Pharmacovigilance NEWSLETTER

4th Issue, January 2019

The Aim of the newsletter:

- Dissemination of drug safety information.
- Dissemination of regulatory decisions.
- Sharing activities of national pharmacovigilance centre (ADRM cell) with stake holders.
- Focusing capacity building, training & awareness programs on pharmacovigilance.

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The Pharmacovigilance newsletter provides the latest information on the safety of medicine & regulatory decisions of the Directorate General of Drug Administration (DGDA), the national drug authority of Bangladesh. It is one of the important means of communication with the Pharmacovigilance stakeholders of Bangladesh, (eg: doctors, nurses, pharmacist, drug manufacturers and importers and for the medicine consumers) and international organizations.

This newsletter includes the outcome of 9th ADRAC meeting, Evaluation of multiple ADR reports coming from different sources & different workshops & awareness programs on Pharmacovigilance organized by DGDA.

Contents:

Honorable Health Minister started Dissemination of the National Guideline on the Pharmacovigilance System in Bangladesh for Implementation:

Adverse Drug Reaction Monitoring (ADRM) Cell of DGDA has been performing as the National Drug Monitoring Centre of Bangladesh as per Ministry of Health and Family Welfare gazette. National PV Guideline of Bangladesh is the guidance documents for conducting Pharmacovigilance in our country. Former honorable Minister, Ministry of Health and Family Welfare, Mohammad Nasim,MP was present in the dissemination program of the National Guideline on the Pharmacovigilance System in Bangladesh among different stake holders on 14 October, 2018 at DGDA conference Hall.

Picture 1: National PV Guideline dissemination program (Chief guest: Mohammad Nasim, MP Former Honorable Health Minister, Mr Salman F Rahman, Advisor to Honorable Prime Minister, private sector investment (right side) and Major General Md. MustafizurRahman, DG, DGDA (left side)

Outcome of the Adverse Drug Reaction Advisory Committee (ADRAC) 9th meeting:

ADRAC, which was formed by Ministry of Health & Family Welfare, 9th meeting was held on 28th November, 2018 at Directorate General of Drug Administration, which was presided by Major General Md. Mustafizur Rahman, DG, Directorate General of Drug Administration. National Pharmacovigilance Centre of Bangladesh received total 423 (Four hundred twenty three) reports from different stakeholders (January - August 2018). These 423 (Four hundred twenty three) ADE reports were primarily evaluated by the ADRM cell. After primary evaluation, ADRM cell placed 345(three hundred forty five)complete reports to the Technical Sub-committee (TSC) of the ADRAC. Out of 345 (three hundred forty five) reports 196 (One hundred ninety six) reports were found Certain, Probable and Possible as per WHO Causality Assessment scale and these reports were then placed to the 9th ADRAC meeting for review.After evaluation, the ADRAC members commented finally 192 (One hundred ninety two) cases as ADRs and gave recommendation for the regulatory actions of some drug safety information based on WHO Pharmaceuticals Newsletter-4 and 5, 2108 and the Pharma World (Pharmaceutical & Health Journal in Bangladesh).

Table 1: Evaluation of reports by different committees

SL. No.	Committee	Number of evaluated reports	Opinion
1.	ADRM Cell	423	Complete reports-345 Incomplete reports-78
2	Technical sub-committee (TSC)	345	Certain, Probable and Possible report-196 Unlikely and Unclassifiable reports -149
3.	ADRAC	196	Has opined with 192 reports as ADR

Detailed reports summary has been graphically depicted below:

