UNIVERSITY of NICOSIA

Course Syllabus

Course Code	Course Title	ECTS Credits
PHAR-620	Pharmacovigilance and Pharmacoepidemiology	10
Prerequisites	**Department**	**Semester**
None	Health Sciences	Spring
Type of Course	**Field**	**Language of Instruction**
Compulsory	Pharmacy	English
Level of Course	**Lecturer(s)**	**Year of Study**
2nd Cycle	Christos Petrou/Panayiotis Petrou	1st
Mode of Delivery	**Work Placement**	**Corequisites**
e-learning	--	none

Course Objectives:

Monitoring drug safety is very important to public health. Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems. Those working in pharmacovigilance must have good working knowledge of the principles of drug safety, its regulations and proactive strategies for risk management. This course provides solid practical foundations for those working in drug safety, and an update for experienced staff. This course will be valuable to a broad range of staff across the pharmaceutical industry and regulatory authorities.

Safety data generated by clinical development programmes is necessarily limited, and experience in this setting does not provide comprehensive information on the safety of a new medicinal product in wider use. Pharmacovigilance and control of medicines' use are required throughout the lifecycle of a product, before and after marketing authorisation. The accruing safety data are to be interpreted in relationship to the benefits of the product as part of the continuous assessment of benefit and risk. A safety risk management plan is required for marketing authorization. It is advisable to start this in the early stages of a product's life cycle as part of the long-term safety risk management strategy for a product. As a dynamic document, it requires regular updating, as a minimum, at the time of the DSUR and (post-authorization) the PSUR. Close, procedural and timely interactions between Regulatory Affairs, Clinical and Pharmacovigilance/Drug Safety are necessary to ensure appropriate safety risk management of products

Pharmacoepidemiology is a key discipline for understanding the safety of medicines. It is also being increasingly recognised as a practical tool for supporting risk management and in planning safety activities at the time medicines are authorised. The course focuses on development of

practical skills and it would benefit staff across industry, regulatory authorities and academia. This introduction will be suitable both for those with no previous experience in pharmacoepidemiology, as well as those with basic knowledge that they wish to expand. Pharmacoepidemiology is a public health discipline that relies on nonexperimental (epidemiologic) methods to assess wanted and unwanted drug effects to support decision-makers in the absence of specific evidence from experimental studies (randomized controlled trials). This will provide an introduction and overview of pharmacoepidemiologic methods, databases and review examples of current research. From case reports to cohort studies, the course will look at specific aspects and potential pitfalls of epidemiologic study designs when applied to the study of drug effects, including the use of administrative databases and novel methods to control for selection bias and confounding.

Learning Outcomes:

After completion of the course students are expected to be able to:

- Analyze the EU regulatory requirements for pharmacovigilance, critically evaluate GVPs and compare and contrast these requirements with other ICH regions
- Critically appraise the roles of the various stakeholders in pharmacovigilance including the role of the EUQPPV
- Distinguish the pharmacovigilance documentation (single case reports, DSUR and PSUR), tools and procedures pre- and post-approval, including Risk Management plan (RMP) handling during the lifecycle of a medicinal product
- Explain the regulatory need for, and implications of benefit-risk assessment of a medicinal product throughout its lifecycle, and describe the regulatory contribution to, and actions resulting from, such assessments
- Devise and co-ordinate appropriate communications to relevant stakeholders on new pharmacovigilance information (e.g from non clinical and clinical study findings)
- Critically discuss the concept of pharmacoepidemiology and compare and contrast typical pharmacoepidemiologic study designs (methods of data collection and design) and explain strengths and weaknesses, and their role in drug safety surveillance and comparative drug effectiveness and safety.
- Debate the threats to validity that are possible in pharmacoepidemiology studies and the variety of solutions available to avert or control for these threats, including understanding the issues involved in selecting sample and recruiting participants.

Course Content:

Introduction to pharmacovigilance:

- From preclinical safety to clinical safety.
- Benefit-risk evaluation in the clinical development and postmarketing phases
- Historical aspects and evolution of drug safety

- Basic terminology and key concepts
- Reporting obligations and definitions
- Seriousness, (Un-)Expectedness, (Un-)Labelled, Spontaneous/(Un-) Solicited, Case origin (clinical trials/marketed product)s), Causality assessment, Periodic Safety Reports (PSUR/DSUR): structure, content, planning, follow-up, National, EU, ICH
- Principles of causality
- Regulatory aspects, including the Clinical Trials Directive
- International Conference on Harmonisation

Pharmacovigilance Regulatory and Procedural Requirements

- Collecting and reporting drug safety information
- Pharmacovigilance planning
- Development of Good Pharmacovigilance Practices (GVP)
- Timetable for implementation and requirements of GVP
- Pharmacovigilance System Master Files
- Reporting of adverse drug reactions; reporting requirements, procedures and roles of stakeholders
- Update of PBRERs, Risk Management Plans and PASS
- Inspections; demonstration of compliance
- Monitoring Safety in Clinical Trials and Drug Development
- Pharmacovigilance planning and monitoring in drug development, including communication to trial subjects
- Development of labelling – the developmental core safety information through to the core data sheet and SPC
- Risk management in drug development – planning and risk minimisation • Monitoring safety in clinical trials
- Reporting to EudraVigilance
- Future drug safety regulatory challenges on the horizon for clinical trials and drug development
- European and national legal and administrative aspects and responsibilities
- Role of Pharmacovigilance Risk Assessment Committee (PRAC) Information exchange within Europe
- Information exchange beyond Europe
- Inspections

