Interview Questions & Answer for Pharmacovigilance

1. What is Pharmacovigilance?

According to WHO, Pharmacovigilance is defined as the Science And Activities Relating To Detection, Assessment, Understanding & Prevention Of Adverse Reactions or any Other Drug Related Problems.

2. Aim of Pharmacovigilance

- Early detection of hitherto unknown adverse reactions and interactions, improvement of patient care and safety.
- Detection of increasing frequency of known adverse reactions.
- Identification of risk factors and possible mechanisms underlying adverse reactions.
- Estimation of quantitative aspects of benefits/risk analysis and dissemination of information needed to improve drug prescribing and regulation.

3. What Are the Types of Pharmacovigilance (pv)?

There are 2 types of PV:

- **Active PV:** It involves active measures to detect the adverse event occurrence after or during the treatment. Patients are directly asked, or patient screening records are checked to find out the any experienced adverse events. The most comprehensive method is cohort event monitoring (CEM)
- **Passive PV:** It won't involve any active measures to detect the adverse events/effects. This is also called as Spontaneous or voluntary reporting. This reporting is mainly depending on initiative and motivation of reporters like Healthcare providers (Doctors, Nurse, Pharmacist etc) and Patients.

4. What Is the Minimum Criterion Required for A Valid Case?

- An identifiable reporter
- An identifiable patient
- A suspect product
- An adverse drug event

Any report which contains the details of only ADR & suspect drug without any information of the details of patient & reporter, such a case is considered as Invalid case.

5. What is GVP?

Good Pharmacovigilance Practices (GVP) are a set of measures drawn up to facilitate the performance of pharmacovigilance in the European Union (EU). GVP apply to marketing-authorisation holders, the European Medicines Agency (EMA) and medicines regulatory authorities in EU Member States. They cover medicines authorised centrally via the Agency as well as medicines authorised at national level.

6. What are the modules associated with GVP

Module I – Pharmacovigilance systems and their quality systems
Module II – Pharmacovigilance system master file
Module III – Pharmacovigilance inspections
Module IV – Pharmacovigilance audits
Module V – Risk management systems
Module VI – Collection, management and submission of reports of suspected adverse reactions to medicinal products
Module VII – Periodic safety update report
Module VIII – Post-authorisation safety studies
Module IX – Signal management
Module X – Additional monitoring
Module XV – Safety communication

7. When were GVP guidelines implemented?

They were implemented from July 2012

8. What is the DSUR Frequency?

The first DSUR period should not be longer than 1 year. The DSUR is always submitted on a yearly basis.

9. 5. What is PADER frequency?

PADERs quarterly during the first 3 years.

10. What is Caveat document?

The formal advisory warning accompanying data release from the WHO Global ICSR Database: it specifies the conditions and reservations applying to interpretations and use of the data.

11. What is Data-mining?

At the UMC, the use of an automated tool, based on Bayesian logic, for the scanning of the WHO database (Vigibase) in the process of detecting drug-adverse reaction associations: the BCPNN. Knowledge-detection is the preferred term for the process.

12. What is an Orphan Drug?

Drug (or biological product) used for the prevention, diagnosis or treatment of a Rare Disease or diagnosis of a disease that is life-threatening or chronically debilitating.

13. Pharmacovigilance centre (PvC):

The PvC of an individual country is responsible for meeting the requirements for pharmacovigilance of all medicines. It is a centre of expertise for the art and science of monitoring and analysis of ADRs, and in use of the information analysed for the benefit of patients. National and regional PvCs should be set up with the approval or involvement of the authority responsible for the regulation of medicines ("regulatory authority"). The centre may function within the regulatory authority, a hospital, an academic institution or as an independent facility such as a trust or foundation.

14. What is Spontaneous reporting?

Spontaneous (or voluntary) reporting means that no active measures are taken to look for adverse effects other than the encouragement of health professionals and others to report safety concerns. Reporting is entirely dependent on the initiative and motivation of the potential reporters. This is the most common form of pharmacovigilance, sometimes termed passive reporting. In some countries this form of reporting is mandatory. Clinicians, pharmacists and community members should be trained on how, when, what and where to report

15. What is Cemflow?

CemFlow is a tool maintained by the UMC for database management in cohort event monitoring (CEM). It is web based and the fields match the data elements on the questionnaires. There are screens for patient demographics, treatment initiation, treatment review and assessment of events. CemFlow as a tool for data entry into an online database maintained by the UMC (Uppsala Monitoring Centre) for CEM. CemFlow provides for entry of cohort data as well as the events.

