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ADR MONITORING AND SAFETY REPORT: AMOXICILLIN

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CLINICAL RESEARCH:

Definition:

Clinical trials are defined as a methodical investigation of a novel medication (therapy regimens, gadgets) in human subjects to provide data for identifying or validating clinical claims or pharmacological and side effects to ascertain the safety and effectiveness of the pharmaceuticals in question.[1]

❑ Phases Of Clinical Trials:

- In phase I trials, new medications are often tested in small groups for the first time in order to determine a safe dose range and detect adverse effects.
- Treatments that were safe in Phase I but now require a larger sample size of human volunteers to monitor for any negative effects are tested in Phase II research.
- Phase III studies, frequently the last stage before a new treatment is authorized, are carried out on bigger populations in various locations and nations.
- Phase IV studies are conducted following national approval, and more research in a larger population over a longer period is required.[1]

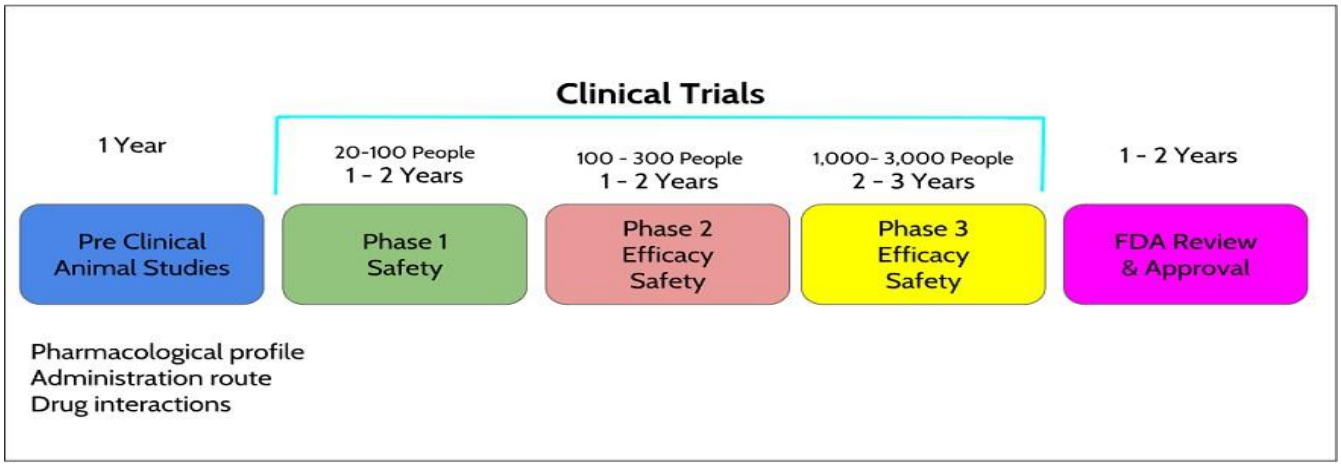


Fig 1. Phases of Clinical Trials

❍ **Functions of Drug Controller General of India (DCGI)**

- Additionally, pharmaceuticals imported into the nation are subject to quality inspection by the DCGI.
- It organizes the actions of several state drug control agencies.
- Foreign manufacturer registration is under its purview. These producers deal in medications and medical equipment that is imported into India.
- It is in charge of issuing permits for the importation of medications. Government hospitals and medical facilities use it for their patients.
- It recommends banning harmful or sub-therapeutic drugs. It does so under section 26A. [2] the Drugs and Cosmetics Act.
- The necessary reference standard for medications is prepared and maintained by it.
- The Drugs and Cosmetics Act of 1940 is applied consistently thanks to the DCGI.
- Training in this area is conducted by the DCGI. It provides training for the State Drug Analysts.
- Cosmetics are also analyzed by the DCGI as survey samples. The Central Drugs Standard Control Organization sent it to us.
- The Medical Device Regulations of 2017 designate the DCGI as the primary licensing body.
- It handles the licensing of the medical devices that fall under this Act's ambit.
- Additionally, it authorizes medications under the Drugs and Cosmetics Act.
- The DCGI handles the conduction of clinical trials. The DCGI also sets standards for drugs.