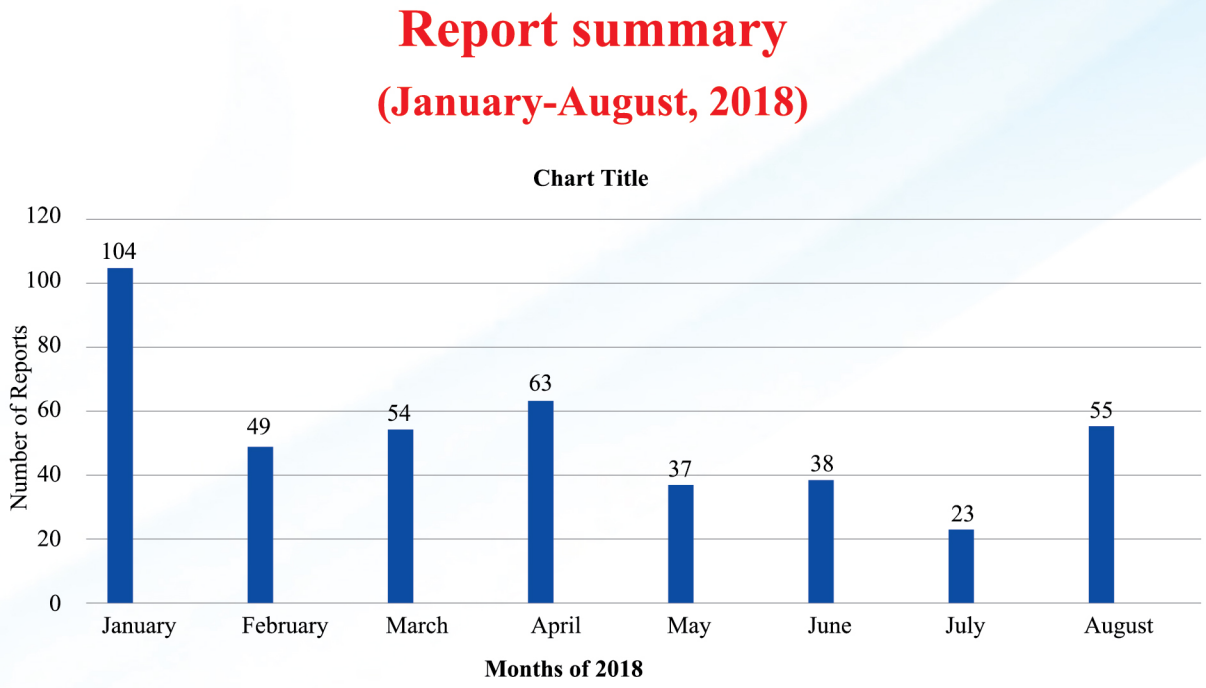


Figure1: Total 423 reports received at ADRM cell from January to August, 2018

Table 2: Sources of reports received at ADRM cell

Sources of Reports		
Sources	**Number of Repots**	**% (n= 423)**
Local Pharmaceutical Companies	34	8%
Multinational Companies	249	58.9%
Importers	115	27.2%
Hospitals	25	5.9%
Total	**423**	**100%**

