

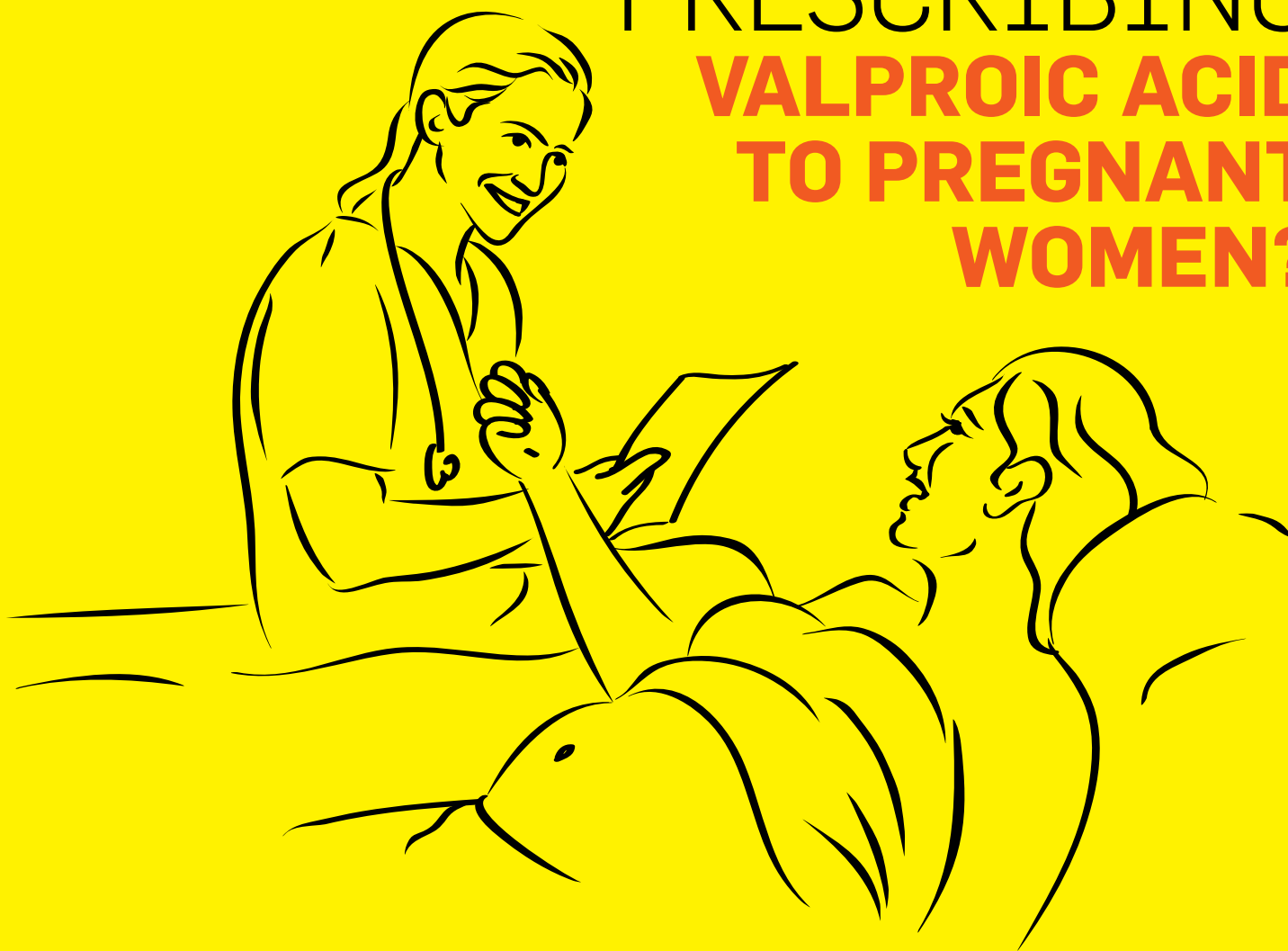


# Newsletter

PHARMACOVIGILANCE PROGRAMME OF INDIA (PvPI)

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## ARE YOU PRESCRIBING **VALPROIC ACID** **TO PREGNANT** **WOMEN?**



**NEED TO OBSERVE CAUTION BEFORE YOU  
PRESCRIBE VALPROIC ACID TO PREGNANT WOMEN**

## DRUG SAFETY REVIEW

- 04 | Valproic acid use in Pregnancy:  
A Necessity of Precaution and  
Pharmacovigilance in India

## IMPORTANT EVENTS

- 06 | It Takes Two to Tango:  
PvPI Join Hands with Industry to  
Strengthen Pharmacovigilance
- 07 | Core Training Panel Meets to Streamline  
Training Programmes
- 07 | Progressing Towards Excellence for  
Awaited National Regulatory Authority  
(NRA) Assessment
- 08 | WHO Experts Concedes, Vaccine  
Pharmacovigilance Fortify Safe  
Vaccination in India
- 08 | Recommendations of  
4<sup>th</sup> Steering Committee
- 09 | Research Based Pharmacovigilance:  
Issue of Letter of Recognition to ICMR  
Institutions
- 10 | Drug Safety Monitoring Committee  
(DSMC) Reviews Bedaquiline Active  
Surveillance Reports
- 11 | Convention of Signal Review Panel (SRP)  
Recommends New Signals

## INTERNATIONAL ARENA

- 11 | Research Based Pharmacovigilance  
for Herbal Drugs: NCC-PvPI to Work  
Jointly with University of Alberta
- 12 | Visit of The Netherlands Pharmacovigilance  
Expert to NCC-PvPI, IPC

- 12 | Visit of UMC Experts to  
NCC-PvPI, IPC
- 13 | Santosh Medical University Interacts with  
Faculty from University of Colorado, USA
- 13 | Visit of Dr. J Christophe Delumeau,  
International Society of Pharmacovigilance  
(ISoP) to NCC-PvPI, IPC
- 13 | PvPI Flickered in 39<sup>th</sup> Annual  
Meeting of WHO-PIDM

## DRUG SAFETY ALERTS

- 14 | Drug Safety Alerts for  
October-December 2016
- 15 | Comparative Status of Global Drug  
Alerts with PvPI Database

## FIELD ACTIVITIES

- 17 | Kurnool Medical College Setting  
Standards of Excellence for  
Pharmacovigilance in Andhra Pradesh
- 18 | Gearing Up with Inspirational  
Achievements: Dr. S. N. Medical  
College, Jodhpur Boosting PvPI  
Activities in Rajasthan
- 19 | Approved New  
Drugs in India



Dear Readers,

It gives me immense pleasure to bring this year's last issue of PvPI's newsletter. Pharmacovigilance Programme of India (PvPI) head quartered at Indian Pharmacopoeia Commission (IPC), Ghaziabad, an autonomous institution under the aegis of Ministry of Health & Family Welfare (MoHFW), Government of India is working with the sole conviction to identify, prevent adverse events associated with medicines and to promote patient safety.

