Newsletter of the Drug Control Authority, Malaysia

BERITA UBAT-UBATAN

VOLUME 59 • No. 37 • ISSN 0128-0627

August 2013

EVENT

National Regulatory Conference (NRC) 2013

The NPCB has successfully organised the National Regulatory Conference (NRC) 2013 on 7 – 9 May 2013 at Istana Hotel, Kuala Lumpur.

The conference, with the theme *Regulatory Innovation towards Transformation*, received an overwhelming response with the presence of nearly 500 local and foreign participants. The objectives of NRC 2013 were as follows:

- To update on developments and challenges in the evolving regulatory landscape
- To strengthen collaboration and understanding among stakeholders
- To enhance competitiveness through regulatory transformation

In conjunction with the conference, an official dinner was held on 7 May 2013. The Industry Excellence Awards were presented during the dinner to local manufacturers of pharmaceutical products, traditional products / health supplements as well as cosmetics.

IN THIS ISSUE

Materials published in this newsletter may not be reproduced without permission or used for any form of advertising, sales or publicity.

DCA EDITORIAL TEAM

ADVISOR:

Datuk Dr. Noor Hisham bin Abdullah
Dato' Eisah A. Rahman

CHIEF EDITOR:

Tan Ann Ling

EDITORS:

Dr. Tajuddin Akasah, Siti Aida Abdullah, Sulaiman Haji Ahmad, Sameerah Shaikh Abd. Rahman, Dr. Kamaruzaman Salleh, Noorizam Ibrahim, Nurulfajar Mohd Jamid, Wayne Wong Guan Wei

NEW DIRECTIVES

Several directives under Regulation 29 of the Control of Drugs and Cosmetics Regulations 1984 (Revised 2006) were issued by the Senior Director of Pharmaceutical Services, Dato' Eisah A. Rahman following decisions made in the 263rd DCA Meeting on 29 April 2013.

1. *Directive 04/2013: New Procedure for the Change of Product Registration Holder [Ref: (3) dlm.BPFK/PPP/07/25]*

The Drug Control Authority (DCA) has revised the procedure for the change of product registration holder (Reference: Drug Registration Guidance Document (DRGD), 16.3 Change of Product Registration Holder).

Implementation

- Application for the change of product registration holder must be submitted by the existing registration holder.
- Product registration can be canceled by the DCA if the product owner terminates the appointment of the existing registration holder by submitting the Letter of Termination (LOT).
- Product owner must submit new product registration application if they wish to continue the registration of the same product (through a different registration holder).

The new procedure for the application for change of product registration holder is available on NPCB's website. The directive above is effective from **3 April 2013** onwards.

2. *Directive 05/2013: To Limit the Use of Products Containing Trimetazidine and Strengthen Warnings Regarding the Risk of Parkinsonian Symptoms (Adverse Reaction) on the Package Inserts of All Products Containing Trimetazidine [Ref: (4) dlm.BPFK/PPP/07/25]*

According to the directive above (effective from **1 May 2013** onwards), the indication of products containing trimetazidine shall be amended as follows:

a) Indication of trimetazidine for treatment of pectoris angina is limited to second-line add on therapy; and the indication in otology and ophthalmology field shall be removed.

b) Permitted indication: **Trimetazidine is indicated in adults as add-on therapy for the symptomatic treatment of patients with stable angina pectoris who are inadequately controlled by or intolerant to first-line antianginal therapies.**

All the package inserts of products containing trimetazidine shall include:

a) Dosage and method of administration:

For products containing trimetazidine 20mg:

The dose is one tablet of 20mg of trimetazidine three times a day during meals.
The benefit of the treatment should be assessed after three months and trimetazidine should be discontinued if there is no treatment response.

Special populations

Patients with renal impairment

In patients with moderate renal impairment (creatinine clearance, CrCl [30-60] ml/min), the recommended dose is 1 tablet of 20mg twice daily, i.e., one in the morning and one in the evening during meals.

Elderly patients

Elderly patients may have increased trimetazidine exposure due to age-related decrease in renal function. In patients with moderate renal impairment (CrCl [30-60] ml/min), the recommended dose is 1 tablet of 20mg twice daily, i.e., one in the morning and one in the evening during meals. Dose titration in elderly patients should be exercised with caution.

For products containing trimetazidine 35mg:

The dose is one tablet of 35mg of trimetazidine twice daily during meals.
The benefit of the treatment should be assessed after three months and trimetadizine should be discontinued if there is no treatment response.

Special populations

Patients with renal impairment

In patients with moderate renal impairment (creatinine clearance, CrCl [30-60] ml/min), the recommended dose is 1 tablet of 35mg in the morning during breakfast.

Elderly patients

Elderly patients may have increased trimetazidine exposure due to age-related decrease in renal function. In patients with moderate renal impairment (CrCl [30-60] ml/min), the recommended dose is 1 tablet of 35mg in the morning during breakfast. Dose titration in elderly patients should be exercised with caution.

b) Contraindications:

- Parkinson disease, parkinsonian symptoms, tremors, restless leg syndrome and other related movement disorders
- Severe renal impairment (CrCl < 30 ml/min)

c) Special warnings and precautions for use:

Trimetazidine can cause or worsen parkinsonian symptoms (tremor, akinesia, hypertonia), which should be regularly investigated, especially in elderly patients. In doubtful cases, patients should be referred to a neurologist for appropriate investigations.

