First Edition

A PRACTICAL GUIDE ON

PHARMACOVIGILANCE FOR BEGINNERS

DR.S.GUNASAKARAN, MBBS, MD
R.SATHEESH KUMAR, M.PHARM

A Practical Guide on Pharmacovigilance for Beginners

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PREFACE

The Authors are pleased to present the First edition of "A Practical Guide on Pharmacovigilance for Beginners". This book is sketched to provide a concise introduction along with practical applications of pharmacovigilance that medical students, post graduates in pharmacology, pharmacy students and life science graduates can impart during their academics as well as during their industrial exposures. This book is expected to provide basic knowledge about the different aspects concerning adverse event reporting and will be an eye opener for beginners who step into the field of pharmacovigilance.

This book details the global and domestic aspects of pharmacovigilance, various drug regulatory bodies guidelines governing the pharmacovigilance, and different reporting systems prevailing among various regulatory agencies along with detailed description of the standard terminologies used in the field of pharmacovigilance. It also covers interesting case scenarios to ignite the minds of bibliomaniacs – the future critiques of this book.

Each chapter is thoughtfully developed to help the reader understand the fundamentals of pharmacovigilance. We are greatly honor-bound to our colleagues who showed interests, encouragement & enthusiasm by devoting their precious time in shape the dream into reality.

Further suggestions, criticisms and elucidation are always welcome from the students and readers, which may be addressed to the author's desk at

Dr.S.Gunasakaran, MBBS, MD
Ph : + 91 98413 12609

Email : drgunasakaran@gmail.com

(Or)

Mr. Satheesh kumar, M.Pharm
Ph : + 91 94431 60516

Email : satheesh_r2001@yahoo.com

AUTHOR'S DESK

With accomplishment of my M.D. Pharmacology from prestigious Madras Medical College and with a couple of years experience in the Pharmacovigilance field, I have desired to pen down my thought-provoking vision and knowledge of Pharmacovigilance to the beginners. Though several books are available in the meadow of pharmacovigilance, I tried to define this book with much versatility and significance.

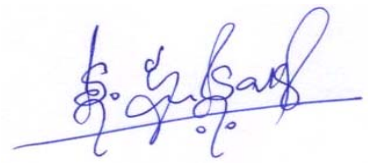
Every person who reads would get their feet wet and definitely persuade in the field of Pharmacovigilance. The book is concise, influencing the beginners to understand the concept meticulously.

This book intends to motivate the students for exploring the depth of this field by answering the ample case studies which will give basic insights to assess an adverse event and mode of reporting to the regulatory agencies. The supporting concept of this book is that, it provides answers to all exercise based questions and case scenarios.

My contribution may be a drop to the ocean of pharmacovigilance but the entire journey of collecting knowledge to exhibit this book flooded me with an ocean of knowledge and clarity about Pharmacovigilance.

The students and professionals who are yet to step into the industrial endeavors may not sense the feel of aliens and may outburst the ignorance in the course of reading this book.

The major objective of writing this book is to present the basic information about pharmacovigilance in a lucid, coherent, condensed and consistent form to furnish the innovative minds of graduates and post graduates of pharmacy, life sciences and medical fields.



AUTHOR'S DESK

From the knowledge acquired through my Masters in Pharmacy from the esteemed Annamalai University and with my experience in the field of Pharmacovigilance, I preferred to share my knowledge in the field of Pharmacovigilance to the young scientists who would like to establish their career in Pharmacovigilance.

Though several resources are available to gain knowledge in Pharmacovigilance, I felt that there was a space left between the beginners and the resources available. This thought provoked me to author a book which would be a big boon for the beginners.

This book contains the fundamentals of Pharmacovigilance, guidance to access the essential resources and exercises to provide hands on experience on various aspects of Pharmacovigilance.

This way I would like to differentiate this book "Practical Guide on Pharmacovigilance for Beginners" from the other resources available. A person who grazes through the book would develop an idea of establishing his / her career in the field of Pharmacovigilance.

This book helps the beginners to understand the concepts of Pharmacovigilance scrupulously.

The passion for persuading in the Pharmacovigilance field for students will increase as they go through the various case studies dealing from the basic concepts of Pharmacovigilance through assessment and reporting of adverse events to various regulatory authorities This process is made easy by providing answers to all exercise based questions.