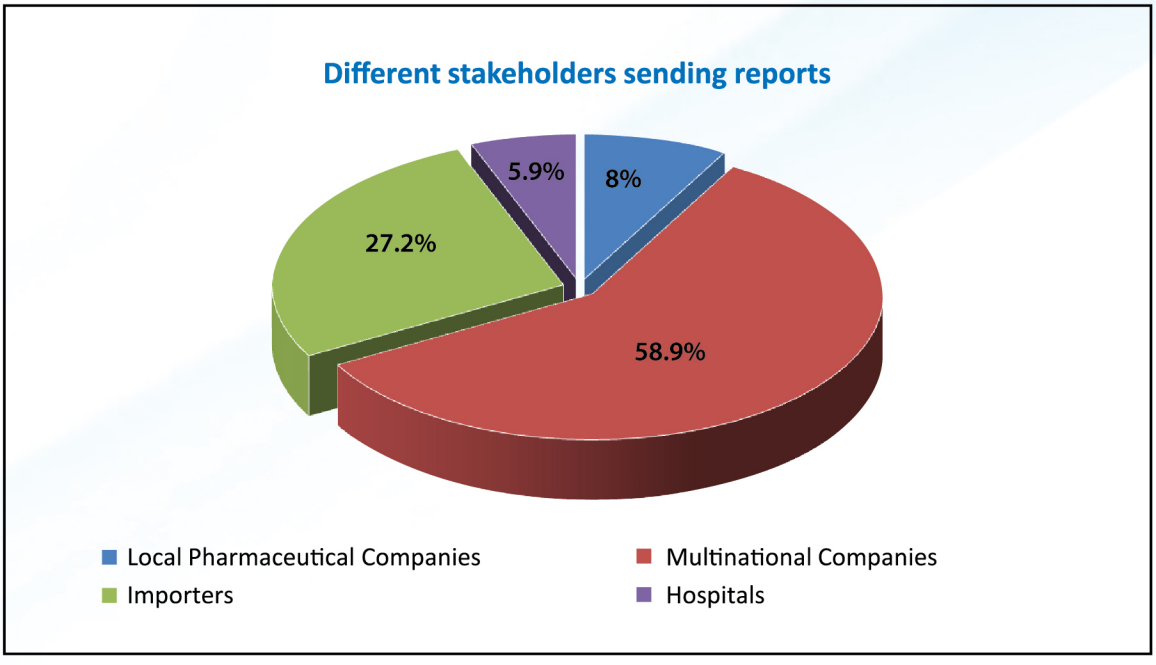


Figure 1: Percentage of received report from different sources

Serious Cases found:

Out of eighteen serious (Death) cases, ADRAC Technical Sub-Committee commented 12 unclassifiable and 06 possible as per WHO Causality Assessment scale. Then six seroius cases were investigated. ADRAC members reviewed these six reports and commented two case are possible and four are unclassified as per WHO causality assessment. These two ADRs were convulsion for Ceftriaxone IV injection and Toxic Epidermal Nacrolysis (TEN) for Allopurinol. ADRAC has given the following recommendations for these two drugs :

Precaution about Ceftriaxone Injection

1. **Ensure sensitivity test before using it.**
2. **Slowly administration for at least 2-4 minutes.**

Picture 2: Ceftriaxone Injection

Precaution about Allopurinol Tablet

1. **Ensure sensitivity test before using it.**

Picture 3: Allopurinol Tablet

Recommendations made by 9th ADRAC based on regulatory decisions of different NRAs published in WHO Pharmaceuticals Newsletter-4 & 5, 2018 and Pharma world

ADRAC recommended for following regulatory actions regarding the following 10 (ten) generic medicines for correction the Product Information Leaflet (PIL) based on the regulatory decisions of the International Agencies/ Authorities published in WHO Pharmaceuticals Newsletter (Issue 4 & 5, 2018) and Pharmaworld, Bangladesh:

Table 3: Recommendation by ADRAC 9th meeting for Regulatory Action

Sl. No	Name of Medicine	Adverse Drug Reaction	Recommendation by ADRAC
1	Benzocaine	Risk of blood disorder (methemoglobinemia) in infants and children	**Warning:** Methemoglobinemia **Contraindication:** Infant & Children younger than two years.
2	Fluoroquinolone antibiotics	Risk of hypoglycemia and adverse effects related to mental health	**Box Warning:** Increased risk of tendinitis and tendon rupture
3	Granulocyte-colony stimulating factor (G-CSF) drugs	Risk of large vessel vasculitis	**Adverse Effects:** Large vessel vasculitis. **Warning:** Allergic reactions, Splenic rupture, Alveolar hemorrhage, hemoptysis and Sickle cell disorders. **Contraindication:** Patients with known hypersensitivity to E-Coli derived proteins.
4	Metronidazole	• Risk of hepatic impairment • Severe hepatotoxicity or acute hepatic failure resulting in mortality was reported in patients with Cockayne's syndrome.	**Adverse Effects:** Chance of severe hepatotoxicity and hepatic failure in patients with Cockayne's syndrome. Risk of hepatic impairment.
5	Erythropoietins	Risk of Severe cutaneous adverse reactions (SCAR)	**Adverse Effects:** Severe cutaneous adverse reactions (SCAR) & Stevens Johnsons Syndrome**.**
6	Desogestrel	Severe psychiatric disorders: panic attack, suicidal ideation and self-induced injurious behavior.	**Adverse Effects:** Panic attack, suicidal ideation and self-induced injurious behavior.
7	Ceftriaxone	Risk of convulsions and involuntary movements	Risk of convulsions and involuntary movements as Adverse Effects.
8	Neuromuscular blocking agents (e.g suxamethonium, pancuronium, and vecuronium)	Prevention of unintended paralysis through medication errors	To **UPDATE** label to include a warning indicating that the product is a **PARALYSING AGENT**.
9	Ulipristal	New measures to minimize risk of liver injury	**Contraindication:** Ulipristal is not recommended for use in patients with liver disease.
10	Amlodepine	Alopecia	**Adverse Effect:** Alopecia.