PvPI's mission is to safeguard the health of Indian population by ensuring the benefit of use of medicine outweighs the risks associated with it. National Coordination Centre (NCC) has undertaken several steps to ensure the effective implementation of PvPI. I would like to take this opportunity to share some significant recent developments of NCC-PvPI.

In the area of research, PvPI has collaborated with Indian Council of Medical Research (ICMR) institutions across the country for research based Pharmacovigilance. These institutions will initiate research in Pharmacovigilance in accordance with their core area of competence to address the gaps and needs in planning with PvPI.

I am delighted to note that NCC-PvPI has implemented Quality Management System (QMS) to ensure Good Pharmacovigilance Practices (GVP) to monitor, report, collect, document and to analysis Adverse Drug Reactions (ADRs). This action is an important step of NCC to ensure patient safety and I feel that it will help to improve the quality of data under PvPI.

As an answer to the challenges posed in spontaneous reporting, NCC-PvPI has kick started with theme of 'Active Surveillance for Bedaquiline'. This step is particularly significant as it will give impetus to India specific signal generation.

I gratefully acknowledge the efforts of each and every member of PvPI, IPC team, with a special mention of physicians, pharmacists, nurses and other healthcare professionals at ADR monitoring centre.

**(Dr. G. N. SINGH)**

Secretary-cum-Scientific Director  
Indian Pharmacopoeia Commission  
Ministry of Health & Family Welfare  
Government of India.

# Valproic acid use in Pregnancy: A Necessity of Precaution and Pharmacovigilance in India

**In India, more than 50% women take prescription and over-the-counter (OTC) drugs during pregnancy and about half of them suffer due to adverse effects.**

**P**regnancy is a distinct physiological phenomenon that requires special concern for complete care and support. Drugs use is unavoidable in pregnancy associated with certain critical conditions like epilepsy, asthma and hypertension. The physiological changes during pregnancy may alter the pharmacokinetics of drugs and hence it becomes liable to attain potentially harmful concentrations in foetus which may lead to certain teratogenic adverse effects.

In India, more than 50% women takes prescription and over-the-counter (OTC) drugs during pregnancy and about half of them suffer due to adverse effects. About 8% of pregnant women need continuous drug treatment due to chronic diseases such as epilepsy, diabetes mellitus, bronchial asthma, hypertension, thyroid disorders, migraine and severe depression.<sup>1</sup>

## CONTOUR OF VALPROIC ACID USE IN PREGNANT WOMEN

Epilepsy is a most common neurologic disorder that requires continuous treatment in pregnancy condition. The use of anti-epileptic drugs (AEDs) pregnancy constitutes one of the most frequent chronic teratogen exposure. It is estimated that over 2.5 million women suffer from epilepsy in India and almost 52% of them belong to reproductive age group. AEDs such as carbamazepine, clonazepam, ethosuximide, phenobarbitone, phenytoin, sodium

valproate, lamotrigine, levetiracetam etc. are used as poly and mono therapy to treat epilepsy.<sup>2</sup>

## SAFETY STUDIES ON VALPROIC ACID USE IN PREGNANCY

Valproic acid (VPA) and sodium valproate was been approved by US FDA in 1967 to treat epilepsy. The semi-salt form of VPA (i.e. Valproate semi sodium) was approved by US FDA in 2003 to treat convulsion and manic condition. Meadow *et al* reported teratogenic effects of VPA in 1970 and Janz in 1976 warned on the cautionary use of VPA based on their findings.<sup>3</sup>

## RECOMMENDATIONS OF INTERNATIONAL REGULATORY AGENCIES ON VALPROATE PRODUCTS DURING PREGNANCY

### UNITED STATES FOOD AND DRUG ADMINISTRATION (US FDA)<sup>4</sup>

- VPA should not be used in pregnant women for prevention of migraine headaches.
- Only be used in extreme circumstances of other regimen failure in pregnant women with epilepsy or bipolar disorders.
- Awareness to pregnant women exposed to VPA for decreased IQ in infants.
- Should not be administered to a woman of

## STUDIES DOCUMENTED THE RISKS OF VALPROIC ACID DURING PREGNANCY

AUTHORS AND YEAR	DRUG	ADVERSE DRUG REACTIONS
Bertollini et al., 1985; Samrén et al., 1999; Arpino et al., 2000	Valproic acid	Increased risk of neural tube defects.
Samrén et al., 1999; Arpino et al., 2000	Valproic acid and its sodium salt	Increased risk of hypospadias.
Wyszynski et al., 2005	Valproic acid	10.7% of birth defects with VPA monotherapy exposure as compared to 2.8% with other AEDs monotherapies in 149 women of first trimester pregnancy.
Vajda et al., 2004; Vajda & Eadie, 2005	Valproic acid and its sodium salt	Greater risk with VPA in comparison to other monotherapies combined. Dose dependant increase in teratogenicity with VPA > 1100 mg/day

- childbearing age unless essential
- Counselling of women planning a pregnancy regarding the relative risks and benefits of valproate use during pregnancy.

### MEDICINES AND HEALTHCARE PRODUCTS REGULATORY AGENCY (MHRA)

MHRA launched a booklet, “Valproate Patient Guide” to ensure that women are properly informed, before they become pregnant, about the risks to their unborn child if they take sodium valproate during pregnancy (MHRA, 2016).

### EUROPEAN MEDICINES AGENCY (EMA)<sup>5</sup>

- Prescribing valproate in pregnant women and in women planning pregnancy is contraindicated.
- Only prescribe valproate medicines for epilepsy and bipolar disorder if other treatments are ineffective or not tolerated.
- Advise patients taking valproate medicines about

effective contraception during their treatment.

- Consider alternative treatments if a female patient becomes or plans to become pregnant during valproate treatment.
- Regularly review the need for treatment and re-assess the balance of the benefits and risks for female patients taking valproate and for girls reaching puberty.
- Inform patients of the risks of taking valproate during pregnancy.

