Drug Regulatory Authority Newsletter

Issue 1 2016

Towards promoting consumers' confidence in medicinal products

RECENT EVENTS

Blood and Blood Product Regulation 2015 has been approved for implementation

DRA is working towards instituting quality system by bringing out a quality manual. It is expected to comply with ISO 9001:2015 standard.

Message from the DrugController

The Drug Regulatory Authority with its mandate to protect consumers' health has for the first time brought this Annual Bulletin as the Drug Regulatory Authority news letter.

As a part of the information service the Post Marketing Control Division (PMCD) has brought out this news letter to share information to the general consumers, stakeholders and the clients.

This news letter in its first attempt gives the background and the history of Drug Regulation in Bhutan and its importance. It also provides medicine safety updates for the consumers and health professionals, highlighting few notifications to create public awareness on the health risk related to complementary herbal products.

The news letter also provide brief information on the medicines registered so far, the registered numbers of retail pharmacies in the country, the inspection conducted so far for regulatory compliance and the Adverse Drug Reaction (ADR) reported so far in the country. The detailed information on its establishment, governance and challenges of Drug Regulatory Authority service that are available on the website www.dra.gov.bt has not been addressed in the news letter.

It is hoped that this first news letter will be useful to the consumers and healthcare professional to get information and thereby have confidence in the service provided by Drug Regulatory Authority.

I am thankful to all the Drug Regulatory Authority staff who are involved in bringing out this first annual news letter and we welcome any feedback for our services for continual improvement.

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CONTENT

Signing of Annual Performance Agreement(APA) 2015-2016 between Drug Controller and Chairman, Bhutan Medicines Board(Hon'ble Minister of Health)

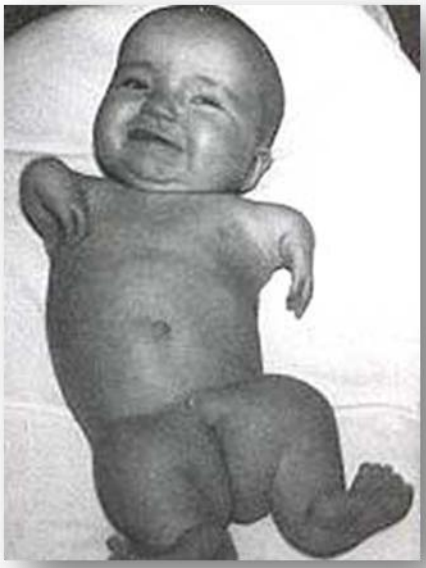
Drug Technical Advisory Committee: Constituted under the Medicines Act to advise Medicines Board and DRA on Technical matters.

Special feature

History of Drug Regulation and its influence in Bhutan health system

Background on global scenario of Drug Regulation

According to an article *Drug Regulation: History Present and Future by Lembit Rägo, and Budiono Santoso*, the modern medicines regulation started in the 19th century and started to flourish after the second World War. Adverse events such as death of the people due to use of medicines poisoning *(Eg when diethylene glycol was used as solvent in sulfanilamide elixir without any safety testing)* have catalysed the development of medicines regulation world wide. The second catastrophe that influenced the development of medicines regulation was thalidomide disaster. Thalidomide was a sedative and hypnotic medicine that first went on sale in Western Germany in 1956. Between 1958 and 1960 it was introduced in 46 different countries worldwide resulting in an estimated 10,000 babies being born with phocomelia(sealed limbs) and other deformities. As a result, the whole regulatory system was reshaped in the UK and also introduced voluntary adverse drug reaction reporting system (Yellow Card Scheme) in 1964.



Eg; Thalidomide used for treatment of morning sickness in pregnant woman has resulted into disaster (1956)

In US, new product registration requirement was initiated requiring compliance with current Good Manufacturing Practices(GMP) in 1962. The need for wider harmonization was discussed during the International Conference of Drug Regulatory Authorities (ICDRA – organized by WHO every second year) in 1989.

In Asia, particularly in India, medicines regulation appears to have begun from 1940s after the enactment of Drugs And Cosmetics Act 1940 and Regulation 1945, and for Thailand, the Drug Act commenced from 1967.

Country Developments on Drug Regulation

Bhutan introduced Essential Drug Program since 1986 and this program took the charge of ensuring quality medicinal products by sending it for testing and monitoring good distribution and storage practices for medicinal products.

With the participation and exposure of officials of Ministry of Health to international conferences on Pharmaceuticals safety and ICDRA, Bhutan recognized the need to introduce National Drug Policy and Medicines Legislation.

Medicines Act of Kingdom of Bhutan was enacted in the year 2003, and Drug Regulatory Authority(DRA) was instituted as a unit under Ministry of Health with **its formal establishment on 14 June 2004**(with the first meeting of the Medicines Board). In the following year, Medicines Regulation was introduced.