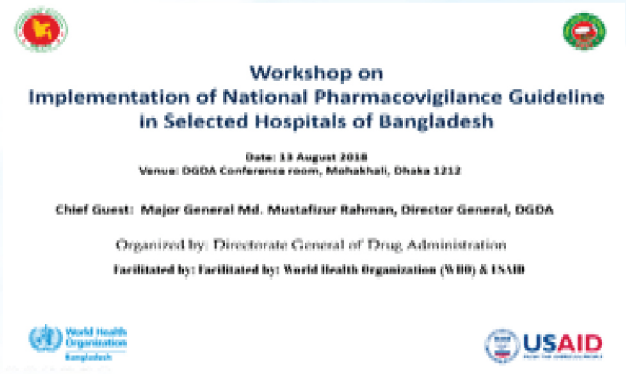
DGDA has already issued letter to the concern Manufacturing /Importing Pharmaceutical Companies and circulated it for updating their Patient Information Leaflet (PIL) including the ADRAC recommended information regarding ADRs. Licensing Authority of Drugs (DGDA) has already informed the related medical/professional associations through official letters to disseminate this safety information among the Health care professionals. A letter has also sent to the Director General of Health Services (DGHS) for informing the concern Healthcare Providers to make them aware regarding safety issues. This information isalso available in the DGDA website link (www.dgda.gov.bd)

Ref: WHO Pharmaceuticals Newsletter No 4 & 5, 2018 and Pharmaworld

Workshop/Training Program on PV Guideline arranged by DGDA

Directorate General of Drug Administration arranged Workshop/Training on Implementation of National Pharmacovigilance Guideline for the focal points of the 50 Hospitals on 13 August, 2018and 50 Pharmaceutical Companies on 16 August, 2018 at DGDA Conference Hall, Dhaka. Nominated Doctors/ Pharmacists/PV experts of the selected Hospitals and Pharmaceutical Companies attended the training workshops arranged by DGDA; jointly facilitated by World Health Organization (WHO) and USAID. The workshops were for dissemination & implementation of National Guideline on the Pharmacovigilance System in Bangladesh and chaired by Major General Md. Mustafizur Rahman, Director General of DGDA. Nayer Sultana, Director (CC) & head of ADRM Cell, Prof. Dr. Md. Saidur Rahman, Pharmacology department, BSMMU, Dr. Md. Akter Hossain, Assistant Director & focal point of ADRM cell, Mr. Mohammed Ramzy Ismail, Technical Officer, Essential Medicine, WHO Country Office, Bangladesh and Dr. Afsana Alamgir Khan, Technical Advisor, USAID took part as resource persons. They presented their valuable presentations and provided hands on training among the participants.

Picture 4: Training for PV focal points of the 50 Hospitals on 13 August, 2018 at DGDA.



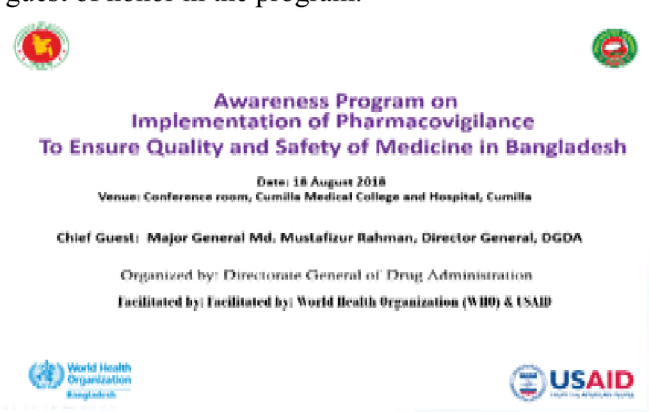
Picture 5: Training for PV focal points of the 50 Pharmaceutical Companies on 16 August, 2018 at DGDA.