### ADRs DURING PREGNANCY: INDIAN SCENARIO

Since, there is paucity of data/ practically no safety data available on risks associated with the use of VPA by females of child bearing potential & during pregnancy in Indian population, the present recommendations aims to address this issue. National Coordination Centre-Pharmacovigilance Programme of India (NCC-PvPI) reviewed its database with respect to VPA and noticed that following ADRs were reported.

### ADRs REPORTED IN PvPI DATABASE DUE TO VALPROIC ACID USE IN PREGNANCY.

YEAR	DRUG & DOSE	ADVERSE DRUG REACTIONS
2013	Sodium Valproate	Congenital anomaly
2013	Sodium Valproate 300 mg daily	Limb malformation
2014	Sodium Valproate 300 mg daily	Foetal Valproate Syndrome-Cardiomegaly, Hepatomegaly
2016	Sodium Valproate 600 mg daily	Spina bifida

### RECOMMENDATIONS OF NCC- PvPI TO HEALTH CARE PROFESSIONALS (HCPs)

- Use of VPA in pregnant women and women of reproductive age must be avoided unless no better alternative is available.
- Regular review of therapy and assessing the balance of benefits & risks in susceptible cases.
- Consider alternative options if a woman on Valproate plans to have children.
- PvPI urges all HCPs like Pharmacists, Nurses and Paramedics to spread awareness in public regarding this serious risk in pregnancy.

PvPI being vigilant and responsible towards ensuring safe medication to Indian public, requests the regulatory authorities and other professional bodies in India to take necessary actions and issue guidelines for the clinical practitioners on safe use of Valproic acid in pregnant women.

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# It Takes Two to Tango: PvPI Join Hands with Industry to Strengthen Pharmacovigilance

**Third interactive session on participating of Marketing Authorization Holders in PvPI:  
A way forward held at NCC-PvPI, IPC, Ghaziabad.**

**T**he “Third interactive session on participation of Marketing Authorization Holders in PvPI: A way forward” was held on 07th October 2016 at NCC-PvPI, IPC, Ghaziabad. As per G.S.R. 287 (E), dated 8th March, 2016, a mandate of Pv system in place for reporting ADR to licencing authority by every manufacturer or market authorisation holder. In order to ensure effective implementation, of the said rule there was an urgent need to deliberate the issues and challenges for the MAHs as well as PvPI in terms of managing ADRs. Involvement of Pharma industry in PvPI is very important to secure comprehensive patient safety data in Indian population.

### RECOMMENDATIONS

- MAHs shall make available their updated package insert leaflets (PIL) on company website.
- MAHs shall start sending ICSRs in E2B, .xml format to NCC-PvPI, IPC
- Development of the medication error module for PvPI with technical support from Lupin Pharmaceutical Ltd.
- MAH shall take the responsibility of ADR reporting of their products manufactured by contract manufacturing.
- MAHs are advised to report all ADRs to PvPI including the unlisted AE/ADRs.



3<sup>rd</sup> interactive session with Indian Pharma Industry representatives

- Quality of ICSRs sent to PvPI need to be improved with special focus on causality assessment.
- Training required for medical representatives of MAHs to improve quality of ICSRs.
- Helpline number of PvPI to be promoted by MAHs (by printing on the last page of PIL of pharmaceutical product).
- Draft version of Pharmacovigilance guideline for MAHs in India may be shared with all participants to get their suggestions/comments.



Delegates from Indian Pharmaceuticals Industry exchanging views with CDSCO and NCC-PvPI officials



# Core Training Panel meets to Streamline Training Programmes

A Core Training Panel (CTP), consisting of five members was constituted by MoHFW, Government of India (GoI) on 31<sup>st</sup> December 2013

Ongoing training is extremely important to update on recent developments and knowledge in the field of Pharmacovigilance besides optimizing the utilization of human resource and achieve organizational goals. A Core Training Panel (CTP), consisting of five members, was constituted by MoHFW, GoI on 31<sup>st</sup> December 2013 to streamline organization of periodic training programmes for the stakeholders of PvPI across the country. The third CTP meeting for PvPI was held on 7<sup>th</sup> November, 2016 at Central Drugs Standard Control Organization (CDSCO), New Delhi to discuss various issues and came out with following recommendations.

## RECOMMENDATIONS

- Regional Training Centres (RTCs) to identify the trainers for continuing medical education (CME)/ Advance level training in pharmacovigilance.
- Recognition of All India Institute of Medical Sciences (AIIMS), Rishikesh as RTC under the guidance of Post Graduate Institute of Medical Sciences (PGIMER), Chandigarh and Institute of Medical Sciences (IMS) BHU, Varanasi as new RTC after they submit the proposal.
- Preparation of training manual on Pharmacovigilance and chapters for the same will be prepared by RTCs coordinators.
- Inclusion of sensitization/awareness activities of each ADR monitoring centre (AMC) in PvPI's monthly progress report and its circulation to all AMCs from NCC to motivate other AMCs for increasing sensitization activities in their region.
- Panel recommended that a calendar of training for 2017 to be prepared for conducting CME/ Advance level training by all regional training centres (RTCs).

# Progressing Towards Excellence for Awaited National Regulatory Authority Assessment

- Pharmacovigilance is one of the key indicators of National Regulatory Authority (NRA) benchmarking tool. This tool contains 6 indicators including 25 sub-indicators which were successfully filled and committed to World Health Organization (WHO).
- The role and responsibilities of all stakeholders (PvPI, AEFI, CDSCO, HCPs) are now set-up for strengthening the vaccine safety.
- External audit was conducted at NCC-PvPI.
- Launch of quality manual for PvPI.
- Field visit to AIIMS, Bhopal & STM, Kolkata was conducted and found satisfactory.



Debriefing meeting for vaccine pharmacovigilance in India with WHO experts at CDSCO (HQ), FDA Bhawan, New Delhi

Immunization (AEFI) committee meeting was conducted on 25<sup>th</sup> November 2016 to review the findings collected in field visit and preparedness of forthcoming WHO-NRA assessment.