Ministry of Health being major stakeholder in procurement and distribution of medicinal products across the country, DRA needed independence from Ministry of Health to deliver its regulatory functions effectively and as per the Act, DRA is also mandated to regulate veterinary medicines, hence in **July 2008,** DRA was de-linked from Ministry of Health.

Medicines Regulation and its accessibility

Medicines registration is the process by which a Regulatory Agency approves the use of a medicine in a particular country, having considered documentary evidence of the medicine's safety, quality and efficacy with the intent of protecting public health. However, since there is always an issue on balancing between the regulatory processes and promoting on availability of medicines. In some cases, regulatory processes may be seen as barrier to access as well as to profits and the growth of the pharmaceutical industry. These issues are higlighted in the international forum as well.

In Bhutan, in the second half of the year 2010, there were frequent stock outs of medicnal products in the country where DRA was blamed for delay in entry of needed medicines due to invoking the clause on medicines registration. *Bhutan Pharmaceuticals in Health Care Delivery Mission Report 8 - 22 June 2011 World Health Organization, SEARO* confirmed the reason as lack of co-ordinated action between Ministry of Health, and DRA and sudden procurement policy changes and lack of training on drug quantitification which caused the sudden shortage of medicines in the country.

The pressure on solving acute shortage of essential medicines triggered the change in policy for DRA to accept un-registered Essential medicines for institutional supplies but strengthening of Post Marketing surveillance. Subsequently, Bhutan Medicines Rules and Regulation 2012 replaced the 2008 version.To this effect, DRA has been facing considerable challenges in provision of greater access to medicines, yet also ensuring that the medicines that are available are safe, of acceptable quality and efficacious.

Success story

On the brighter side, DRA has been successful in regulating all manufacturing premises, pharmacies and the persons handling the pharmacy business and there is increased in compliances to the "Good Storage Practices", distribution practices and management of Defective medicines. We have increased our routine sampling and testing and reporting of Adverse Drug Reaction thereby ensuring that medicines are of the required quality, safety, efficacy. We have started the publication of Bhutan National Formulary so that

Healthcare professionals and patients have the necessary information for rational use of medicines. Good Manufacturing Practice(GMP) inspection overseas have been initiated from 2011 to ensure that imported medicines are appropriately manufactured to its standards. Regulatory procedures have been developed to ensure promotional activities of medicines is fair, balanced, aimed at rational drug use. DRA is also obliged to share the local ADR data to the global data base for the purpose of signal detection globally after Bhutan became member to WHO International Drug monitoring system in December 2014. Overall, the access to medicines are not hindered by unjustified regulatory work and we have observed neutrality in regulatory procedures by involving external advisory committees such as Bhutan Medicine Board and Drug Technical Advisory Committee.

DRA has also committed to ensure safety of Blood and Blood Products from 2015 with medical devices in the pipeline for future.

DRA with Competent Persons for Pharmacies after completion of Pharmacy Competency Course in 2011

The outlook of the Livestock extension centres where veterinary medicines are stored and medicinal products stored at Basic Health Units have improved over the time. The attitude of Healthcare professionals have changed over the past years with various sensitization workshops organized by DRA. They contribute to safe use of medicines by reporting of Adverse Drug Reactions and visually detective medicines to DRA for regulatory actions.

Consumers have become more aware and concerned about the quality of health services and medicines and have started reporting to DRA for dispensation of expired medicines or defective medicines.

With plans of introducing Quality Management System in DRA by June 2016, we intent to provide quality services to our clients (Market Authorization Holders, Licensees, Competent persons and consumers) thereby fulfilling our DRA's mission i.e *"Protect consumer's health by regulating safety, efficacy and quality of medicinal products including vaccines while promoting availability of quality medicinal products in the country through efficient and transparent regulatory mechanism".*

Compiled by:

- Ngawang Dema (She is an employee of DRA since 2005)

Medicines Safety Updates

Note: Updates on commonly medicines available in Bhutanese market are shared from the WHO Pharmaceuticals Newsletter 2015

METROCLOPRAMIDE: Risk of Neurological adverse events

According to Therapeutic Goods Administration(TGA) of Australia, there are many case reports of extrapyramidal disorders and tardive dyskinesia as well as rare cardiac cardiac conduction disorders.

Metroclopramide is widely used antiemetic and gastro-prokinetic drug.

Therefore, Australia has announced for update of product information to include the following contraindications for Metoclopramide:

- It is contraindicated for children under one year
- For young adults (Aged under 20 years) and children over 1 year, it is only indicated as second line therapy and dosage should not normally exceed 0.5mg/kg body weight with maximum of 30 mg daily.
- The maximum dose for adults is 10 mg three times daily.
- The maximum recommended treatment duration is now five days in all age groups

In December 2013, the European Commission also adopted the Europeran Medicines Agency's recommended changes to restrict the dose and duration of use of metroclopramide to reduce the the risk of portentially serious neurological advserse events.