Awareness program on PV among the stakeholders arranged at Cumilla district

Directorate General of Drug Administration arranged two awareness programs on Pharmacovigilance among the stakeholders in Cumilla district on 17 and 18 August, 2018 at Cumilla Club and Cumilla Medical College Hospital respectively. Programs were jointly facilitated by World Health Organization (WHO) and USAID. In both programs Major General Md. Mustafizur Rahman, Director General, DGDA was present as a Chief Guest and Chairperson.

Successful Awareness Program on Implementation of Pharmacovigilance to ensure quality and safety of medicine in Bangladesh held among Model Pharmacy / Medicine shop / retail Pharmacy Owners, Pharmaceutical Marketing Senior Representatives, Bangladesh Chemist's and Druggist's Samity (BCDS), and some local graduate physicians. The program was held in Cumilla Club conference Hall dated on 17th September 2018. More than 100 participants attended in this program. Additional District magistrate (ADM), Cumilla, local renowned Doctors, Lowers and Professionals were present as guest of honor in the program.

Successful Awareness Program on Implementation of Pharmacovigilance to ensure quality and safety of medicine in Bangladesh held among medical practitioners of Cumilla Medical College and Hospital. The program held in Cumilla Medical College conference Hall dated on 18th September 2018. Total 120 participants attended in this program. Vice Chancellor of the Chottogram Medical University Prof. Dr Md. Ismail Khan, Principal of Cumilla Medical College, Director of Cumilla Medical College Hospital were present as guest of honor in the program.



Picture 6:Awareness program on PV implementation at Cumilla Medical College Hospital Conference Hall, Cumilla on 18 August, 2018.

Picture 7: Awareness program on PV implementation at Sher-E-Bangla Medical College Hospital, Barisal on 06 December, 2018.

Major General Md. Mustafizur Rahman mentioned that Pharmacovigilance activities contribute to the safer use of drugs. It is the way of searching adverse effects of the medicine which have not yet been identified. So pharmacovigilance is crucial for ensuring safe, efficacious & quality medicine which impacts on the improved health services. Other guests and participants delivered & discussed on the importance of PV implementation and role of healthcare providers in this regard.

DG Health Services Issued letter to conduct Pharmacovigilance in all Hospitals:

Directorate General of Drug administration has taken initiatives for extending Pharmacovigilance in Bangladesh to all Hospitals having 100 or more beds as per the Drug Poilicy-2016. As per request of DG, Drugs, Directorate General of Health Services (DGHS) issued a letter to all the 100 or more beded hospital authorities to form PV committee and selecting focal points for conducting pharmacovigilance within the hospitals. The committee will organize and implement a system for monitoring adverse drug reactions (ADRs) found in the patients of the hospitals and will generate suspected Adverse Event reports. The reports have to be sent to the ADRM Cell of DGDA regularly. The hospital committee will conduct meeting monthly for evaluating the reports to find out the causes of the events.

গণপ্রজাতন্ত্রী বাংলাদেশ সরকার
স্বাস্থ্য অধিদপ্তর
মহাখালী, ঢাকা-১২১২।

স্মারক নং-স্বাঃ অধিঃ/হাসঃ/চাঃ ও সরঃ/বিবিধ/ঢাঃ বিঃ-৩/২০১৮/ ৫১১৩ তারিখঃ ৩/১২/২০১৮

প্রাপকঃ

১। পরিচালক
মেডিকেল কলেজ হাসপাতাল(সকল)
২। পরিচালক
বিশেষায়িত হাসপাতাল(সকল)
৩। তত্ত্বাবধায়ক/সিভিল সার্জন কাম তত্ত্বাবধায়ক
জেলা/সদর হাসপাতাল(সকল)

বিষয়ঃ জাতীয় ঔষধনীতি ২০১৬ মোতাবেক একশত বেড বা তদুর্ধ্ব হাসপাতাল সমূহের ফার্মাকোভিজিল্যান্স সংক্রান্ত কার্যক্রম পরিচালনার জন্য অফিস আদেশ জারি করণ প্রসংগে।