16. What is Number needed to harm (NNH)?

The number needed to harm (NNH) is an epidemiological measure that indicates how many patients on average need to be exposed to a risk-factor over a specific period to cause harm in an average of one patient who would not otherwise have been harmed. It is defined as the inverse of the attributable risk.

17. What are SSFFCs?

There is currently no universally agreed definition of what used to be widely known as 'Counterfeit medicine'. Since the 70th World Health Assembly in 2017, WHO is using the term "Substandard and Falsified (SF) medical products.

18. What is Post-authorization safety study (PASS)?

A post-authorisation safety study (PASS) is a study that is carried out after a medicine has been authorised to obtain further information on a medicine's safety, or to measure the effectiveness of risk-management measures. The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) is responsible for assessing the protocols of imposed PASSs and for assessing their results.

19. What Is an Adverse Drug Reaction (ADR)?

ADR is defined as response to drug that is noxious and unintended, and it occurs due to normal dose of drug used in men for prophylaxis, diagnosis and therapy of diseases.

20. What is the difference between ADE and ADR?

ADE means noxious and unintended effect of a drug which have causal relationship between suspect drug and adverse event.

ADE (Adverse event) means noxious and unintended effect of a drug which may or may not have any causal relationship between suspect drug and event.

21. What is MedWatch?

A system maintained by the U.S. Food & Drug Administration (FDA) for the voluntary reporting of adverse events, potential and actual medical product errors, and product quality problems associated with the use of FDA-regulated medicines, biologics, devices, and dietary supplements.

22. When do you consider an event to be serious?

i. Death
ii. Life threatening
iii. Hospitalization or prolongation of hospitalization.
iv. Congenital anomaly
v. Disability
vi. Medically significant

23. What are sources of Adverse Event Reports?

i. Clinical Trial/Phase Reports:
ii. Post Marketing Phase Reports:
    - Solicited Reports
    - Spontaneous Reports

Solicited Study Reports: Any study conducted with a marketed product with same intervention but for different indication. Hence, they are also known as Non interventional Studies.

Spontaneous Reports: Any Voluntary reports that is submitted to MAH (Marketing Authorization Holders) or by any Health Care team such as Physicians, Pharmacists, nurses or any other volunteers is called as Spontaneous Reports.

24. TIME LINES:

SUSAR cases should be submitted within **7 Calendar Days**.

All serious cases should be submitted within **15 calendar days**.

All Non serious cases should be submitted within **30 Calendar Days**.

There are no Global Guidelines Regarding Non-Serious Cases.

In the European Region, all non-serious cases should be submitted within **90 Calendar days**, & **According to FDA** the Non-Serious cases should be submitted within **30 calendar days**.

25. What are the due dates for safety reporting?

Safety reporting due dates are 7days for IND Reporting and 15 days for NDA Reporting.

26. Initial receipt date (IRD) / day 0

It is the Day on which we receive the report.

27. What are the Different forms of reporting an ADR/AE?

CIOMS- (Council for International Organization of Medical Sciences). It is used globally.
US- Med Watch (Form 3500)
UK – Yellow Card iv.
Australia- Blue Card
India- SARRF (Suspected Adverse Reaction Reporting Form)

28. What is SUSAR (Suspected Un Expected Serious Adverse Reaction)?

Serious cases can be seen only in clinical trial reports but not in solicited and spontaneous reports. It should be from clinical trial report, would be serious, it is unexpected, and the reports were not found in IB the causality should be possible.

29. Name the regulatory bodies in USA, UK, Japan and India?

USA: United States Food and drug administration (USFDA).
UK: Medicines and Healthcare Product Regulatory Authority (MHRA)
Japan: Ministry of Health, Labour and Welfare (MHLW).
India: Central Drugs Standard Control Organization (CDSCO)
Canada: Health Canada
Australia: Therapeutics Good Administration (TGA)
China: State Food and Drug Administration
Europe: Europe Medicine Agency (EMA)
France: AFSSAPS

30. What is Medically Significant Event?

Medically significant event means, the events may be always serious or sometimes serious but will not fulfil any of the other criteria.

31. When do you consider a case to be medically confirmed?

A case is considered to be medically confirmed if it contains at least one event confirmed or reported by an HCP (Health Care Professional).
Note: HCP can be a physician, nurse, pharmacist, coroner or psychologist (only in Germany).

32. What do you mean by causality?

It is the relationship between Suspect drug and the Adverse Event. Generally, it is of two types:

- Reporters Causality: When Reporter asses the causality towards an event, it is Reporters causality.
- Company causality: When the company assesses the causality, towards an event, it is Company causality.

