457
• Research and Development Section	8448
• Pharmaceutical Chemistry Testing Section	5463, 5456, 5450
• Laboratory Services Section	5431
• Natural Product Testing Section	5471
• Reference Standard Section	5468
Centre for Administration	8458

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