❑ **Function of Central Drugs Standard Control Organization (CDSCO)[1]**

- Approval of drugs: New medications and clinical studies are approved by CDSCO.
- Regulatory control: CDSCO oversees the quality of imported medications and regulates their importation.
- Setting standards: Drug standards are established by CDSCO.
- Licensing: Certain specialist medications, including blood, blood products, vaccinations, and sera, are licensed by CDSCO.
- Coordination: State drug control organizations' operations are coordinated by CDSCO.
- Enforcement: CDSCO is responsible for enforcing the 1940 Drugs and Cosmetics Act and other relevant laws.
- Public authority: CDSCO responds to RTI inquiries as a public authority..

❍ **Types of application:** [3]

1. Investigational new drug:

An application to the Food and medication Administration (FDA) for approval to use a biological product or experimental medication in people is known as an experimental New Drug (IND) application. Before any novel medication or biological product is delivered or used over state boundaries, an IND is necessary.

2. New drug application: -

A request to the Food and Drug Administration (FDA) for authorization to sell and promote a novel medication in the US is known as a novel Drug Application (NDA). When the pharmaceutical company feels they have sufficient proof to satisfy the FDA's approval standards, they submit the NDA.

3. Abbreviated new drug application: -

The U.S. Food and Drug Administration (FDA) receives requests for reviews and possible approval of generic drugs through the Abbreviated New Drug Application (ANDA).

GOOD CLINICAL PRACTICE: [4]

A global ethical and scientific quality standard for planning, carrying out, documenting, and disclosing research involving human beings is called Good Clinical Practice (GCP). Under the principles derived from the Declaration of Helsinki, adherence to this standard gives the public confidence that the rights, safety, and welfare of trial participants are safeguarded and that the clinical trial data are reliable.

Objectives and scope:

ICH-Good Clinical Practice:

- Keep the patient safe.
- Establishing a common standard for the US, Japan, and EU to enable reciprocal acceptance of clinical data by these jurisdictions' authorities. Facilitate the mutual acceptance of clinical data across ICH GCP regions
- Steer clear of trial duplication to save resources, money, and time.
- Encourage worldwide contributions by accepting data from both parties.
- Technical specifications for medications that contain novel

Scope:

To safeguard trial participants and ensure the validity of trial findings, the ICH GCP guidelines included scientific and ethical requirements for planning, carrying out, documenting, and reporting studies involving human beings.

New Drugs and Clinical Trial Rules 2019: [5]

- To support clinical research and trials in India and to improve the efficiency and transparency of the drug approval process, the New Drugs and Clinical Trials Rules, 2019 (NDCT Rules) were developed**.**
- Increase the accessibility of medications
- Control clinical trials.
- Give precise parameters for compensation.

Protocol designing for clinical trials:

- Background and rationale: outlines the goals of the investigation and the research issues it attempts to answer.
- Design: explains the methodology behind the study.
- Methodology: describes the actions to be done during the research.
- Statistical considerations: Includes details about data recording and analysis.
- Safety assessment: addresses issues such as data handling, ethics, and adverse occurrences.
- Project timetable: contains references and a flowchart.
- Process of clinical trials: -

Fig 2. Clinical trial process

CONCEPT OF PHAMACOVIGILANCE: [6]

Definitions:

The study and practice of identifying, evaluating, comprehending, and preventing side effects or any other issue pertaining to medications or vaccines is known as pharmacovigilance. Clinical trials are used to test the safety and effectiveness of all medications and vaccines before they are approved for use.

Objectives: -

- To establish a nationwide patient safety reporting system.
- To find and examine the newly reported instances' ADR signal.
- To evaluate the benefit-risk ratio of pharmaceuticals that are sold.
- To produce data based on evidence about medication safety.
- To aid regulatory organizations in making decisions on the use of pharmaceuticals.
- To minimize risk, inform different stakeholders about the safety information regarding the use of medications.
- Objective To become the nation's premier hub for pharmacovigilance initiatives.

- To cooperate with other national centres for data management and information exchange.

Types of pharmacovigilance:

- Surveillance for drug safety.
- Surveillance of drug misuse and side effects.
- Monitoring the safety of new goods.