R. Sathish Kumar

ACKNOWLEDGEMENTS

It is with great pleasure, we record our deep respects, gratitude and indebtedness to Dr. Vikas soni, MD, Orchid Chemicals and Pharmaceuticals, for his remarkable guidance, encouragement and selfless support which enabled us to pursue the work with perseverance and a skillful mind to view and analyze things. His contagious enthusiasm was a source of energy to us in successfully completing this book under this generous guidance.

We wish to express our sincere and heartful thanks to Mr. Ragavendra Rao, Managing Director, Orchid Chemicals and Pharmaceuticals and Dr. C.B.Rao, Deputy Managing Director, Orchid Chemicals and Pharmaceuticals for their untiring support, continuous suggestions and enduring encouragement in writing this book.

We extend our sincere thanks and gratitude to our contributory author Dr. Praveena Pearl, MD for her contribution in writing the chapter “Global perspective of Pharmacovigilance“.

Our wholehearted thanks and gratitude to Dr. Abdul Hameed Khan, Mr. Srinivasa Reddy, Mrs. Narmadha Vijayaraja, Ms. Veena and Dr. Mohammad Shahid for their encouragement and continuous help in bringing out this book.

We also extend our sincere thanks to our family members (Mrs.Radha Sambandan, Er.Inbasakaran, BE, ME, Mrs.Priyadarsini Inbasakaran, Mrs. Sakthi Satheesh & Ms. Deeksha) and our friends for their appropriate suggestions, moral support and timely adjustments in bringing out this book.

We also extend our personal thanks and gratefulness to all professors and directors who enlightened us during our graduation and post graduation studies.

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CHAPTER 1

CHAPTER 1

STANDARD TERMS AND DEFINITIONS IN PHARMACOVIGILANCE

This chapter discuss in detail about the various standard terminologies and definitions used in adverse event reporting system and pharmacovigilance. The standard terms are defined based on various drug regulatory guidelines and modified for better ease of understanding to the readers. The glossary of terms described here covers most of the terminologies which are in use in the field of pharmacovigilance and risk management.

Pharmacovigilance

WHO defines Pharmacovigilance as "the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems."

Pharmacovigilance is the process and science of monitoring the safety of medicines and taking action to reduce risks and increase benefits from medicines.

Drug

A drug includes any substance or mixture of substances manufactured, sold or represented for use in:

- the diagnosis, treatment, mitigation or prevention of a disease, disorder or
- abnormal physical state, or its symptoms, in human beings or animals,
- restoring, correcting or modifying organic functions in human beings or animals, or disinfection in premises in which food is manufactured, prepared or kept.

Adverse Event (or Adverse Experience)
Any untoward medical occurrence in a patient or clinical investigation subject administered a pharmaceutical product and which does not necessarily have to have a causal relationship with this treatment.

An adverse event (AE) can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding, for example), symptom, or disease temporally associated with the use of a medicinal product, whether or not considered related to the medicinal product.

Adverse Drug Reaction (ADR)
In the pre-approval clinical experience with a new medicinal product or its new usages, particularly as the therapeutic dose(s) may not be established:
all noxious and unintended responses to a medicinal product related to any dose should be considered adverse drug reactions.

The phrase "responses to a medicinal product" means that a causal relationship between a medicinal product and an adverse event is at least a reasonable possibility, i.e., the relationship cannot be ruled out.

Regarding marketed medicinal products, a well-accepted definition of an adverse drug reaction in the post-marketing setting is found in WHO Technical Report 498 [1972] and reads as follows:

A response to a drug which is noxious and unintended and which occurs at doses normally used in man for prophylaxis, diagnosis, or therapy of disease or for modification of physiological function.

Unlisted / Unexpected Adverse Drug Reaction
An adverse reaction, the nature or severity of which is not consistent with the applicable product information (e.g., Investigator's Brochure for an unapproved investigational medicinal product and prescribing information / Summary of Product Characteristics (SmPC) for marketed products).

Listed / Expected Adverse Drug Reaction
An ADR whose nature, severity, specificity, and outcome are consistent with the information in the CCSI.

Challenge
Administration of a suspect product by any route.

Dechallenge
Withdrawal of a suspect product from a patient's therapeutic regimen.

Negative Dechallenge
Continued presence of an adverse experience after withdrawal of the suspect product.

Positive Dechallenge
Partial or complete disappearance of an adverse experience after withdrawal of the suspect product.

Rechallenge
Reintroduction of a suspect product suspected of having caused an adverse experience following a positive dechallenge.