The occurance of movement disorders such as parkinsonian symptoms, restless leg syndrome, tremors, gait instability should lead to definitive withdrawal of trimetazidine.

These cases have a low incidence and are usually reversible after treatment discontinuation. The majority of the patients recovered within 4 months after trimetazidine withdrawal. If parkinsonian symptoms persist more than 4 months after drug discontinuation, a neurologist opinion should be sought.

Falls may occur, related to gait instability or hypotension, in particular in patients taking antihypertensive treatment.

Caution should be exercised when prescribing trimetazidine to patients in whom an increased exposure is expected:
- moderate renal impairment,
- elderly patients older than 75 years old

d) Side effects

Nervous system disorders: Frequency not known:
Parkinson symptoms (tremor, akinesia, hypertonia), gait instability, restless leg syndrome, other related movement disorders, usually reversible after treatment discontinuation

ANNOUNCEMENT

1. Food-Drug Interface (FDI) Products That Require Registration [Ref: Bil (4) dlm. BPFK/PPP/01/03 Jld 3]

The Food-Drug Interface (FDI) Committee Meeting between NPCB and Food Safety and Quality Division (BKKM) has decided in 2013 that all FDI products containing one of the following active ingredients or combination (taken orally in any percentage) are classified as drug and must be registered with the DCA:

Red Yeast Rice, Natto extract, Placenta, Bile, Glucosamine, Hyaluronic Acid, Glutathione, Gamma-Amino Butyric Acid (GABA), Resveratrol

Hence, all companies involved in the manufacturing, marketing or importing of such products that are yet to be registered should submit their registration application through the NPCB online registration system.

FDI products that were previously classified as non-drug have to be reclassified to ensure the product category. A period of 6 months will be given to the companies to finish up existing stocks in the market.

2. Banning the Use of Methylene Chloride or Dichloromethane (DCM) in the Manufacturing Process of Local Products [Ref: (2) dlm.BPFK/30/06/2 Bhgn 2]

As stated in the DRGD, 8.2 List of Prohibited and Restricted Excipients, the use of Methylene Chloride or Dichloromethane (DCM) in the manufacturing process of local products has been prohibited. Therefore, local manufacturers shall ensure that their manufacturing process is free from such solution. The implementation will be as follows:

Product Registration Status	Implementation
New application	Implemented immediately. Application for the registration of product containing these substances will not be entertained.
Under screening stage	Implemented immediately. Application for the registration of product containing these substances will be rejected.
Under evaluation process	Registration holder is required to replace Methylene Chloride or DCM with alternative substance or solution such as non-halogenated solvents and water-based solutions for safety purposes. Failure to meet the above requirement may result in rejection of registration application.
Registered	Registration holder will be given until 31 December 2014 to comply with the requirement by submitting variation application (before product registration renewal).

SUMMARY OF PRESS RELEASES

1. *The Acceptance of Malaysia as Non-Organisation for Economic Cooperation And Development (OECD) Member Adhering to the Mutual Acceptance of Data (MAD) in the Assessment of Chemicals on Good Laboratory Practice (GLP)*

Effective from March 2013, Malaysia is officially a Non-OECD Member adhering to MAD system on GLP. With the MAD system, the data generated in the testing of chemicals in an OECD Member and non-member countries adhering to MAD system in accordance with OECD Principles of GLP shall be accepted in other Member Countries for purposes of assessment and other uses relating to the protection of mankind and the environment.

The acceptance of Malaysia as a Non-OECD Member adhering to MAD system on GLP will benefit Malaysia in many ways including:

a. International acceptance of non-clinical data developed in Malaysia
b. Trade facilitation by reducing marketing time for local manufactured products marketed internationally
c. Exemption of non-clinical research being repeated in OECD countries
d. Saving costs for development of product
e. Overcoming existing technical barriers
f. Increasing local and foreign investments in research and development of products involving pharmaceutical, biomedical, biotechnology and biochemical in Malaysia.
g. Making Malaysia a research and development (R&D) hub for non-clinical research.

2. *Cosmetic Products Containing Scheduled Poisons*

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

No.	Product Name	Notification Number	Scheduled Poison Detected	Name of Product Holder	Name of Manufacturer
1.	Cellnex Anti-Sensitive Essence Treatment	NOT120905219K	Betamethasone	Europe Cosmeceutical Industries Sdn. Bhd.	Centre De Recherches Biocosmetiques S.A, Switzerland
2.	Natural 99 Night Cream	NOT120300526K	Mercury	Auraqu Enterprise	CV Raja Kosmetik, Indonesia
3.	Natural 99 Day Cream	NOT120300524K	Mercury	Auraqu Enterprise	CV Raja Kosmetik, Indonesia
4.	SF Beauty Night Cream (Facial)	NOT120602462K	Mercury	SF Infinity Resources	Yamni Industries Sdn. Bhd.
5.	SF Beauty Day Cream (Facial)	NOT120602461K	Mercury	SF Infinity Resources	Yamni Industries Sdn. Bhd.
6.	Aveana Night Revival Cream	NOT110404581K	Tretinoin	Owi Lab (M) Sdn. Bhd.	Owi Lab (M) Sdn. Bhd.
7.	Blemished Skin Ampoules	NOT110204305K	Azelaic Acid	Noble Aspect Sdn. Bhd.	Noble Aspect Sdn. Bhd.
8.	Golden Horse B&W Cream – GH902-1	NOT120905460K	Mercury	Chee Sing (Labuan) Sdn. Bhd.	Chin San Chemical Works, Taiwan