Components of pharmacovigilance: [7]

- Quality system: A pharmacovigilance system's quality objectives are to avoid adverse drug reactions (ADRs), encourage the safe use of medications, and adhere to legal requirements.
- Risk management: Creating a Risk Management Plan that outlines a drug's dangers and how to manage them is a crucial component of pharmacovigilance.
- Signal: Information that indicates a potential connection between a medication and negative outcomes is called a signal. Because it assists in identifying ADRs that were previously unknown or not completely reported, signal detection is crucial.

- Pharmacovigilance System Master File (PSMF): A PSMF is a thorough document with a wealth of information.
- Post-authorization safety studies: The purpose of these studies is to investigate the safety of medications.
- Regulatory bodies: Another essential component of pharmacovigilance is regulatory affairs.

Constitution and Objectives of the Pharmacovigilance Program of India (PvPI): -

- To establish a national mechanism for reporting patient safety.
- To recognize and evaluate fresh warning signs.
- To produce data based on evidence about medication safety.
- To assist regulatory bodies in making decisions on the use of drugs
- To provide safety information about the use of medications to diverse stakeholders to decrease the risk of becoming a premier national hub for pharmacovigilance initiatives.
- To establish pharmacovigilance as a national centre of expertise.
- To cooperate with other national centres for data management and information sharing.
- To provide training and consultancy support to other national pharmacovigilance centres across the globe.
- To promote the rational use of medicines.

List of adverse drug monitoring centres:

- Dr. AL Nair Road, Mumbai Central, Mumbai-4; TN Medical College & Byl Nair Hospital.
- Pune Cantonment, Solapur Road, next the Race Course, Armed Forces Medical College, Pune-411040.
- N.K.P. Salve Institute of Medical Sciences & Lata Mangeshkar Hospital, Digdoh Hills, Hingna Road, Nagpur-440019.
- Jawaharlal Nehru medical College, Datta Meghe Institute of Medical Sciences, Sawangi (Meghe),

Wardha-442004

- Smt. Kashibai Navale Medical College & General Hospital, Sr. No. 49/1, Narhe, Off Mumbai-Pune bypass, Pune-411041

Function of adverse drug monitoring centres: [8]

- Perform a follow-up with the complaint to ensure that everything complies with SOP.
- Importing data into Vigiflow.
- through Vigiflow, reporting to the PvPI National Coordinating Centre (PVPI NCC) with each ADR case's source data attached.
- Physicians get training, sensitization, and feedback via newsletters distributed by the PVPI NCC Center coordinator, who is in charge of providing NCC with monthly updates on their AMC.

INTERNATIONAL CONFERENCE OF HORMONISATION (ICH) E2e GUIDELINES:[9]

- **Harmonization:** to create a uniform strategy for pharmacovigilance planning on a worldwide scale.
- **Risk Management:** to guarantee the efficient identification, assessment, and mitigation of any risks to pharmaceutical safety.
- **Efficient Resource Utilization:** to better allocate resources and reduce effort duplication in pharmacovigilance duties.
- **Enhanced Patient Safety:** to enhance marketed medications' safety profile in order to safeguard the public's health.

Elements of the non-clinical and clinical safety specification: -

- Pre-Clinical
- Toxicity
- General Pharmacology
- Drug Interactions
- Other toxicity-related information
- Clinical
- Limitations of the Human Safety Database
- Populations not studied in the pre-approval phase
- Adverse events/adverse drug reactions
- Identified risks that require further evaluation
- Potential risks that require further evaluation.
- Identified and potential interactions
- Identification and evaluation of risks including drug-drug interactions and drug-food interactions
- Identification of Drug- Drug interaction

Clinical studies

- DDI clinical trials are an essential part of the licensing process for new medications since they assist detect possible adverse responses.
- Experiments that test a model's capacity for learning using a test set are typically used to assess a model's performance.

Social network analysis

- Using graph theory, this program describes networked structures in terms of nodes, which are chemicals or proteins, and edges, which are interactions.