Causality Assessment Means:

i. WHO UMC (Uppsala Monitoring Centre),
ii. Naranjo Scale,
iii. French Imputability Scale.

WHO UMC (Uppsala Monitoring Centre) Scale: It is most widely used in causality assessment. It involves:

a) **Certain / likely**: Any Adverse Event can only be explained with Drug.
b) **Probable**: Mostly Explained by Drug (95%) and might be less chances of other medical condition (5%) and other factors.
c) **Possible**: We can Assess Drug and Other factors i.e. 50;50
d) **Unlikely**: It is reversal of Probable.
e) **Un classifiable**: We need more information to access the case.
f) **Un assessable**: We cannot make out the Causality assessment with the data i.e. no data is available to assess the causality.

33. Suspect Drug:

The Drug which causes an Adverse Event / Suspects to cause an ADR is known as a Suspect Drug.

34. Co-Suspect Drug:

Drugs Other than the Suspect drug in a case arte known as Co suspect/ non-Company Drug.

35. Concomitant Medication:

It is the Drug, which is taken along with the Suspect Drug, but it is not a Suspect Drug.

36. Treatment Drug:

Drug which is given for any treatment or to treat any ADR is known as Treatment Drug.

37. Historical Drug:

Any drug that is withdrawn by the patient before administration of the suspect drug, is known as Historical Drug.

38. Historical Event / Condition:

Any Medical condition that is started and Stopped before administration of a Suspect Drug.

39. Concomitant Condition:

Any medical condition that is started earlier to or after Administration of the Drug & is Continuing with the Administration of Suspect Drug.

40. MedDRA (Medical Dictionary for Regulatory Activities)

Med DRA is a dictionary used for the coding of adverse events. It maintained by **Maintenance and Support Service Organization (MSSO).** It mainly written in to two languages: English and Japanese.
Med DRA gets updated twice in a year.
Major Update = in March of every year.
Minor Update = In September of every year.
The current version of Med DRA is 23.1 (As per Sep 2020)

41. Explain the Hierarchy In MedDRA?

System Organ Class (SOC)
High Level Group Term (HLGT)
High Level Term (HLT)
Preferred Term (PT)
Lower Level Term (LLT)

42. Role of Drug Safety Associate:

Manage and relay d rug safety information, maintain current knowledge of global drug safety regulations, summaries clinical safety data, participate in meetings with potential and actual study sponsors, write narratives

with medical input from a physician, report SADRs to the Regulatory Authorities, participate in the training of operational staff on drug safety issues, quality control work of other staff in the department, take on any other task as assigned by the manager or Medical Director within the capabilities of the Drug Safety Associate.

43. Name some data elements in ICSR?

Patient demographics : Age, gender and race.
Suspect product details : Drug, dose, dosage form, therapy dates, therapy duration and indication.
Adverse event details : Event, event onset date, seriousness criterion, event end date and latency.

44. What should a narrative consist of?

A narrative should consist of precise and concise information about the source of report, patient demographics, patient's medical history, concomitant medications, suspect product details and adverse event details in an orderly manner.

45. What are Data assessments in Pharmacovigilance?

Data assessments are:

- Individual case report assessment
- Aggregated assessment and interpretation
- Signal detection
- Interactions and risk factors
- Serial study
- Frequency
- Estimation

46. Suitable methods of reporting:

- Telephone
- Fax
- E-mail
- Internet

47. Seriousness criteria based on intensity?

Not severe, mild, moderate, severe.

48. Synonyms for relatedness (causality-related)?

Related: Certain, possible, probable, likely

49. Synonyms for relatedness (causality- unrelated)?

Not related: Unlikely, Unclassified (or conditional), Unassessable.

50. Odd scenarios in PV?

- Pregnancy
- Overdose (>MTD)
- Off label use
- Medication error
- Lack of efficacy

51. What is Co-morbid conditions?

Patients may be more susceptible to particular ADRs if they also have other health problems, either because of the concomitant condition or from the interaction of the medicines being used to treat the other condition(s).

52. What is a signal?

Signal is defined as: Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously (WHO).

53. Methods of signal detection?

There are four methods for identifying signals:

- Clinical assessment of individual events
- Clinical review of collated events
- Record linkage
- Automated signal detection.

54. Periodic Safety Update Report (PSUR)

A systematic review of the global safety data which became available to the manufacturer of a marketed drug during a specific time period. Produced in an internationally agreed format.

55. Define aggregate reporting?

It is a procedure that collects all the cumulative safety data of a medical product on a periodic basis from a wide verity of sources. These data submitted to regulatory authority.