Obligations of Marketing Authorisation Holders and Competent Authorities

- Qualified Person for Pharmacovigilance (QPPV)
- Quality system requirements
- Company Core Safety Information (CCSI)
- Company Core Data Sheet (CCDS)
- Relationship to SmPC

Regulatory action and procedures, Safety variations

- Periodic Safety Update Report (PSUR) and Periodic Benefit-Risk Evaluation Report (PBRER) •

- Rationale for writing PSURs/PBRERs • Format and content of PSURs/PBRERs • Planning, writing and reviewing of PSURs and PBRERs
- Risk communication (e.g. direct healthcare professionals communication)
- Benefit-risk communication to all stakeholders (why, what and when) Building the concept of safe use of medicinal products
- Benefit-risk by indication at the individual and population level Pharmacovigilance crisis management

Pharmacovigilance Planning and Risk Management

- Current regulations and guidance relevant to global risk management • Safety specification and pharmacovigilance planning • Risk management activities and the drug development programme • Stakeholder perspectives on construction and execution of risk management plans • Workshops to analyse recent challenges in the implementation of risk management plans • Development of best practice techniques • Management of drug safety after reclassification
- Assessment and Medical Evaluation of Individual Case Safety Reports •
- Assessment of reports from various sources both from a regulatory and a clinical perspective • Evaluation of a cluster of reports/ case series • Coding of atypical events • Current and future requirements for the production of case narratives

Risk Benefit Assessment in Pharmacovigilance •

- Principles of risk benefit assessment and management
- Implications of the EU PV Legislation
- Evaluating signals
- Reporting and summarising safety data at registration and for the periodic safety report
- Variations, urgent safety restrictions, licence suspension and withdrawal Regulations and guidelines governing risk benefit
- Methods and tools for formal risk benefit assessment
- SPCs and PILs
- DSMBs and crisis management

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Monitoring the Effectiveness of Risk Minimisation
Pharmacoepidemiology

- Overview of study designs for pharmacoepidemiology
- Measurements in pharamacoepidemiology - including outcomes, exposures, co-variates and issues of validation
- Study methods and data resources
- Interpretation of pharmacoepidemiological data

- Use of pharmacoepidemiology in the detection and investigation of signals
- Pharmacoepidemiology and risk management planning
- Public health, clinical trials of drugs, experimental and observational studies, causality, epidemiological study design, the outcome of pharmacotherapy (efficacy and effectiveness), meta-analyses, random and systematic errors (bias), confounders, statistical analysis and register epidemiology.
- The practicalities of study design and subsequent feasibility testing
- Overview of data resources for pharmacoepidemiology & factors covering the choice of database
- Overview of methods for handling bias and confounding - including matching, regression models and propensity scores
- The practicalities of data analysis using data from the General Practice Research Database
- Overview of clinical trials in pharmacoepidemiology, including real world randomisation
- Use of registries in pharmacoepidemiology
- Meta-analysis - overview and practical application
- Development of quantitative harm-benefit models
- Overview of methods for dealing with missing data in pharmacoepidemiology studies

Learning Activities and Teaching Methods:

Teaching material including PowerPoint presentations with extended descriptions and explanations, asynchronous video presentations, additional readings (journal articles and ebooks), access to additional videos related to the course, synchronous meetings (WebEx), forums, chats, quizzes, case studies, wikis, and major assignments.

Assessment Methods:

Continuous Assessment (major assignments and weekly activities), Final Exam

Required Textbooks / Readings:

Title	Author(s)	Publisher	Year	ISBN
Understanding Pharmacoepidemiology. Eds.	Yang Y, West-Strum D	McGraw Hill, New York	2011	9780071766678

Regulation 726/2004EC		EMA		
Directive 2001/83EC		EMA		
Individual Case Safety Report (ICSR)1 Implementation Guide March 2021 EMA/51938/2013 Rev 2* EU		EMA	2013	
Stephens' Detection and Evaluation of Adverse Drug Reactions : Principles and Practice 6th edition.	John Talbot, Jeffrey K. Aronson, and M. D. B. Stephens	Wiley		9780470986349 |Online ISBN:9780470975053
Pharmacoepidemiology; 5th Edition.	Eds. Strom BL, Kimmel SE, Hennessy S	Wiley	2012	9781119413417 |Online ISBN:9781119413431
Mann's Pharmacovigilance, 3rd Edition,	Elizabeth B. Andrews (Editor), Nicholas Moore (Editor),	Wiley-Blackwell	2014	9780470671047 Online ISBN:9781118820186
Cobert's Manual of Drug Safety and Pharmacovigilance, 2nd Edition	Barton Cobert	Jones & Bartlett Publishers	2011	9780763791599
WHO & ICH Guidelines in Pharmacovigilance				