Evaluation of Risk of drug-drug interaction: [7]

- Study of design, Study of variables, Inhibition study.
- Drug interaction analysis
- Cytochrome p-450 enzyme inhibitors
- Interactions with transmembrane protein transporters
- Patient cohort

Design and conduct of observational studies

Creating and carrying out observational studies requires a methodical approach to comprehending and evaluating the connections between variables in practical contexts. Instead of the researcher intervening or manipulating, observational studies watch and record individuals as they spontaneously occur.

SELECTION OF DRUG CLASS.

Introduction: -

A class of drugs called an antibiotic is used to treat bacterial infections. Either killing germs or preventing their development is how antibiotics function. They do not work against viral illnesses, such as the common cold or the flu. Effective drugs that cure specific infections, and antibiotics have the potential to save lives when taken as directed. They either eliminate germs or prevent their reproduction. In most cases, the immune system can eliminate germs before they grow and produce symptoms. Even if symptoms appear, the immune system can often handle and fight off the infection because white blood cells (WBCs) fight dangerous germs.However, the immune system may not be able to eradicate all of the dangerous germs when their numbers are too high. Under these circumstances, antibiotics are helpful. Penicillin is the first antibiotic. Amoxicillin, penicillin G, and ampicillin are among the penicillin-based antibiotics that have been used for many years and are still available to treat a range of illnesses. In the United States, there are a number of contemporary antibiotic varieties that are often only accessible with a prescription. Creams and ointments that are sold over-the-counter (OTC) include topical antibiotics.[1,2,3]

Antibiotic work: [2,3]

There are different types of antibiotics, which work in their unique way. However, the two main they work include:

- Penicillin is an example of a bactericidal antibiotic, which destroys microorganisms. These medications typically disrupt the development of the bacterial cell wall or the contents of the cell.
- A bacteriostatic prevents the growth of bacteria.

Mechanism of action: -

1. The inflexible cell wall of bacteria provides them with protection and structure. The enzymes that make the bacterial cell wall are disrupted by some antibiotics. Bacteria that lack a functional cell wall are unable to hold their form and are more likely to rupture as a result of osmotic pressure.

2. Interference with Cell Membrane Function

Mechanism: The membrane of the bacterial cell, which regulates the flow of chemicals into and out of the cell, is damaged by these antibiotics. The antibiotics create holes or faults in the membrane by binding to it.

2. Inhibition of Protein Synthesis

Mechanism: Protein synthesis is carried out by the bacterial ribosome, which is the target of these antibiotics. Because bacterial and human cells have distinct ribosomes, these medications can specifically target the production of proteins in bacteria without endangering human cells.

Effect: When bacterial development is stopped or faulty proteins are produced as a result of protein synthesis disruption, the bacteria are eventually killed or inhibited.

3. Inhibition of Nucleic Acid Synthesis

Mechanism: These antibiotics target the enzymes that bacteria need to replicate their DNA or to do transcription. For instance, fluoroquinolones block the enzymes topoisomerase and DNA gyrase, which are essential for DNA replication and repair. By blocking RNA polymerase, rifamycins stop bacteria from transcription.

Contraindication: [7]

- Hypersensitivity or allergy.
- Antibiotics should not be administered to patients who have a known allergy to any of its ingredients.
- Being pregnant and nursing Certain antibiotics are unsafe to take while pregnant because they might damage the growing fetus. Similarly, certain medications can infect the nursing child through breast milk.
- Neurological Disorders
- Patients who have experienced seizures or other neurological diseases in the past should use antibiotics with caution since they may produce neurological side effects, including seizures.
- Myasthenia Gravis.
- Certain antibiotics, especially macrolides and fluoroquinolones (like ciprofloxacin), might exacerbate the symptoms of myasthenia gravis, a neuromuscular condition that results in voluntary muscle weakening.