56. Vigi-Base

The name of the WHO Global ICSR Database.

57. Vigi-Flow

Vigi-Flow is a complete ICSR management system created and maintained by the UMC. It is web-based and built to adhere to the ICH-E2B standard. It can be used as the national database for countries in the WHO Programme as it incorporates tools for report analysis, and facilitates sending reports to Vigi-Base.

58. Vigi-med

Share point based conferencing facility, exclusive to member countries of the WHO Programme for International Drug Monitoring for fast communication of topical pharmacovigilance issues.

59. Vigi-Mine

A statistical tool within Vigi-Search with vast statistical material calculated for all Drug- ADR pairs (combinations) available in Vigi-Base. The main features include the disproportionality measure (IC value) stratified in different ways and useful filter capabilities.

60. Vigi-Search

A search service for accessing ICSRs stored in the Vigi-Base database offered by the UMC to national pharmacovigilance centres and other third-party inquirers.

61. WHO-ART

Terminology for coding clinical information in relation to drug therapy. WHO-ART is maintained by UMC.

62. WHO Drug Dictionary (WHO DD)

The WHO Drug Dictionary is an international classification of drugs providing proprietary and non-proprietary names of medicinal products used in different countries, together with all active ingredients.

63. Explain different phases in clinical trails?

3 phases involved in the Clinical Trials.

Phase I : Determines the drug safety and dosage by the help of pharmacokinetics of the drug. Except chronic disease (AIDS/Cancer) drugs, most of the remaining drugs tested in healthy volunteers.

Phase II : Once the drug safety confirmed, this phase starts to find out the effectiveness of the drug along with its side effects.

Phase III : This phase tested on a huge number (1000 to 3000) of patients. Before going to drug in the market, this phase confirm/ verifies the effectiveness of the drug in the trial.

Note: Phase 0 also belongs to the clinical trial phase known as micro dosing. Very small amount of the drug is administered in the human body to check whether the drug is behaving same as it is tested in the animals in the preclinical studies.

64. Expand the following terms?

ICSR- Individual Case Safety Report

DSUR- Development Safety Update Report

PSUR- Periodic Safety Update Report: European Medicines Evaluation Agency (EMEA) needs this PSURs.

PADER- Periodic Adverse Drug Experience Report: USFDA needs this PADERs.

SUSAR- Suspected Unexpected Serious Adverse Reaction

MedDRA- Medical Dictionary for Regulatory Affairs, MedDRA developed by ICH (International Conference on Harmonisation) and maintained by Maintenance Support Services Organisation (MSSO).

GVP- Good Pharmacovigilance Practices.

IBD- International Birth Date

ESTRI- Electronic Standards for the Transfer of Regulatory Information

WHO-ART- World Health Organisation- Adverse Reaction Terminology: It is a dictionary for coding adverse reactions. WHO ART maintained by Uppsala Monitoring Centre (UMC), Sweden.

CIOMS- Council for International Organizations of Medical Sciences.

ICD- International classification of diseases

WHO-DDE- World Health Organisation -Drug Dictionary of Enhanced

65. What do you know about Thalidomide disaster?

Thalidomides used as a mild sleeping agent and to treat morning sickness in pregnant women in 1960s. The major side effect of this drug is Phocomelia (severe Birth defects affecting the upper and/ lower limbs and foetal death. Thousands of babies affected by the malformed limbs.

66. Action Taken:

It refers to the action taken to suspect drug with that of an event. The possible actions taken to the drug is:

i. Drug withdrawal/ Drug Discontinuation

ii. Dose not change

iii. Dose increases

iv. Dose decreases

v. Unknown i.e. we do not know about the action taken.

67. Dechallenge / Re challenge:

They both are applicable when the drug is discontinued due to an AE.

68. Dechallenge:

The withdrawal of a drug from a patient; the point at which the continuity, reduction or disappearance of adverse effects may be observed. When the Event is Resolved, it is known as Positive Dechallenge When the event is not resolved, it is known as Negative Dechallenge.

69. Re challenge:

The point at which a drug is again given to a patient after its previous withdrawal. It is applicable only when there is Positive Dechallenge. When the Event is reoccurred, it is known as Positive Re challenge, and when the event not occurred it is known as Negative Re challenge.

70. Listedness/ Unlistedness:

Any reaction which is not included in the Company Core Safety Information within a company's core data sheet for a marketed product is called unlisted. If it is included, it is termed listed.