The 4<sup>th</sup> Annual National Adverse Events Following

# WHO Experts Concede, Vaccine Pharmacovigilance Fortify Safe Vaccination in India

**Experts in two teams overviewed AMCs of Madhya Pradesh and West Bengal along with state immunization offices to analyse the functions and progress involved in Pharmacovigilance of vaccines.**

**T**eam of experts from WHO Headquarters, Geneva visited India from 13<sup>th</sup>-16<sup>th</sup> December 2016 to review the function of vaccine Pharmacovigilance system by using the WHO-NRA assessment tool. Experts in two teams overviewed AMCs in Madhya Pradesh and West Bengal along with State immunization offices to analyse the functions and

progress in Pharmacovigilance of vaccines.

Debriefing meeting of above inspection was held on 15<sup>th</sup> December, 2016 at CDSCO, New Delhi and following outcomes were discussed:

- Experts appreciated the efforts of PvPI in enhancing awareness among HCPs regarding safe vaccination.
- Committee admitted that most of the indicators of Pharmacovigilance tool were fulfilled and found satisfactory.
- The progress was remarkable in comparison to last NRA assessment during the year 2012.
- WHO addressed the need of improvement in quality of AEFI reporting and also pointed about the requirements of additional human resources for effectiveness of vaccine reporting.
- Joint Secretary (R) assured WHO experts for taking necessary steps to strengthen the Pharmacovigilance system of vaccines.



NRA assessment review session at CDSCO (HQ), FDA Bhawan, New Delhi

## Recommendations of 4<sup>th</sup> Steering Committee

**Pharmacovigilance Programme of India (PvPI) is guided and monitored by the steering committee.**

**T**he 4th steering committee meeting was held on 28th December 2016 at CDSCO, New Delhi under the chairmanship of Dr. G. N. Singh, Drugs Controller General (India). The steering committee's objective is to supervise and give proper direction to the Pharmacovigilance Programme of India.

During its 4th meeting the steering committee recommended-

- i. For the appointment of Pharmacovigilance Officers & Senior Pharmacovigilance Associates.
- ii. Conception of drug safety research fellowship (DSRF) under PvPI for undertaking research



based studies that will help to strengthen PvPI and bolster regulatory decisions taken by CDSCO. The recommendation was agreed in principle.

- iii. Medical Superintendent to be Chief-Coordinator of ADR monitoring centre under PvPI for better implementation of the programme in hospitals.
- iv. Pharmacy colleges/ institutions attached with

hospitals may be recognised as ADR monitoring centres upon examining the capacity and strength in Pharmacovigilance.

- v. MTNL to develop anew Mobile app for ADR reporting to NCC-PvPI. The committee recommended for expedited action in this regard.

## Research Based Pharmacovigilance: Issue of Letter of Recognition to ICMR Institutions

**Letter of recognition was issued to Indian Council of Medical Research (ICMR) institutions pursuant to first meeting on 'Optimising the safety of medicines through research based Pharmacovigilance.'**

**A**n existence of ample opportunity and understanding the importance of research in Pharmacovigilance, NCC-PvPI, IPC, Ghaziabad aligned with ICMR institutions. Recently, letter of recognition as collaborating centre were issued to seven ICMR institutions by NCC-PvPI, IPC. This step was taken in pursuance of the decision taken in a meeting 'Optimising the

safety of medicines through research based Pharmacovigilance' held on 28th July, 2016 under the Chairmanship of Dr. Soumya Swaminathan, Secretary, Department of Health Research (DHR) & Director General, ICMR wherein the following ICMR institutes expressed their interest in participation in nationwide programme to monitor drug safety.

S. No.	NAME OF ICMR INSTITUTE	DOMAIN OF RESEARCH
1	National Institute of Epidemiology (NIE), Chennai	Pharmacoepidemiology & data management platforms.
2	National Institute for Research in Reproductive Health (NIRRH), Mumbai	Safety monitoring of drugs & devices for reproductive health.
3	National Institute of Nutrition (NIN), Hyderabad	Nutraceuticals' safety monitoring.
4	National Institute for Research in Tuberculosis (NIRT), Chennai	Research in tuberculosis.
5	National Institute of Cholera & Enteric Diseases (NICED), Kolkata	Safety monitoring of vaccines & drugs used in communicable diseases.
6	National Institute of Malaria Research (NIMR), New Delhi	Safety of anti-malarial drugs.
7	National AIDS Research Institute, (NARI), Pune	Monitoring the safety of Anti-HIV drugs.

The collaborating centres will initiate research in Pharmacovigilance in accordance with their core area of competence to address the gaps and needs that may be fulfilled by the respective institution.

The above centres will also submit a concept note and phase-wise plan of work on research based pharmacovigilance to NCC-PvPI.

# Drug Safety Monitoring Committee Reviews Bedaquiline Active Surveillance Reports

Dr. Nilima Kshirsagar, Chairperson, DSMC while appreciating the team work of all partners, made a point to the TB treatment providers as well as PvPI team to gather complete drug safety information in case ADR is encountered.

**T**he Bedaquiline (BDQ) Drug Safety Monitoring Committee (DSMC) was constituted by Director General of Health Services (DGHS) to review the ADRs associated with the use of BDQ. The second meeting was held under the Chairmanship of Dr. Nilima Kshirsagar, was held on 5<sup>th</sup> December 2016 in New Delhi. Present were, Dr. V S Salhotra, Additional Deputy Director General-TB appreciated the efforts of PvPI, WHO and RNTCP for effectively establishing an operational and technical system to roll out BDQ in 6 AMCs. It was also proposed to develop channels to monitor

and report ADRs particularly by developing IT tool to bridge the gap between Nikshay and Vigiflow (web-based ICSR management system).

Dr. Nilima Kshirsagar while, appreciating the team work of all partners, made a point to the TB treatment providers as well as PvPI team to gather complete drug safety information in case any ADR is encountered.

After reviewing drug safety data, the committee opined that the use of BDQ is safe in Indian population; however further safety data needs to be strengthened.

## BEDAQUILINE SAFETY UPDATES

**2<sup>nd</sup> February 2016:** DSMC was constituted and approved by DGHS, MoHFW, GoI

**11<sup>th</sup> March 2016:** 1<sup>st</sup> DSMC Meeting held, Discussion regarding the CAC committee at Bedaquiline CEM Site

**21<sup>st</sup> March 2016:** Bedaquiline was launched on World TB Day

**6<sup>th</sup>-9<sup>th</sup> September 2016:** RNTCP, PvPI, WHO and MoHFW met with the aim to strengthen the operational & technical aspects to effectively implement CEM of Bedaquiline.