Adverse effect: -

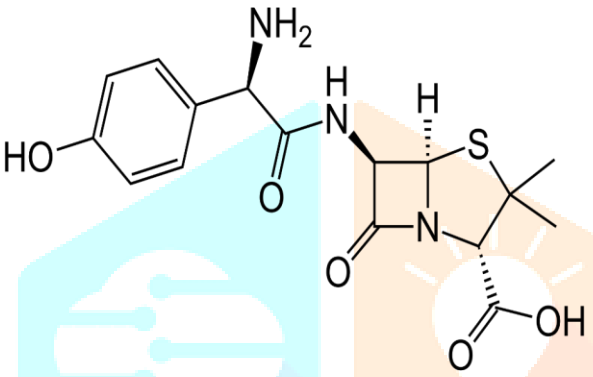
The specific side effects that an antibiotic can cause depend on the drug. However, some common side effects of antibiotics include:

- nausea
- sleepiness
- dizziness
- lightheadedness
- diarrhea
- Alcohol can also cause side effects. These include:

- an upset stomach
- digestive problems, such as stomach pain, diarrhea, and ulcers
- tiredness
- Signs of a negative alcohol-antibiotic reaction include:
- flushing (reddening and warming of your skin)
- severe headache
- racing heart rate

SELECTION OF DRUG:[8]

Drug name: - amoxicillin



Amoxicillin:

It is an antibiotic drug that is a member of the penicillin family's aminopenicillin class. The medication is used to treat bacterial infections, including urinary tract infections, odontogenic infections, pneumonia, strep throat, middle ear infections, and skin infections. It is administered orally, or less frequently by intramuscular injection or IV bolus injection, which is a brief intravenous infusion that lasts anywhere from a few seconds to several minutes**.** After being developed in 1958, amoxicillin was first used in medicine in 1972. Both the United States and the United Kingdom granted medical approval for amoxil in 1974 and 1977, respectively. It is listed as one of the essential medicines by the WHO. In 14 children, it is among the most often administered antibiotics. A generic form of amoxicillin is available. It received almost 20 million prescriptions in 2022, ranking it as the 26th most prescribed drug in the US.[7,8,9]

Mechanism of action

Among other high molecular weight penicillin binding proteins, amoxicillin competitively inhibits penicillin-binding protein 1. Penicillin-binding proteins are in charge of the transpeptidase and glycosyltransferase activities that cause D-alanine and D-aspartic acid in bacterial cell walls to cross-link. The bacteriocidal effect results from bacteria overexpressing autolytic enzymes and being unable to form and repair the cell wall in the absence of penicillin-binding proteins.

The suppression of bacterial cell wall production is part of amoxicillin's mode of action. The process by which amoxicillin kills germs is broken down here

1. Targeting Penicillin-Binding Proteins (PBPs) [8]

- The last steps of the bacterial cell wall's formation, particularly the cross-linking of the peptidoglycan layers, depend heavily on the enzymes known as penicillin-binding proteins (PBPs).
- Peptidoglycan is the primary structural element of the bacterial cell wall, giving the cell strength and rigidity.
- Amoxicillin inhibits PBPs by binding to them, stopping the peptidoglycan chains from being cross-linked by the enzymes.

❖ **Inhibition of Cell Wall Cross-Linking:**

- Peptidoglycan strands must cross-link for the bacterial cell wall to remain strong and structurally sound.
- When amoxicillin inhibits PBPs, the peptidoglycan chains are unable to cross-link correctly.
- As a result, the bacterial cell wall becomes weaker.

2. Bacterial Cell Lysis:

- Osmotic pressure, or the force produced by the fluid inside the cell, is particularly vulnerable to the protective barrier that the bacterial cell wall offers, preserving the integrity of the cell.
- The bacteria cannot tolerate this osmotic pressure without a healthy cell wall, and they will rupture (lyse).
- Because it causes cell death when the cell wall structure is not maintained, amoxicillin is regarded as bactericidal (it kills germs).

3. Selective Toxicity

- Human cells are immune to amoxicillin because they lack cell walls.
- Amoxicillin destroys germs without causing damage to human cells because it selectively targets the cell walls of bacteria.

4. Effect on Growing Bacteria

- The most effective use of amoxicillin is against bacteria that are actively dividing.
- Bacteria are continuously constructing and modifying their cell walls as they proliferate. This process is hampered by amoxicillin, which results in bacterial mortality and cell wall collapse.