Negative Rechallenge
Failure of the product, when reintroduced, to produce signs or symptoms similar to those observed when the suspect product was previously introduced.

Positive Rechallenge
Reoccurrence of similar signs and symptoms upon reintroduction of the suspect product.

Serious Adverse Event or Adverse Drug Reaction
A serious adverse event (experience) or reaction is any untoward medical occurrence that at any dose:

* results in death,
* is life-threatening,

The term "life-threatening" in the definition of "serious" refers to an event in which the patient was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

* requires inpatient hospitalisation or prolongation of existing hospitalisation,
* results in persistent or significant disability/incapacity,
* is a congenital anomaly/birth defect.

CASE SCENARIOS

Case scenarios:

Case 1

A Dermatologist called KA pharmaceuticals and reported that a 21 year old male patient named Johnson had urticaria after intake of Terbinafine tablets.

Check the criteria of identifiable patient in this case.

	Yes	No
1. Name/Initials	☐	☐
2. Patient ID	☐	☐
3. Age /D.O.B	☐	☐
4. Age category	☐	☐
5. Sex	☐	☐

Whether this case report fulfills the criteria of an identifiable patient..?

Yes/No

Case 2

Dr. Johnson mailed PJ pharmaceuticals that a young man complained of severe abdominal pain after the intake of amoxicillin tablets.

Check the criteria of identifiable patient in this case.

	Yes	No
1. Name/Initials	☐	☐
2. Patient ID	☐	☐
3. Age /D.O.B	☐	☐
4. Age category	☐	☐
5. Sex	☐	☐

Whether this case report fulfills the criteria of an identifiable patient..?

Yes/No

Case 9

A Physician called CFC pharmaceuticals and informed that few patients complained of severe burning sensation at the injection site after administration of methylcobalamin injection in the gluteal region in the past one week.

Check the criteria of identifiable patient in this case.

	Yes	No
1. Name/Initials	□	□
2. Patient ID	□	□
3. Age /D.O.B	□	□
4. Age category	□	□
5. Sex	□	□

Whether this case report fulfills the criteria of an identifiable patient..?

Yes / No

Case 10

A nurse informed that a patient named Mr. IK complained of diarrhea after intake of erthyromycin tablets.

Check the criteria of identifiable patient in this case.

	Yes	No
1. Name/Initials	□	□
2. Patient ID	□	□
3. Age /D.O.B	□	□
4. Age category	□	□
5. Sex	□	□

Whether this case report fulfills the criteria of an identifiable patient..?

Yes / No

Case 70

A published article states that 2 cancer patients was admitted in a multispecality hospital in Mexico with history of metastatic carinoid tumors for the past 3 years. Treatment with octreotide was started at the dose of 100-600 mcg per day in 2-4 divided doses. One of the patient complained of tremors, palpitations and giddiness 20 min after the intravenous infusion of octreotide Assess the case based on the Product Information provided in the next page.

Check the criteria of reportability:

	Yes	No
• Identifiable patient	☐	☐
• Identifiable source	☐	☐
• Suspect medication	☐	☐
• Event / outcome	☐	☐

Whether this case is reportable or not..?
Yes / No

Assessment of seriousness:

Serious ☐ Non-serious ☐

If serious, check the appropriate box (es) below:

- Death ☐
- Life-threatening ☐
- Hospitalization – Initial or prolonged ☐
- Disability or permanent damage ☐
- Required intervention to prevent permanent impairment damage (device) ☐
- Congenital anomaly with child ☐
- Other serious (important medical events) ☐

Assessment of Expectedness:

Expected ☐ Unexpected ☐

Product information of Octerotide:

Hypo/Hyperglycemia
Hypoglycemia and hyperglycemia occurred in 3% and 16% of acromegalic patients, respectively, but only in about 1.5% of other patients. Symptoms of hypoglycemia were noted in approximately 2% of patients.

Hypothyroidism
In acromegalics, biochemical hypothyroidism alone occurred in 12% while goiter occurred in 6% during Sandostatin therapy. In patients without acromegaly, hypothyroidism has only been reported in several isolated patients and goiter has not been reported.

Pain on injection was reported in 7.7%, headache in 6% and dizziness in 5%. Pancreatitis was also.

Adverse Events 1%-4%
Other events (relationship to drug not established), each observed in 1%-4% of patients, included fatigue, weakness, pruritus, joint pain, backache, urinary tract infection, cold symptoms, flu symptoms, injection site hematoma, bruise, edema, flushing, blurred vision, pollakiuria, fat malabsorption, hair loss, visual disturbance and depression.