**5<sup>th</sup> December 2016:** 2<sup>nd</sup> DSMC meeting, Committee reviewed drug safety data which was presented by PvPI and RNTCP, the committee opined that as per the information available till date on BDQ it is considered to be safe & suggested for further safety data needs to be generated to establish its safety profile.

**21<sup>st</sup> May 2015:** Meeting among the 6 sites regarding the use of Bedaquiline

**1<sup>st</sup> -3<sup>rd</sup> July 2015:** Skill development and Harmonisation of the activities of CEM for all 6 DRTB active sites from Delhi **LRSITRD**, Delhi **RBIPMT**, Delhi **GHTM**, Tambaram, Tamil Nadu **GTB KEM**, Sewri, Mumbai **BJMC**, Ahmedabad **GMC**, Guwahati

## MILESTONES OF ACTIVE SURVEILLANCE OF BEDAQUILINE

# Convention of Signal Review Panel Recommends New Signals

The ninth Signal Review Panel (SRP) meeting of PvPI was held on 29<sup>th</sup> November, 2016 at CDSCO West Zonal Office, Mumbai with an objective to detect signal(s) from Indian safety database and promote safety. SRP recommended to CDSCO about new signals, drug safety label change and drug alerts for the following pharmaceutical products which are marketed in India.

S. No.	DRUGS	ADVERSE DRUGS REACTIONS	RECOMMENDATIONS
1	Furosemide	Dermatitis lichenoid	Signal
2	Itraconazole	Acute generalised exanthematous pustulosis	Signal
3	Lithium carbonate	Drug reaction with eosinophilia and systemic symptoms (DRESS)	Signal
4	BCG vaccine	Lymphadenopathy	Drug safety label change
5	Docetaxel	Candidiasis	Drug safety label change
6	Phenytoin	Acute generalised exanthematous pustulosis	Drug safety label change
7	Meropenem	Hypokalaemia	Drug alert
8	Montelukast	Hypokalaemia	Drug alert

## INTERNATIONAL ARENA

### Research Based Pharmacovigilance for Herbal Drugs: NCC-PvPI to Work Jointly with University of Alberta

**This joint work is deemed to provide a platform to carry out research and analysis along with expertise of faculties from University of Alberta**

To initiate the research based Pharmacovigilance and to monitor the safety of herbal drugs, NCC-PvPI is going to jointly work with University of Alberta (UAlberta). This will foster to generate drug-herbal interaction data and will strengthen the Indian regulatory system to take appropriate regulatory interventions on marketed herbal drugs.

Integrative Health Institute under UAlberta is already fostering upon conventional medicines/

therapies. And it is equally important to monitor the safety of herbal drugs/phytopharmaceuticals in Indian context too. This also posed a responsibility to the HCPs to carry out vigilance studies on such herbal products being consumed/ utilized in India. This collaboration will provide a platform to carry out research and analysis along with expertise of faculties from University of Alberta.



### Visit of The Netherlands Pharmacovigilance Expert to NCC-PvPI, IPC

Prof. (Dr.) Eugene van Puijenbroek, Head, Science and Research at the Netherlands Pharmacovigilance Centre and Dr. Wil Hilgersom, Vaccine Safety Expert, Lareb, Netherlands visited Indian Pharmacopoeia Commission (IPC) on 20th October 2016 to exchange the ideas on AEFI Pharmacovigilance. This was second visit of Prof. (Dr.) Eugene and he shared insights on recent Pharmacovigilance experience in Netherlands. Dr. Wil Hilgersom highlighted on AEFI signals. Both experts overviewed the reporting culture of adverse events occurring due to vaccines and were highly impressed about the way of working and reporting by NCC-PvPI.

Prof. Eugene on behalf of Netherlands Pharmacovigilance Centre, Lareb agreed to provide training resource material to educate the personnel's on Pharmacovigilance and develop methodology to identify new signals from Indian database. Replying to queries of QA officials he had also insisted for adopting other methods of statistical analysis like Proportional Reporting Ratio (PRR), IC values analysis etc. as the case by case study may become very



Prof. (Dr.) Eugene van Puijenbroek (Left) and Dr. Wil Hilgersom (Lareb, The Netherlands) (Right) reviewed the process of vaccine ADR reporting system under PvPI

lengthy for such a huge data from Indian population. The efforts of PvPI officials in preparation of Quality Manual, and the commitment of PvPI towards achieving excellence in quality data was highly appreciated by the experts. .

### Visit of UMC Experts to NCC-PvPI, IPC

**Uppsala Monitoring Centre (UMC) has recognized India's rapid growth & contribution to global drug safety database.**

Dr. Marie Lindquist, Director, UMC and Prof. Edward, Senior Advisor, UMC visited NCC-PvPI, IPC on 21st October 2016 to review the progress and initiatives taken by PvPI. The dignitaries were impressed by the steps taken

by NCC-PvPI and appreciated that Pharmacovigilance activities under NCC are at par with the global standards. Dr. Marie on behalf of UMC proposed for collaboration on medication errors and reporting of lack of efficacy of drugs. She stated that NCC-PvPI may be identified as a hub for Asian countries to lead the research and development of neglected diseases. The UMC will seek to establish links between PvPI and international medical services for better patient safety. She also emphasized the importance of regular training, quality data generation and to compete with other regulatory authorities. She invited PvPI work force to join training programmes at UMC. On behalf of PvPI Dr. V. Kalaiselvan, Principal Scientific Officer requested Director, UMC to organize skill development training in India in the areas of signal detection, statistical analysis and publication of quality reports.



Dr. Marie Lindquist (Center) and Prof. Edward (WHO - UMC) (Left) interacting with NCC-PvPI officials

## Santosh Medical University Interacts with Faculty from University of Colorado, USA

Dr. Kari L. Franson, Associate Dean, Professional Education & Dr. Jodie V. Malhotra, International Affairs Coordinator, University of Colorado, U.S.A. visited Santosh Medical University (SMU), one of the AMCs under PvPI, Ghaziabad on 10th November 2016 to understand the Pharmacovigilance activities in India. Under the aegis of University of Colorado, Dr. Jodie V. Malhotra agreed to provide necessary technical support to PvPI and SMU in Pharmacovigilance activities.