The cosmetic products mentioned above have been tested and were found to contain scheduled poisons betamethasone, mercury, tretinoin and azelaic acid. The usage of such substances in cosmetic products is strictly prohibited. All these products are no longer allowed to be sold in Malaysia. The companies responsible for placing these products in the market have been instructed to immediately halt the sale and supplies of the product mentioned and remove all physical stocks from the market within 72 hours.

Betamethasone is a type of corticosteroid that is usually used in the treatment of skin conditions such as eczema, seborrhoeic dermatitis, psoriasis and allergic skin conditions. Preparations containing betamethasone can only be supplied by medical doctors and pharmacists. Prolonged unsupervised use of betamethasone on facial skin can cause thinning and skin can be easily irritated, stretch marks, acne, changes in skin pigmentation and increase the risk of systemic absorption that may cause undesirable effects.

Mercury is not allowed in cosmetic products as it can cause harm to human health. Exposure to mercury can cause damage to the kidneys and the nervous system. It may also interfere with the brain development in foetuses and very young children. Furthermore, using products containing mercury can also result in skin rashes, irritation, and other changes to the skin.

Products containing azelaic acid is usually used for acne treatment and rosacea. The unsupervised use of preparations containing azelaic acid can cause burning, stinging and reddening of the skin.

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

3. *Response to Newspaper Article Regarding Product That Contains Mercury*

• CHINA PRESS (9 MAY 2013)

"TONG REN TANG JIAN TI WU BU WAN CONTAINS HIGH LEVEL OF MERCURY"

According to the local newspaper article stated above, the Department of Health Hong Kong has ordered for the recall of Jian Ti Wu Bu Wan after the product was found to contain high levels of mercury. However, the product recall only involves one product batch (1033946). Jian Ti Wu Bu Wan is not registered with the Drug Control Authority (DCA), Ministry of Health Malaysia. Therefore, the public are advised not to buy or take this product as its quality and safety is not ensured. Those who are taking this product are advised to stop using it immediately.

4. *Response to Newspaper Article Regarding Cosmetic Products That Contain Banned Substances*

• BERITA HARIAN (26 APRIL 2013)

"NASIHAT USAH GUNA PRODUK KOSMETIK TABITA"

The local newspaper above has quoted a statement issued by the Health Sciences Authority (HSA), Singapore regarding Tabita cosmetic products containing banned substances. Tabita Skincare Smooth Lotion, Tabita Skincare Daily Cream and Tabita Skincare Nightly Cream were tested and found to contain hydroquinone, tretinoin, salicylic acid and mercury.

The statement was released following an adverse events received by the HSA in which a patient had developed rashes on the face and neck as well as other reports suggesting rapid whitening of the skin after using Tabita products. These products are not marketed in Singapore but are currently sold from oversea sources through internet. Tabita products are not notified with the Ministry of Health (MOH) Malaysia. Therefore, these products are not allowed in the market. Consumers who have purchased or are using Tabita products are advised to stop using and discard the products immediately as they may cause deleterious effects. Consumers are also reminded to be more careful while making cosmetic product purchases online. Cosmetic products that are not notified may contain undeclared or banned substances which can cause serious harm.

**Source: Health Sciences Authority (HSA) Singapore*

CONTACTS & MAP

National Pharmaceutical Control Bureau + 603 - 7883 5400

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
• Variation Section	5588
• 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 Diretor	5564
• GMP Section	5566
• Quality, Certification, Licensing and GDP Section	5569
Centre for Organisational Development – Deputy Director	5553
• Information, Communication & Technology Section	8577
• Helpdesk	5561
Centre for Quality Control – Deputy Director	5429
• Bio-Pharmaceutical Testing Section	8457
• Research and Development Section	8448
• Pharmaceutical Chemistry Testing Section	5462
• Laboratory Services Section	5431
• Natural Product Testing Section	5471
• Reference Standard Section	5468
Centre for Administration	8458

National Pharmaceutical Control Bureau (NPCB), Ministry Of Health Malaysia
Biro Pengawalan Farmaseutikal Kebangsaan (BPFK), Kementerian Kesihatan Malaysia

Lot 36, Jalan Universiti,
46200 Petaling Jaya,
Selangor Darul Ehsan,
MALAYSIA

Tel: + 603 - 7883 5400
Fax: + 603 - 7956 2924

Website:

http://www.bpfk.gov.my
This newsletter is also available on our website