Adverse Events < 1%
Events reported in less than 1% of patients and for which relationship to drug is not established are listed: Gastrointestinal: hepatitis, jaundice, increase in liver enzymes, GI bleeding, hemorrhoids, appendicitis, gastric/peptic ulcer, gallbladder polyp; Integumentary: rash, cellulitis, petechiae, urticaria, basal cell carcinoma; Musculoskeletal: arthritis, joint effusion, muscle pain, Raynaud's phenomenon; Cardiovascular: chest pain, shortness of breath, thrombophlebitis, ischemia, congestive heart failure, hypertension, hypertensive reaction, palpitations, orthostatic BP decrease, tachycardia; CNS: anxiety, libido decrease, syncope, tremor, seizure, vertigo, Bell's Palsy, paranoia, pituitary apoplexy, increased intraocular pressure, amnesia, hearing loss, neuritis; Respiratory: pneumonia, pulmonary nodule, status asthmaticus; Endocrine: galactorrhea, hypoadrenalism, diabetes insipidus, gynecomastia, amenorrhea, polymenorrhea, oligomenorrhea

Case 71

A Scientific literature states that a 45 year old male patient who was suffering from parkinsonism for the past 2 years was started with Ropinirole 2mg extended release tablets once daily. After two weeks, the dose of Ropinirole was incremented at the rate of 2mg/day. The patient experienced hallucinations, dyskinesia and dizziness after the titration of dosage. Assess the case based on the Product Information provided in the next page.

Check the criteria of reportability:

	Yes	No
• Identifiable patient	☐	☐
• Identifiable source	☐	☐
• Suspect medication	☐	☐
• Event / outcome	☐	☐

Whether this case is reportable or not..?

Yes / No

Assessment of seriousness:

Serious ☐ Non-serious ☐

If serious, check the appropriate box (es) below:

- Death ☐
- Life-threatening ☐
- Hospitalization – Initial or prolonged ☐
- Disability or permanent damage ☐
- Required intervention to prevent permanent impairment damage (device) ☐
- Congenital anomaly with child ☐
- Other serious (important medical events) ☐

Assessment of Expectedness:

Expected ☐ Unexpected ☐

Product Information of Ropinirole Extended Release Tablets:

The following adverse reactions are described in the product information label:

- Falling asleep during activities of daily living
- Syncope
- Symptomatic hypotension, hypotension, postural/orthostatic hypotension
- Elevation of blood pressure and changes in heart rate
- Hallucination
- Dyskinesia
- Major psychotic disorders
- Events with dopaminergic therapy
- Retinal pathology

Cardiovascular: palpitation, vasodilation, tachycardia, heart failure, hyperkalemia, myocardial infarction, cerebrovascular accident, hypertensive crisis, angina pectoris, orthostatic hypotension, cardiac rhythm disturbances, cardiogenic shock

Hematology: hemolytic anemia

Gastrointestinal: flatulence, dry mouth or throat, constipation, gastrointestinal hemorrhage, pancreatitis, abnormal liver function tests, dyspepsia

Nervous/Psychiatric: somnolence, vertigo, syncope, nervousness, depression, insomnia, paresthesia

Integumentary: alopecia, increased sweating, pemphigus, pruritus, exfoliative dermatitis, photosensitivity reaction, dermatopolymyositis

The incidence of adverse reactions was not clearly different between women and men.

Case 103

Dr. Viswanthan M.D. D.M., a cardiologist prescribed digoxin tablets for 56 year old male suffering from grade II congestive cardiac failure according to NYHA classification. 3 days after the initiation of therapy the patient complained shortness of breath, chest pain, dizziness, nausea, nervousness and feelings of impending doom. On auscultation, the heart rate found to be 240 beats / min. The plasma concentration of digoxin is found to be 12 microgram / ml. EEG showed characteristic features of type I atrial flutter. Cardioversion was done to revert back to sinus rhythm. Atrial flutter was not mentioned in the product information of digoxin.