Dr. Sharmila Anand, Managing Director, SMU showed keen interest to promote PvPI and was ready to boost Pharmacovigilance activities up to primary health centre level in Ghaziabad district. NCC will engage SMU for further capacity building and drug safety research to outreach the scope of pharmacovigilance to community.



PvPI officials & experts from Santosh Medical University interacted with faculties from University of Colorado.

## Visit of Dr. J Christophe Delumeau, International Society of Pharmacovigilance (ISoP) to NCC-PvPI, IPC

Dr. J. Christophe Delumeau, Executive committee member, ISoP visited IPC on 21st October, 2016 to understand the functioning of NCC-PvPI. He appreciated the progress of PvPI over the years and briefed about the scope and objectives of ISoP. He on behalf of his organization agreed to collaborate with NCC-PvPI to provide training programmes for the



NCC officials for signal detection, benefit-risk and medication errors assessment. He also committed to extend his support

to develop advanced version of mobile ADR application and develop IT tools for Pharmacovigilance.

## PvPI Flickered in 39<sup>th</sup> Annual Meeting of WHO-PIDM

WHO-PIDM was organized in Sultanate of Oman by Ministry of Health, Oman between 14th -17th November 2016. Officials from India participated in the world class

meeting and showcased the PvPI activities in international arena. Oral presentations were presented to showcase the Pv activities in the country.



# Drug Safety Alerts for October-December 2016

The preliminary analysis of Suspected Unexpected Adverse Drug Reactions (SUSARs) from PvPI database revealed that following drugs are associated with risk

## CABERGOLINE

**Indication:** Hyperprolactinemia and inhibition of lactation

**ADR:** Steven Johnson Syndrome

## AMLODIPINE

**Indication:** Angina, hypertension, Coronary artery disease

**ADR:** Alopecia

## NITROFURANTOIN

**Indication:** Urinary tract infections, cystitis

**ADR:** Drug reaction with eosinophilia and systemic symptoms (DRESS)

## ATENOLOL

**Indication:** Angina, Myocardial infarction, Arrhythmias, Hypertension, Migraine prophylaxis.

**ADR:** Dermatitis Lichenoid

## CEFIXIME

**Indication:** Otitis media, RTI, Uncomplicated UTIs, Effective against infections caused by *Enterobacteriaceae*, *H.influenza* species.

**ADR:** Anal Ulcer

## OLANZAPINE

**Indication:** Schizophrenia and other psychotic disorders, Mania/mixed episode, Psychomotor agitation and violent behaviour.

**ADR:** DRESS

## MONTELUKAST

**Indication:** Prophylaxis of mild to moderate asthma

**ADR:** Tinnitus

## CEFOPERAZONE, SULBACTAM

**Indication:** Upper and lower respiratory tract infection (RTI) and urinary tract infection (UTI), Septicemia, Meningitis, Skin & Soft tissue infection, Endometritis, Other infection of genital tract, Intra-abdominal infection, Bone & joint infection, Intra-abdominal infection, Acute Generalised Exanthematous Pustulosis (AGEP)

**ADR:** Acute Generalised Exanthematous Pustulosis

## MEROPENEM




**Indication:** Nosocomial infections like septicaemia, Febrile neutropenia, Intra-abdominal and pelvic infection etc., caused by cephalosporin's resistant bacteria, Meningitis cystic fibrosis.

**ADR:** Hypokalaemia






Healthcare Professionals, Patients/Consumers are advised to closely monitor the possibility of above adverse events while prescribing/consuming above suspected drugs and report to the NCC-PvPI either by filling of Suspected Adverse Drug Reactions Reporting Form/ Medicines Side Effect Reporting Form for Consumer (<http://www.ipc.gov.in>) or by PvPI **Helpline No. 1800-180-3024**.



# Comparative Status of Global Drug Alerts with PvPI Database

NAME OF DRUG	RISK	INTERNATIONAL STATUS	INDIA STATUS
<b>ATYPICAL ANTIPSYCHOTICS</b>	 Sleep apnoea	Health Canada had carried out a safety review to investigate risk of sleep apnoea with the use of atypical antipsychotics. It recommends that current product labels for atypical antipsychotics (Aripiprazole, Asenapine, Clozapine, Lurasidone, Olanzapine, Paliperidone, Quetiapine, Risperidone and Ziprasidone) are updated to include the risk of sleep apnoea.	A total of 3 reports were received on atypical antipsychotics for the risk of sleep apnoea.
<b>BCR-ABL TYROSINE KINASE INHIBITORS</b>	 Hepatitis B virus reactivation	Therapeutic Goods Administration (TGA), Australia worked with manufacturers to update the product information documents of Bcr-Abl tyrosine kinase inhibitors (TKIs) such as Imatinib, Nilotinib, Dasatinib and Ponatinib by including a precautionary statement about the risk of HBV reactivation. The Ministry of Health, Labor & Welfare (MHLW) and Pharmaceutical & Medical Devices Agency (PMDA), Japan announced that package inserts for Bcr-Abl TKIs (Imatinib, Nilotinib, Dasatinib, and Bosutinib) have been updated to include the risk of reactivation of HBV as an important precaution. The Health Sciences Authority (HSA), Singapore stated that local package inserts for Bcr-Abl TKIs (Dasatinib, Imatinib, and Nilotinib) updated to include the risk of HBV reactivation.	Two cases of hepatitis B virus reactivation were received for Imatinib
<b>ETANERCEPT</b>	 Potential harm due to in utero exposure during pregnancy	Health Canada's safety review noted that taking Etanercept during pregnancy associated with potential risk of experiencing a miscarriage. It is also working with the manufacturer of Etanercept on updating the product safety information to include information on the risks of birth defects due to in utero exposure during pregnancy.	One case of abortion due to etanercept was reported.