In Bhutan, it is only cautioned for young adults and children(as per National Essential Medicines Formulary & Bhutan National Formulary), but not contra-indicated hence it will be discussed in the Drug Technical Advisory Committee or National Drug Committee for its edition in the National Formulary.

ORAL DICLOFENAC : No longer available without prescription in United Kingdom

The Medicines and Healthcare products Regulatory Agency(MHRA) has announced that oral diclofenac is no longer available over the counter(without prescription) as it is associated with small increased risk of cardiovascular side effects(eg: myocardial infarction and stroke). Hence, it is recommended that patients should have medical assessment to determine if it is suitable for them.

Diclofenac is non-steroidal anti-inflammatory drug used to treat pain and inflammation.

A recall has been issued for non-prescription diclofenac. However topical formulations of diclofenac(gel and cream) are available without prescription.

In Bhutan, it is available without prescription and it will be discussed in the Drug Technical Advisory Committee if it is required to be removed from the list of Non-prescription medicines List "schedule A".

AMBROXOL AND BROMHEXINE EXPECTORANTS : Risk of allergy and skin reactions

The European Medicines Agency(EMA) has announced that for updating Product Information(PI) on ambroxol and bromhexine –containing medicines with information about the small risk of severe allergic reactions and severe cutaneous adverse reactions(SCARs).

Ambroxol and bromhexine are mainly used as expectorants to make the mucus thinner for disease of lungs and airways. As ambroxol is metabolite of bromhexine, the risk of anaphylactic and severe cutaneous reaction is condisdered to apply also to bromhexine.

Health-care professionals are to advise patients that they should stop the treatment immediately if symptoms of progressive skin rash occur.

In Bhutan National Formularly, it is mentioned under adverse effects as "very rarely allergic skin rashes". Hence counselling must include for patients that they should stop the treatment immediately if symptoms of progressive skin rash occur.

DRA DIRECTIVES AND NOTIFICATION

i. Herbal Products with the medicinal claims

From the post market surveillance, we notice that herbal medicines/ remedies are flourishing in the market with certain medicinal claims/ indications/ claiming to alter body function or cure certain disease. *(Eg: Slim tea, ……).* Consumers may assume that, "If natural, it is harmless." But it may be adulterated *(addition of substances not noted on the label).*

Any products with therapeutic claims are to be considered medicinal products and hence registered with DRA with scientific evidence about the claims.

Hence, the consumers may take note of such products with exaggerated claims about the health benefits and refrain from self medication with the use of such products.

ii. Promotion/advertisement of medicinal products

According to Bhutan Medicines Rules and Regulation 2012, "Advertisement means whatsoever for the purpose of promotion directly or indirectly, the sale or distribution of any medicinal products". Only the Board shall approve advertisement as per section 27 of the Act.

The intention for control of advertisement of medicinal products is to screen the contents of the "ad" and not to mislead our consumers on the exaggerated medicinal claims without any scientific evidence.Therefore, we would request public and our clients not to publicly advertise any product with therapeutic/ medicinal value claims even on the social media sites without prior approval.

A year review January 2014- December 2015

Drug Regulatory Authority (DRA) was assessed as part of Global Alliance for Vaccines Initiatives (GAVI)-Bhutan graduation plan along with relevant programs of Ministry of Health. National Regulatory Authority strengthening was identified as one of the priorities to ensure quality of vaccines in the country. Introduction of Quality System in compliance to ISO9001 was also initiated.

Technical Cooperation between Thai FDA and Bhutan was signed on 21 October 2015

First meeting of Blood Technical Advisory Committee (BTAC) with the Regulators to finalize the Blood Regulation: 24 -26 May 2015

REGISTRATION DIVISION

No. of medicines registered:	Modern Human Medicines	Veterinary medicines	Herbal /Traditional medicines
Jan 2015 – December 2015	**425**	**40**	**5**
Total medicines registered till date	3363	288	140
No. of medicines imported:			
Jan 2015 – December 2015	**504**	**87**	**Nil**

No. of Registered Pharmacies, MAH & Competent Persons	Retailers	Market Authorization Holders	No. of Competent Persons
Current status	**51**	**24 (National wholesalers)** **15 (Manufacturers)**	**138**

INSPECTION DIVISION

Number of inspections

Year	Health Centres (Ministry of Health)	Livestock Extension centres	GMP inspections in-country and excountry
Jan 2015 – December 2015	**64**	**28**	**2**
Number of Inspections till Date	529	165	48

POST MARKETING CONTROL DIVISION

Number of Adverse Drug Reaction Reported and Defective Products Reported

	Jan 2015 – December 2015	Till Date
ADRs Reported (Human medicines)	**36**	151
Products Defective Reported (Human medicines)	**4**	59(Human medicines)
Products Recall Notification Served	**1**	25
Drug Tested	**109**	242 (since 2009)

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