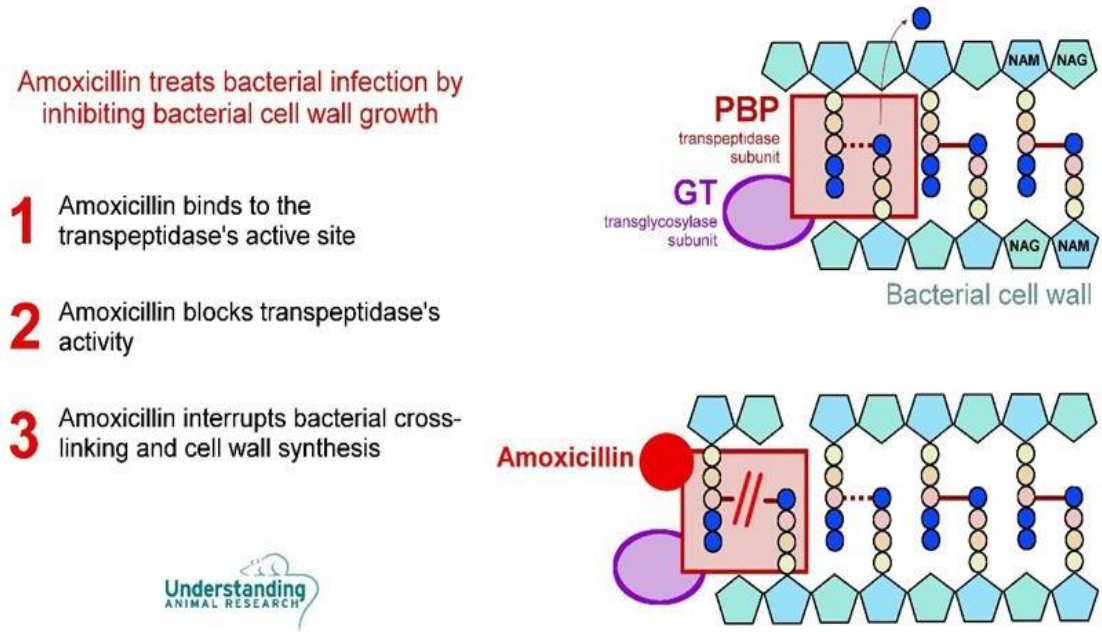


Fig 3. MOA of amoxicillin

Pharmacokinetics: [8,9]

Amoxicillin's pharmacokinetics describes how the medication enters the body, moves throughout it, is digested, and is eliminated.

Here's a breakdown of its pharmacokinetic properties:

1. Absorption.[9]

- • Administration Route: Amoxicillin is usually taken orally as a liquid solution, pill, or capsule.
- Absorption When taken orally, amoxicillin has a bioavailability of around 93% and is well absorbed from the gastrointestinal (GI) tract. This indicates that a sizable amount of the medication enters the circulation undamaged.
- Effect of Food**:** meals may cause a minor delay in absorption, but this has no effect on overall bioavailability, and it can be taken with or without meals.

2. Distribution

- Volume of Distribution (vd)**:** With a volume of distribution of around 0.3 to 0.4 L/kg, amoxicillin is broadly dispersed throughout the body.
- Tissue Penetration: The following bodily fluids and tissues are permeable to amoxicillin: blood, lungs, kidneys, skin, middle ear (used to treat otitis media), sinuses, and urine.
- It is not well disseminated into the CSF unless there is inflammation of the meninges. Higher levels of CSF may be obtained in instances of bacterial meningitis..
- Protein Binding: About 17% to 20% of amoxicillin is bonded to plasma proteins, meaning that some of the medication is still free and active.

3. Metabolism

- The liver does not substantially process amoxicillin. It doesn't significantly change metabolically and stays mostly unaltered in the body.
- A small fraction of amoxicillin may be metabolized to an inactive compound, penicilloic acid**.**

4. Excretion

- Elimination Half-Life: In healthy people, the elimination half-life of amoxicillin is just 1 to 1.5 hours.
- Route of Elimination: Urine is where amoxicillin is mostly eliminated unaltered. Between 60 and 70 per cent of a dosage is eliminated unaltered by the kidneys.
- Renal Clearance: Amoxicillin's clearance may be decreased in those with renal impairment since it is mostly removed via the kidneys. Patients with renal illness may require dose modifications.
- Excretion in Breast Milk: Amoxicillin can be excreted into breast milk in small amounts, though generally considered safe for use during breastfeeding.
- Impact of Hepatic and Renal Impairments
- Renal Impairment: Amoxicillin excretion may be hindered in people with compromised renal function, which might result in increased plasma concentrations. Changes in dosage can be required.
- Hepatic Impairment: Since the medication does not experience substantial hepatic metabolism, people with liver disorders usually do not need to modify their dosage.