Check the criteria of reportability:

	Yes	No
• Identifiable patient	☐	☐
• Identifiable source	☐	☐
• Suspect medication	☐	☐
• Event / outcome	☐	☐

Whether this case is reportable or not..? Yes / No

Assessment of seriousness:

Serious ☐ Non-serious ☐

If serious, check the appropriate box (es) below:

- Death ☐
- Life-threatening ☐
- Hospitalization – Initial or prolonged ☐
- Disability or permanent damage ☐
- Required intervention to prevent permanent impairment damage (device) ☐
- Congenital anomaly with child ☐
- Other serious (important medical events) ☐

Assessment of Expectedness:

Expected ☐ Unexpected ☐

Encircle the appropriate score:

Questions	Yes	No	Unsure
Previous conclusive reports on this reaction	+1	0	0
Did the ADR appear after the suspected drug was administered?	+2	-1	0
Did ADR improve when the drug was discontinued or a specific antagonist was given	+1	0	0
ADR appearance after drug readministration	+2	-1	0
Are there alternative causes other than the incriminated drug	-1	+2	0
Did the reaction appear when placebo was given?	-1	+1	0
Was the drug detected in blood at toxic levels?	+1	0	0
ADR more severe with large dose, less severe with small dose	+1	0	0
Did the patient have a similar reaction to the same or similar drug in any previous exposure?	+1	0	0
Was the ADR confirmed by any objective evidence?	+1	0	0
Total Score			

Naranjo's score: .....

Causality assessment: Doubtful / possible / probable / definite

WHO probability scale: Certain / probable / possible / unlikely / unclassified / unassessable

Time frame of reporting to licensing authority

Expedited 7 days □ Expedited 15 days □ PSUR □ DSUR □

Case 104

A 72 year old female patient suffering from nosocomial pneumonia was admitted in ICU of Chennai Medical centre. She was started on intravenous ceftriaxone 2 g twice daily along with amikacin intramuscular injection. The patient complained nausea, dyspepsia, giddiness and blurring of vision two days later. The physician reduced the dose of ceftriaxone to 1 g in two divided dose daily. The symptoms resolved and the patient had mild nauseating sensation only. All the foresaid side effects are mentioned in the summary of product characteristics of ceftriaxone injection.

Check the criteria of reportability:

	Yes	No
• Identifiable patient	☐	☐
• Identifiable source	☐	☐
• Suspect medication	☐	☐
• Event / outcome	☐	☐

Whether this case is reportable or not..? Yes / No

Assessment of seriousness:

Serious ☐ Non-serious ☐

If serious, check the appropriate box (es) below:

- Death ☐
- Life-threatening ☐
- Hospitalization – Initial or prolonged ☐
- Disability or permanent damage ☐
- Required intervention to prevent permanent impairment damage (device) ☐
- Congenital anomaly with child ☐
- Other serious (important medical events) ☐

Assessment of Expectedness:

Expected ☐ Unexpected ☐

Encircle the appropriate score:

Questions	Yes	No	Unsure
Previous conclusive reports on this reaction	+1	0	0
Did the ADR appear after the suspected drug was administered?	+2	-1	0
Did ADR improve when the drug was discontinued or a specific antagonist was given	+1	0	0
ADR appearance after drug readministration	+2	-1	0
Are there alternative causes other than the incriminated drug	-1	+2	0
Did the reaction appear when placebo was given?	-1	+1	0
Was the drug detected in blood at toxic levels?	+1	0	0
ADR more severe with large dose, less severe with small dose	+1	0	0
Did the patient have a similar reaction to the same or similar drug in any previous exposure?	+1	0	0
Was the ADR confirmed by any objective evidence?	+1	0	0
Total Score			

Naranjo's score: .....

Causality assessment: Doubtful / possible / probable / definite

WHO probability scale: Certain / probable / possible / unlikely / unclassified / unassessable

Time frame of reporting to licensing authority

Expedited 7 days □ Expedited 15 days □ PSUR □ DSUR □

Case 105

A scientific literature states that a 47 year old male patient was prescribed cephalexin capsules 500 mg twice daily for the treatment of upper respiratory tract infections. Ten minutes after the intake of cephalexin capsule the patient developed itching, eczema, tightness in the chest and hypotension. He was rushed to the nearby hospital. The drug was discontinued and was given symptomatic treatment for anaphylactic reaction. The family physician noted that the patient had previous history of hypersensitivity to penicillin two years back. The patient had no relevant medical or treatment history.