# DRUG SAFETY ALERT

NAME OF DRUG	RISK	INTERNATIONAL STATUS	INDIA STATUS
<b>METOCLOPRAMIDE CONTAINING PRODUCTS</b>	 Restriction on dose and duration of use due to neurological and cardiovascular adverse effects	European Union review confirmed a relationship between high doses or long-term use of Metoclopramide and an increase in the risk of neurological and serious cardiovascular adverse reactions (I.V. route). HSA noted that nearly one in five neurological adverse reports associated with Metoclopramide from 1993 to August 2014 were reported in children. Hence, HSA had recommended that the package inserts for Metoclopramide containing products are updated to include restrictions on dose and duration of use.	Multiple report of neurological ADR and two report of cardiovascular ADR due to Metoclopramide administration were documented in PvPI.
<b>NATALIZUMAB</b>	 Progressive multifocal leukoencephalopathy, granule cell neuronopathy and acute retinal necrosis	MHLW and PMDA, Japan had announced that package insert for Natalizumab (Tysabri®) updated to include the risk of progressive multifocal leukoencephalopathy (PML), granule cell neuronopathy and acute retinal necrosis in patients as clinically significant adverse reactions.	One case of PML was reported to NCC.
<b>OLANZAPINE</b>	 Drug induced hypersensitivity syndrome	MHLW and PMDA, Japan had announced that package inserts for Olanzapine (Zyprexa® and others) updated to include the risk of drug-induced hypersensitivity syndrome (DIHS) as a clinically significant adverse reaction.	Two cases of DIHS were reported to NCC.
<b>ALLOPURINOL</b>	 Serious cutaneous adverse reactions (SCAR) and role of genotyping	HSA found evidence of a strong association between HLAB*5801 allele and allopurinol-induced SCAR (100 times high risk) compared to others. This is consistent with international data. Hence, HSA issued advice to health-care professionals about cautions required with the use of allopurinol to minimize risk of allopurinol-induced SCAR.	44 cases of SCAR (SJS and TEN) were reported to NCC.
<b>ISOTRETINOIN</b>	 Psychiatric adverse events	Isotretinoin (Roaccutane® and generics) is indicated for the treatment of severe cystic acne. Therapeutic Goods Administration, Australia (TGA) stated that psychiatric adverse reactions, including depression and suicidality, are a known risk associated with the use of isotretinoin. TGA advised healthcare professionals to perform careful psychological assessment before and during treatment with isotretinoin.	NCC-PvPI received six cases of psychiatric disorders with the use of isotretinoin.



# Kurnool Medical College Setting Standards of Excellence for Pharmacovigilance in Andhra Pradesh

Kurnool Medical College is a tertiary level medical college with 1000 bedded hospital and it provides specialty healthcare services to approximately 50 million people of Andhra Pradesh.

**K**urnool Medical College (KMC) is a multi-speciality hospital in Kurnool district of Andhra Pradesh. KMC was recognized as ADR Monitoring Centre (AMC) under PvPI in the year 2014 under the leadership of Dr. G.S. Ram Prasad, MD (Paediatrics), Principal, Dr.Y. Vijaya Bhaskar Reddy, Professor & Head, Dept of Pharmacology and Dr. S. Sharon Sonia, Professor, Dept. of Pharmacology. Later two holds the responsibilities of Coordinator and Deputy Coordinator, respectively. KMC is a tertiary level medical college with 1000 bedded

hospital and health institution which provides specialty health services to approximately 50 million people of Andhra Pradesh. Average attendance in Out-patient Department is more than 1700 patients per day and more than 80 major and minor surgical procedures are performed daily in 10 fully equipped operation theaters. The AMC has effectively translated the concept of Pharmacovigilance amongst medical and paramedical fraternity during last few years. The AMC is driving force to bring positive changes in ADR reporting and anticipate adopting Pharmacovigilance practices by stakeholders.

## ACTIVITIES OF AMC, KURNOOL MEDICAL COLLEGE, KURNOOL

- Incorporated the stamp of PvPI Toll free number in the Out Patient slip, RNTCP treatment card and Identity card of GGH, Kurnool.
- Total of eleven sensitization camps conducted for all the departments in GGH/KMC.
- Distribution of ADR forms and pamphlets containing the contact numbers and E-mail id of AMC to the public and HCPs for effective communication.
- Demonstration of ADR reporting app during the workshops, sensitization programmes and seminars to promote ADR reporting.
- Prepared a video on PvPI sensitization and importance of Pharmacovigilance.
- Distribution of newsletter and other promotional handouts.
- Display of English and Telugu posters (containing toll free number, PvA number) in all OPD and IPD wards.
- Installed 6 PvPI ADR drop boxes in IPD and OPD.





### MESSAGE FROM CLINICIANS

Patient safety is of prime importance at Kurnool Medical College, Kurnool. We at KMC, with combined untiring efforts of all physicians & healthcare professionals strive hard to positively contribute towards vital issue of patient safety. The contribution from our college is commendable in reporting adverse drug reactions.

**Dr. G. S. Rama Prasad, MD** (Paediatrics),  
Principal, Kurnool Medical College, Kurnool.

Indian healthcare system is a unique of its kind, so its challenges. In particular, I wish to highlight the challenges as to public awareness, voluntary participation of physicians & healthcare professionals with reference to pharmacovigilance. We at KMC, help the stakeholders in identifying, recognising, recording & reporting of adverse events to our AMC in concerted manner that will surely bring enormous benefits to patients & society at large.

**Dr. S. Sharon Sonia,**  
Professor,  
Deputy Coordinator, KMC, Kurnool.

At our ADR monitoring centre we have been able to get wholehearted support from our clinicians as we propagate that the main objectives of the Pharmacovigilance Program of India is to collectively ensure "Patient Safety".

**Prof. Suparna Chatterjee,**  
Dept. of Pharmacology, IPGME&R, Kolkata.



Post marketing activities involves assessing & reviewing the safety of medicines used in clinical set up. At our centre we are able to effectively communicate safety issues related with drugs with all stakeholders through innovative models.

**Dr. J. Veera Swamy, MCh** (Paediatric Surgery),  
Medical Superintendent, GGH, Kurnool.

Monitoring of Adverse Drug reaction at all levels is necessary. That is to say, starting from the drug development process till its clinical use. Therefore, post marketing surveillance is necessary in day to day practice of our physicians. To ensure patient safety at KMC, Kurnool we assure that all our physicians & other healthcare professionals are well sensitized on the issue of reporting. Our physicians also sensitize the patients/ care givers on this issue.

**Dr. Y. Vijaya Bhaskar Reddy, MD,**  
Professor & HOD, Coordinator, KMC, Kurnool.

PvPI is surging ahead in our institution and we are receiving full cooperation from the majority of our clinical colleagues. However, there is need for continued sensitization and motivation of both faculty and residents, in order to sustain the current momentum and improve upon it.