সূত্রঃ নং-ডিজিডিএ/পিভি-কম/হাস-২০১৮/০০২৭ তারিখ ২৪/১০/২০১৮খ্রিঃ

উপরোক্ত বিষয় ও সূত্রের প্রেক্ষিতে মহাপরিচালক, ঔষধ প্রশাসন অধিদপ্তর, ঔষধ ভবন, মহাখালী, ঢাকা কর্তৃক প্রেরিত পত্রের ছায়ালিপি এতদসংগে সংযুক্ত করা হলো(কপি সংযুক্ত)।

এমতাবস্থায়, সংযুক্ত পত্রের মর্মানুযায়ী প্রয়োজনীয় ব্যবস্থা গ্রহণের জন্য অনুরোধ করা হলো।

ইহাতে মহাপরিচালক মহোদয়ের অনুমোদন রয়েছে।

সংযুক্তঃ ২ (দুই) পাতা।

(অধ্যাপক ডাঃ মোঃ আলী খান)
পরিচালক, হাসপাতাল ও ক্লিনিক সমূহ এবং
লাইন ডাইরেক্টর
হসপিটাল সার্ভিসেস ম্যানেজমেন্ট।
ফোন নং-০২-৫৫০৬৭১৫০ ,ফ্যাক্সঃ ০২-৫৫০৬৭১৫১

স্মারক নং-স্বাঃ অধিঃ/হাসঃ/চাঃ ও সরঃ/বিবিধ/ঢাঃ বিঃ-৩/২০১৮/ তারিখঃ
অনুলিপি অবগতি ও প্রয়োজনীয় ব্যবস্থা গ্রহণের জন্য প্রেরন করা হলো।
১। মহাপরিচালক, স্বাস্থ্য অধিদপ্তর, মহাখালী, ঢাকা। দৃঃ আঃ সহকারী পরিচালক(সমন্বয়)।
২। মহাপরিচালক, ঔষধ প্রশাসন অধিদপ্তর, ঔষধ ভবন, মহাখালী, ঢাকা।

(অধ্যাপক ডাঃ মোঃ আলী খান)
পরিচালক, হাসপাতাল ও ক্লিনিক সমূহ এবং
লাইন ডাইরেক্টর
হসপিটাল সার্ভিসেস ম্যানেজমেন্ট।

Fruitful discussion for PV collaboration with EPI and WHO:

Picture 8: Meeting for PV collaboration between ADRM cell, DGDA with EPI and WHO

A successful meeting between National Pharmacovigilance Center (NPC) and Extended Programme for Immunization (EPI) held at DGDA Conference Hall on 14 November 2018 for pharmacovigilance collaboration for vaccines (AEFI monitoring). Major General Md. Mustafizur Rahman, Director General, DGDA; Dr. Sultan Md. Shamsuzzaman, Line Director, MNC&AH (DGHS),Mr. Md. Ruhul Amin, Director(cc), DGDA; Nayer Sultana, Director and Head of ADRM cell, DGDA; Dr. Moula Box Chowdhury, Program Manager of EPI; Dr. Md. Akter Hossain, focal point of ADRM cell; Dr. Rezaur, Deputy Program Manager of EPI; Dr Selina Ahmed,WHO; Dr Aysha Siddiqua, Pharmacologist, DGDA; Mahbub Hossain, Superintendent of Drugs, DGDA; Farzana Shabnam Baishakhi Superintendent of Drugs, DGDA were present in the meeting. Both parties agreed that the EPI will provide the delail reports and summary of Expert Review Committee (ERC) meeting comments on the serious events. After the meeting EPI is sharing the AEFI reports with ERC meeting minutes to DGDA.

Piloting AEFI data integration into national District Health Information System 2 (DHIS2) based Health Management Information System (HMIS) initiated:

In September 2018, Bangladesh initiated rolling out vaccine adverse events information management system (VAEIMS) integration with the country's own DHIS2 based EPI tracker (EPI software) system.