Check the criteria of reportability:

	Yes	No
• Identifiable patient	☐	☐
• Identifiable source	☐	☐
• Suspect medication	☐	☐
• Event / outcome	☐	☐

Whether this case is reportable or not..? Yes / No

Assessment of seriousness:

Serious ☐ Non-serious ☐

If serious, check the appropriate box (es) below:

- Death ☐
- Life-threatening ☐
- Hospitalization – Initial or prolonged ☐
- Disability or permanent damage ☐
- Required intervention to prevent permanent impairment damage (device) ☐
- Congenital anomaly with child ☐
- Other serious (important medical events) ☐

Assessment of Expectedness:

Expected ☐ Unexpected ☐

Encircle the appropriate score:

Questions	Yes	No	Unsure
Previous conclusive reports on this reaction	+1	0	0
Did the ADR appear after the suspected drug was administered?	+2	-1	0
Did ADR improve when the drug was discontinued or a specific antagonist was given	+1	0	0
ADR appearance after drug readministration	+2	-1	0
Are there alternative causes other than the incriminated drug	-1	+2	0
Did the reaction appear when placebo was given?	-1	+1	0
Was the drug detected in blood at toxic levels?	+1	0	0
ADR more severe with large dose, less severe with small dose	+1	0	0
Did the patient have a similar reaction to the same or similar drug in any previous exposure?	+1	0	0
Was the ADR confirmed by any objective evidence?	+1	0	0
Total Score			

Naranjo's score: .....

Causality assessment: Doubtful / possible / probable / definite

WHO probability scale: Certain / probable / possible / unlikely / unclassified / unassessable

Time frame of reporting to licensing authority

Expedited 7 days □ Expedited 15 days □ PSUR □ DSUR □

Case 106

Dr. Alexander called LND laboratories and informed that his 55 year old known hypertensive patient was on enalapril 5 mg once daily for the past two years. On routine follow up, his blood pressure was found to be 154 / 96 mmHg. The physician added 5 mg amlodipine besylate twice daily along with enalapril. Two days after the initiaton of treatment with amlodipine, the patient experienced anorexia, constipation, dyspepsia, dysphagia and dysuria. The patient called upon his family physician and informed him of the adverse reactions. The physician advised him to reduce the dose of amlodipine 5 mg to once daily. The symptoms resolved on the next day of reduction of dosage. Assess the case based on the product information provided in the next page.

Check the criteria of reportability:

	Yes	No
• Identifiable patient	☐	☐
• Identifiable source	☐	☐
• Suspect medication	☐	☐
• Event / outcome	☐	☐

Whether this case is reportable or not..? Yes / No

Assessment of seriousness:

Serious ☐ Non-serious ☐

If serious, check the appropriate box (es) below:

- Death ☐
- Life-threatening ☐
- Hospitalization – Initial or prolonged ☐
- Disability or permanent damage ☐
- Required intervention to prevent permanent impairment damage (device) ☐
- Congenital anomaly with child ☐
- Other serious (important medical events) ☐

Assessment of Expectedness:

Expected ☐ Unexpected ☐

Encircle the appropriate score:

Questions	Yes	No	Unsure
Previous conclusive reports on this reaction	+1	0	0
Did the ADR appear after the suspected drug was administered?	+2	-1	0
Did ADR improve when the drug was discontinued or a specific antagonist was given	+1	0	0
ADR appearance after drug readministration	+2	-1	0
Are there alternative causes other than the incriminated drug	-1	+2	0
Did the reaction appear when placebo was given?	-1	+1	0
Was the drug detected in blood at toxic levels?	+1	0	0
ADR more severe with large dose, less severe with small dose	+1	0	0
Did the patient have a similar reaction to the same or similar drug in any previous exposure?	+1	0	0
Was the ADR confirmed by any objective evidence?	+1	0	0
Total Score			

Naranjo's score: .....

Causality assessment: Doubtful / possible / probable / definite

WHO probability scale: Certain / probable / possible / unlikely / unclassified / unassessable

Time frame of reporting to licensing authority

Expedited 7 days □ Expedited 15 days □ PSUR □ DSUR □

The following adverse events are listed in the product information of amlodipine besylate:

Cardiovascular: arrhythmia (including ventricular tachycardia and atrial fibrillation), bradycardia, chest pain, hypotension, peripheral ischemia, syncope, tachycardia, postural dizziness, postural hypotension, vasculitis.

Central and Peripheral Nervous System: hypoesthesia, neuropathy peripheral, paresthesia, tremor, vertigo.

Gastrointestinal: anorexia, constipation, dyspepsia, dysphagia, diarrhea, flatulence, pancreatitis, vomiting, gingival hyperplasia.