**Prof. Avijit Hazra**  
Dept of Pharmacology, IPGME&R, Kolkata.

## Gearing Up with Inspirational Achievements: Dr. S. N. Medical College, Jodhpur Boosting PvPI Activities in Rajasthan

**D**r. S. N. Medical College, Jodhpur was established in 1965 and is a tertiary level medical college with four attached groups of hospitals viz;

1. Mahatma Gandhi Hospital (MGH)
2. Umaid Hospital
3. Mathura Das Mathur Hospital (MDMH)
4. K. N Chest Hospital

Average attendance in OPD is more than 5000 patients in OPD and 1500 patients in IPD.

It was established as an AMC under PvPI in 2016 under the leadership of Dr. Ami Lal Bhat, Principal & Controller and Dr Anusuya Gehlot, Professor & HoD (Pharmacology) as a Coordinator for NCC-PvPI.

### Activities of AMC

1. Displaying of PvPI helpline number on prescription(s).
2. Regular meetings with various departments to improve reporting of ADRs.
3. Appointment of nodal officers in each department to take care of pharmacovigilance (Pv) activities.
4. Sensitization of residents and doctors via Continuous Medical Education (CME) meetings, how to fill the ADR report & importance of ADR reporting on regular basis.

5. Installation of 20 ADR drop boxes in various OPD/ IPD of attached hospitals, satellite hospitals & PHCs.

Dr. Anusuya Gehlot, Coordinator for NCC-PvPI is keen to conduct, CMEs on regular basis. She was invited as speaker from different institutes to conduct CME on “Pharmacovigilance need of the hour” and “Pharmacovigilance plus hands on training to fill ADR form.”

Pharmacovigilance is based on sound scientific principles and is an integral part of effective clinical practices. Such monitoring will help in assessing, monitoring and detecting adverse effects of drugs, their interactions. This measure will help to maximize benefits and minimize risks associated with drugs in Indian scenario.

**Dr. A. L. Bhat**  
Principal & Controller  
Dr. S.N. Medical College,  
Jodhpur.



Pharmacovigilance is an essential component of patient care & rational use of medicines. It is also variously referred to as, adverse drug reaction monitoring, drug safety surveillance, side effect monitoring, spontaneous reporting and post marketing surveillance. Further the long term safety of medicine is important when the drug is being used widely in a population. PvPI has been involved to monitor both the known and unknown effect of medicines in order to determine any new information available in relation to their safety profile.

**Dr. Anusuya Gehlot**  
Coordinator-AMC,  
Dr. S.N. Medical College,  
Jodhpur.



## Approved New Drugs in India

CDSCO has approved the following new drugs from October 2016 to December 2016.

S No.	DRUG	INDICATION
1	Dolutegravir 50 mg Tablet & Bulk (Dolutegravir Sodium)	Indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults weighing more than 40 kg.
2	Alcaftadine Eye Drops (0.25% w/v) & Bulk	For prevention of itching associated with allergic conjunctivitis in patients between the age group 10 to 60 years.
3	Lenvatinib 4mg/10mg Hard Gelatin Capsules (Lenvatinib Mesylate)	For the treatment of patients with locally recurrent or metastatic, progressive, radioactive iodine-refractory differentiated thyroid cancer.
4	Perampanel 2mg/4mg/6mg/8mg/10mg/12mg Tablets	Adjunctive treatment of partial-onset seizures with or without secondarily generalized seizures in patients with epilepsy aged 12 years and older.
5	Azilsartan Medoxomil Bulk & 40mg/80mg Tablets	Indicated for the treatment of hypertension in adults patients, either alone or in combination with other antihypertensive agents.

- Healthcare professionals are urged to closely monitor the safety of above drugs.
- ADRs, if any to be reported to PvPI.



### Duration of Training Programme

Duration of the training programme is 10 days and the training is available round the year as per training calendar.

### Training Calendar

State/Union Territory	Training Schedule 2017	Last Date for Application
• Uttar Pradesh • Uttarakhand • Manipur • Chandigarh • Delhi	16 <sup>th</sup> -25 <sup>th</sup> Jan	20 <sup>th</sup> Dec 2016
• Himachal Pradesh • Tripura • Arunachal Pradesh • Bihar • Jammu & Kashmir	01 <sup>st</sup> -10 <sup>th</sup> Mar	31 <sup>st</sup> Jan 2017
• Madhya Pradesh • Haryana • Tamil Nadu • Odisha • Meghalaya • Nagaland • Puducherry	01 <sup>st</sup> -10 <sup>th</sup> May	31 <sup>st</sup> Mar 2017
• Chhattisgarh • Karnataka • Andhra Pradesh • Dadra and Nagar Haveli • Assam • Lakshadweep • Goa	03 <sup>rd</sup> -12 <sup>th</sup> Jul	31 <sup>st</sup> May 2017
• Maharashtra • Kerala • Telangana • Mizoram • Sikkim • Rajasthan	04 <sup>th</sup> -13 <sup>th</sup> Sep	31 <sup>st</sup> Jul 2017
• Punjab • West Bengal • Gujarat • Jharkhand • Daman and Diu • Andaman & Nicobar	06 <sup>th</sup> -15 <sup>th</sup> Nov	30 <sup>th</sup> Sep 2017

Note: Aspirants are encouraged to apply as per the schedule of their respective States/UTs however the request may be considered in the other slots depending on the availability of seats.

#### Venue:

Indian Pharmacopoeia Commission  
National Coordination Centre-Pharmacovigilance Programme of India  
Ministry of Health & Family Welfare, Govt. of India  
Sector-23, Rajnagar, Ghaziabad-201 002, Email: [pvpi@ipcindia@gmail.com](mailto:pvpi@ipcindia@gmail.com), [pvpi@ipc.gov.in](mailto:pvpi@ipc.gov.in)  
Tel.: 0120-2783400, 2783401, 2783392, Fax: 0120-2783311

# We Learn Practice Educate Pharmacovigilance

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*Skill Development Programme on  
Basics and Regulatory Aspects of Pharmacovigilance  
Striving for Excellence*

2017  
January | March | May | July | September | November

Organized By:



Indian Pharmacopoeia Commission (IPC)  
National Coordination Centre-Pharmacovigilance Programme of India (NCC-PvPI)  
Ministry of Health & Family Welfare (MoHFW), Govt. of India (GoI), Ghaziabad

## ACKNOWLEDGEMENT

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**Website:** [www.ipc.gov.in](http://www.ipc.gov.in)

*let us join hands with PvPI to ensure patient safety*  
**ADR reporting Helpline (Toll Free): 1800-180-3024**