Picture 9: DGDA officials attended training with EPI and National & International AEFI Experts *(Source: WHO)*

Dhaka district and Dhaka North City Corporation initiated the pilot roll-out following "Hands-on" training exercises for National EPI managers, staff of health management information system (HMIS), Directorate General of Drug Administration (DGDA), WHO country office, AEFI Expert Review Committee and staff of pilot districts.

Implementation of PV Monitoring Activities:

As part of regular monitoring of the ongoing PV activities, a team of ADRM cell members, DGDA are visiting different Hospitals and Marketing Authorization Holders (MAH) of Bangladesh. During the visit, the team monitors the ADE reporting status and PV systems within the organizations. They share and exchange the ideas about how to strengthen medicine safety reporting, planning on risk management and risk mitigation. ADRM cell also emphasized on conducting the activities and awareness on PV as per plan and schedule of the facilities/institutions. The Management and PV team officials of those hospitals & companies highly cooperated and appreciated DGDA's support and directives for the PV program and committed to continue ADE reporting related activities.

Picture 10: ADRM Cell of DGDA visited the BEXIMCO Pharmaceuticals Ltd. as a part of PV awareness activities.

Presently the following Marketing Authorization Holders (MAH), Govt. & Non-Govt. Hospitals and National Health Programmes are sending ADR reports to National PV Centre (DGDA) in Bangladesh:

Marketing Authorization Holders (MAH):
ACI Limited
The ACME Laboratories Ltd.
Alco Pharma Ltd.
Aristo Pharma Ltd.
Beacon Pharmaceuticals Ltd.
Beximco Pharmaceuticals Ltd.
Delta Pharma Ltd.
Discount pharma Ltd.
Eskayef Pharmaceuticals Ltd.
General Pharmaceuticals Ltd.
Healthcare Pharmaceuticals Ltd.
Incepta Pharmaceuticals Ltd.
Janata Traders Ltd.
Jayson Pharmaceuticals Ltd.
NIPRO JMI Pharma Ltd.
Novartis BD Ltd.
Nuvista Pharma Ltd.
One Pharma Ltd.
Orion Pharma Ltd.
Pharmacil Limited
Pharmasia Limited
Radiant Pharmaceuticals Ltd.
Reckitt Benckiser Ltd.
Roche BD Ltd..
Sanofi BD Ltd.
Square Pharmaceuticals Ltd.
The IBN Sina pharmaceuticals Ltd.
UniMed & UniHealth Ltd.
Zenith Pharmaceuticals Ltd.

Govt. & Non-Govt. Hospitals:
Dhaka Medical College and Hospital (DMCH)
National Institute of Cardiovascular Disease (NICVD)
National Institute of Diseases of the Chest and Hospital (NIDCH)
BGB Hospital
Central Police Hospital, Dhaka
Faridpur Medical College and Hospital
Square Hospital Ltd.
Apollo Hospital Ltd.
Anwar Khan Modern Medical College Hospital

Public Health Programmes:
Expanded Program on Immunization (EPI)
National Tuberculosis Control Programme (NTP)
Kala-azar Program

ADRM Cell members attend 2018 KIDS-APEC Pharmacovigilance training in South Korea:

Korea Institute of Drug Safety (KIDS) invited DGDA officials for attending the 2018 KIDS-APEC Pharmacovigilance training in South Korea on September4-5, 2018. Two members of ADRM cell joined the seminar. They are Dr. Md. Akter Hossain, Assistant Director and Focal Point of ADRM cell and Mohammed Nayeem Golder, Assistant Director, DGDA.

Some imprtant topics of the seminar were listed below:

- Overview of Pharmacovigilance
- Regulation on Lableling in ASIA/EU/USA
- Safety specification and Pharmacovigilance Plan
- Risk Management Plans from Industry perspective
- International safety data collection
- Pharmacovigilance and Pharmacoepidemiology
- Benifit-Risk Assessment through product life cycle
- Risk communication of safety information with patients and Healthcare professionals.
- Future Direction on Pharmacovigilance

Picture-12: ADRM Cell members attend Pharmacovigilance Training 2018 in Seoul, Korea