General: allergic reaction, asthenia, back pain, hot flushes, malaise, pain, rigors, weight gain, weight decrease.

Musculoskeletal System: arthralgia, arthrosis, muscle cramps, myalgia.

Psychiatric: sexual dysfunction, insomnia, nervousness, depression, abnormal dreams, anxiety, depersonalization.

Respiratory System: dyspnea, epistaxis.

Skin and Appendages: angioedema, erythema multiforme, pruritus, rash, rash erythematous, rash maculopapular.

Special Senses: abnormal vision, conjunctivitis, diplopia, eye pain, tinnitus.

Urinary System: micturition frequency, micturition disorder, nocturia.

Autonomic Nervous System: dry mouth, sweating increased.

Metabolic and Nutritional: hyperglycemia, thirst.

Hemopoietic: leukopenia, purpura, thrombocytopenia

The following events occurred in <0.1% of patients: cardiac failure, pulse irregularity, extrasystoles, skin discoloration, urticaria, skin dryness, alopecia, dermatitis, muscle weakness, twitching, ataxia, hypertonia, migraine, cold and clammy skin, apathy, agitation, amnesia, gastritis, increased appetite, loose stools, coughing, rhinitis, dysuria, polyuria,

parosmia, taste perversion, abnormal visual accommodation, and xerophthalmia.

Other reactions occurred sporadically and cannot be distinguished from medications or concurrent disease states such as myocardial infarction and angina.

Amlodipine therapy has not been associated with clinically significant changes in routine laboratory tests. No clinically relevant changes were noted in serum potassium, serum glucose, total triglycerides, total cholesterol, HDL cholesterol, uric acid, blood urea nitrogen, or creatinine.

In the clinical studies conducted in patients with coronary artery disease, the adverse event profile was similar to that reported previously, with the most common adverse event being peripheral edema.

The following post-marketing event has been reported infrequently where a causal relationship is uncertain: gynecomastia. In post-marketing experience, jaundice and hepatic enzyme elevations (mostly consistent with cholestasis or hepatitis) in some cases severe enough to require hospitalization have been reported in association with use of amlodipine.

Amlodipine has been used safely in patients with chronic obstructive pulmonary disease, well-compensated congestive heart failure, coronary artery disease, peripheral vascular disease, diabetes mellitus, and abnormal lipid profiles.

Assessment of case report as a Reportable one or Not

There are minimum requirements need to be present in the case reports for reportability such as

1. Identifiable patient
2. Identifiable source
3. Suspect medication(s)
4. An Event or Outcome

Identifiable patient and Identifiable Source:

The identifiablility of the patient and reporter is important to avoid duplication of cases, detection of fraudulent ones, and facilitation of follow-up of appropriate genuine cases.

A patient can be identified either by

- Initials/Name
- Age/Date of Birth (D.O.B)
- Age category
- Sex/gender
- Patient Identification number

The sources of information can be categorized into primary and secondary source. The primary reporting source(s) of the information is a person/source from which an adverse event report arises. Secondary sources are the one who will transmit the information (e.g., industry to regulatory authority).

The identifiable reporting source may be any one of the following

- Consumers
- Health care professionals
- Lawyers
- Care takers
- Literature reports
- Clinical study reports etc

Suspect Medicinal Product:

A Suspect medicinal product is the one which is suspected at first to be the reason for the reported adverse event.

An Event or Outcome:
An event or outcome should be present for the case to be reportable to the regulatory authorities.

All the above four criteria should be present to make the adverse event as reportable one. In some cases, both the reporting source and identifiable patient will be the same.

Exercise 5:

Dr. Dinesh called TH manufacturers and stated that 21 year old male patient had rigor after administration of tablet diclofenac manufactured by them, which is also marketed in US. As a Medical affairs executive,

- To which regulatory body will you report this case?

  (a) DCGI

  (b) FDA

  (c) Both

Exercise 6:

Dr. Ramachandran, MD called LEL drug pharmaceuticals and stated that 29 year old female patient had giddiness, vomiting and shortness of breath after administration of codeine cough syrup manufactured by them, which is also marketed in US.

- *Which forms need to be filled in this case?*

  (a) *MedWatch 3500*

  (b) *MedWatch 3500 A*

  (c) *SADRRF*

  (d) Both a and c

  (e) Both b and c

Dr.S.Gunasakaran, MD

Satheesh kumar,MPharm

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