71. Expectedness:

Expectedness refers to the AE whether serious or being previously observed and documented in Reference Safety Information (i.e. IB, SmPC, Package Insert, CCSI).

72. Unexpectedness:

Unexpectedness refers to AE not being observed or documented in the Reference Safety Information (i.e. IB, SmPC, Package Insert, CCSI).

73. Reference Safety Information:

RSI is a document for identification of AE. It is very unique and may vary from company to company. Here we check the safety information in an RSI.

74. International Society of Pharmacovigilance (ISOP)

This is an important international society. Their web site gives information about meetings and training courses.

75. Absolute risk

Risk in a population of exposed persons; the probability of an event affecting members of a particular population (e.g. 1 in 1,000). Absolute risk can be measured over time (incidence) or at a given time (prevalence).
Incidence: Rate of occurrence of disease
Prevalence: condition of being prevalent

76. Drug Misuse:

Wrong use of drug by a consumer and it is not an accordance to the prescription and also it is intentionally and inappropriately use of medication.

77. Drug Abuse:

Intentional excessive use of a medical product which is accompanied by harmful physical and psychological effects. Ex: Excessive Morphine cause Hallucination.

78. Medication Error:

The unintended failure in the treatment process that leads to harm the patient. Ex: Prescription error, Dispensing error or Administration error.

79. Off label use:

Medical product used for the unapproved age group, dosage form and ROA intentionally.

80. What Is Volume 9a?

European Union prepared this Volume 9A. It provides guidance on pharmacovigilance roles, requirements, procedures and activities. These guidelines are for both MAH (Marketing Authorisation Holders) and Human use medicinal product competent authorities. It incorporates international agreements reached within the framework of the International Conference on Harmonisation (ICH). Volume 9A is presented in four parts:

- Part I deals with Guidelines for Marketing Authorisation Holders
- Part II deals with Guidelines for Medicinal product competent authorise.
- Part III provides the Guidelines for the electronic exchange of pharmacovigilance in the EU
- Part IV provides Guidelines on pharmacovigilance communication

81. What are the ICH guidelines related to Pharmacovigilance?

ICH E2A to E2F guidelines deals with pharmacovigilance.

E2a: E2a give guidelines for Clinical Safety Data Management. It also gives guidance on mechanisms for handling expedited (rapid) reporting of adverse drug reactions in the investigational phase of drug development.
E2b: E2B guidelines for Data elements transmission of ICSRs (Individual Case Safety Reports). It provides guidelines on clinical safety data management and ICSR data elements transmission.
E2c: It provides guidelines on PSURs (Periodic Safety Update Reports) of marketed drugs which are having role in Periodic benefit risk evaluation report
E2D: It provides guidelines for Post approval safety data management.
E2E: It provides guidelines on Pharmacovigilance planning.
E2F: Development Safety Update Report: It provides guidance on DSUR. It is the data from the Investigational drugs in the clinical trials with or without having a market approval. Sponsors required to submit DSUR on every year.

82. What Should A Narrative Consist Of?

A narrative should consist of precise and concise information about the source of report, patient demographics, patient's medical history, concomitant medications, suspect product details and adverse event details in an orderly manner.

There is no standard template and Global Guideline for Narrative. Ideally it should be within 5-8 Paragraphs.
1st Paragraph = Opening paragraph.
2nd Paragraph = Patient's height & weight.
3rd Paragraph = Patients medical history.
4th Paragraph = Patient's concomitant medication.
5th Paragraph = Body of Narrative
6th Paragraph = Action taken to suspect Drug
7th Paragraph = Outcome of the Event.
8th Paragraph = Causality of the event.

Opening Paragraph: It should give validity of the case. It should contain:

- Reporter of the Case
- Details of the Patient
- Suspect Drug
- Reported ADR

If there is no information regarding the patient, then it should be mentioned as not reported.
Example: Physician, Germany, 24 females, hypertension, atenolol, Headache.

1st paragraph = This spontaneous case was reported from a physician from Germany and Confirmed a 24 years old female patient who experienced headache while taking Atenolol for hypertension.
2nd Paragraph= The patient's height & weight were not reported
3rd Paragraph= The patient's medical history included hypertension.
4th Paragraph= Patient's concomitant medication were not reported.
5th Paragraph= On an unspecified date, the patient started Atenolol (formulation, dose, route of administration, frequency of ADR were not reported). On an unspecified date the patient experienced headache.
6th Paragraph= The action taken with atenolol was not reported.
7th Paragraph= The outcome for headache was not reported.
8th Paragraph= The causality between Atenolol and headache were not reported. (In case of CT & solicited Reports)