○ **Adverse effect: -**

1. Gastrointestinal Issues: -

- **Nausea**: When taken on an empty stomach, some people may feel queasy.

- **Vomiting**: Although less often, it can happen.
- **Diarrhea**: one of the most common adverse reactions. It is often mild and can affect up to 10% of people. Prolonged or severe diarrhoea, however, might indicate a more serious illness.
- **Abdominal pain or cramps**: Some folks could feel uneasy in their stomach.

2. Skin Reactions:

- **Rash**: Children are particularly susceptible to a moderate maculopapular rash, which consists of flat, red patches with tiny bumps.
- **Pruritus (Itching)**: Itching could be mild.
- **Hypersensitivity Reactions (Allergic Reactions):**
- **Anaphylaxis**: Although uncommon, a strong allergic response can be fatal. The symptoms include a weak or fast pulse, facial and throat oedema, and trouble breathing. Emergency medical care is necessary.
- **Rash**: A more serious rash might appear, such as urticaria, which is a type of hive. An allergic response may be indicated by this..
- **Angioedema**: Swelling beneath the skin, often around the eyes and lips, can also occur.

3. Severe Gastrointestinal Effects:

- **Clostridium difficile-associated diarrhoea (C. difficile)**: Amoxicillin, like other antibiotics, can upset the delicate balance of intestinal flora, causing C. difficile to proliferate. This can result in severe and occasionally fatal colitis, or colon inflammation. Severe, watery diarrhea (frequently accompanied by blood or mucus), fever, and stomach discomfort are among the symptoms.

4. Liver Toxicity:

Amoxicillin seldom results in liver damage, hepatitis, or jaundice, which is a yellowing of the skin or eyes. Liver poisoning manifests as yellowing of the skin and eyes, pale faeces, and black urine.

5. Contraindication:

Despite being a widely used antibiotic, amoxicillin should be administered carefully or avoided in some circumstances. They are referred to as contraindications. These are the main reasons why amoxicillin should not be used.

- An allergy to beta-lactam antibiotics, such as penicillin
- Amoxicillin-Related Severe Allergic Reaction History
- Infectious Mononucleosis (Mono)
- Severe Renal Impairment (Kidney Failure)
- Clostridium difficile Colitis (C. difficile-associated Diarrhea)

IDENTIFICATION OF ADVERSE DRUG REACTION:[3,4] [9-11]

Adverse effects of amoxicillin: -

Amoxicillin can have certain adverse effects, however, it is usually well tolerated. These are amoxicillin's most frequent side effects.:

Common Side Effects:

- **Gastrointestinal:** Nausea, vomiting, diarrhoea, and stomach pain.
- **Skin Rash:** A mild, itchy rash is possible.

Serious Side Effects (Less Common):

- **Allergic Reactions:** In rare cases, amoxicillin can cause severe allergic reactions, including:
- **Hives**
- **Swelling of the face, lips, tongue, or throat**
- **Difficulty breathing**
- **Anaphylaxis (a life-threatening allergic reaction) Severe Skin Reactions: -**

- **Stevens-Johnson syndrome**
- **Toxic epidermal necrolysis**

Diarrhoea:
Severe diarrhoea may occasionally be brought on by amoxicillin and might indicate a major intestinal illness.

If you experience any of the following symptoms, stop taking amoxicillin and seek immediate medical attention:

- Difficulty breathing
- Hives
- Swelling of the face, lips, tongue, or throat
- Severe diarrhea
- Skin rash or blistering

ADR MONITORING FORM

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

INDIAN PHARMACOPOEIA COMMISSION
(National Coordination Centre-Pharmacovigilance Programme of India)
Ministry of Health & Family Welfare
Government of India
Sector-23, Raj Nagar, Ghaziabad-201002
www.ipc.nic.in

(AMC/ NCC Use only)
AMC Report No.
Worldwide Unique

A. PATIENT INFORMATION

1. Patient Initials _____
2. Age at time of Event or date of birth _____
3. Sex ☐ M ☐ F
4. Weight ___ Kgs

12. Relevant tests / laboratory data with dates

B. SUSPECTED ADVERSE REACTION

5. Date of reaction started (dd/mm/yyyy)
6. Date of recovery (dd/mm/yyyy)
7. Describe reaction or problem

13. Other relevant history including pre-existing medical conditions (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/ renal dysfunction etc)

14. Seriousness of the reaction
- ☐ Death (dd/mm/yyyy)
- ☐ Life threatening
- ☐ Hospitalization/prolonged
- ☐ Disability
- ☐ Congenital anomaly
- ☐ Required intervention to prevent permanent impairment / damage
- ☐ Other (specify)

15. Outcomes
- ☐ Fatal
- ☐ Recovering
- ☐ Unknown
- ☐ Continuing
- ☐ Recovered
- ☐ Other (specify)

C. SUSPECTED MEDICATION(S)

S.No	8. Name (brand and /or generic name)	Manufacturer (if known)	Batch No./ Lot No. (if known)	Exp. Date (if known)	Dose used	Route used	Frequency	Therapy dates (if known, give duration)		Reason for use of prescribed for
								Date started	Date stopped	
i.										
ii.										
iii.										
iv.										

S.No As per C	9. Reaction abated after drug stopped or dose reduced					10. Reaction reappeared after reintroduction				
	Yes	No	Unknown	NA	Reduced dose	Yes	No	Unknown	NA	If reintroduced dose
i.										
ii.										
iii.										
iv.										

11. Concomitant medical product including self medication and herbal remedies with therapy dates (exclude those used to treat reaction)

D. REPORTER (see confidentiality section on first page)

16. Name and Professional Address : _____
Pin code: _____ E-mail _____
Tel. No. (with STD code): _____
Occupation _____ Signature _____

17. Causality Assessment

18. Date of this report (dd/mm/yyyy)

HOSPITAL VISIT

PATIENT REVIEW

1. Is there any administration of IV fluid?

➢ Ans: - yes DNS and NS

2. What precautions are advised by a physician to be taken?

➢ Ans: - use insect repellant, and avoid insect bites or sting

3. Is there any change in diet during treatment?

➢ Ans: - prevent alcohol, avoid food with high VIT K

4. Is there any gastric problem after medication?

➢ Ans: - yes, acidity sometimes causes nausea

5. Is there any irritation at the site of administration?

➢ Ans: - yes at the injection site but cover after ice therapy

6. What are the problems observed in daily routine?

➢ Ans: - not welling to eat, hair fall, thrust

7. What way drug is administrated regularly?

➢ Ans: - parenteral route

ASSESSMENT OF ADR

- Widely accepted method
- Patient information: Include the patient's initials, age, sex, and weight
- It consists of ten questions that are answered as "yes", "no", and "unknown" (don't know) These

answers are assigned via a score termed Definite, Probable, Possible Or Doubtful.

i. Definite-when a total score of 29
ii. Probable- when a total score of 5-8
iii. Possible-when a total score of 1-4

The Naranjo Algorithim

This questionnaire was designed by Naranjo et al. for determining whether a suspected adverse drug reaction (ADR) is actually caused by the drug, as opposed to other factors. Probability is determined to be definite, probable, possible, or doubtful. This algorithm is sometimes used to verify conclusions regarding ADRs. It is also called the Naranjo Scale or Naranjo Score.

Clinical Question	Yes	No	Do not know or not done
1. Are there previous conclusive reports on this reaction?	+1	0	0
2. Did the adverse event appear after the suspected drug was given?	+2	-1	0
3. Did the adverse reaction improve when the drug was discontinued or a specific antagonist was given?	+1	0	0
4. Did the adverse reaction appear when the drug was readministered?	+2	-1	0
5. Are there alternative causes that could have caused the reaction?	-1	+2	0
6. Did the reaction reappear when a placebo was given?	-1	+1	0
7. Was the drug detected in any body fluid in toxic concentrations?	+1	0	0
8. Was the reaction more severe when the dose was increased, or less severe when the dose was decreased?	+1	0	0
9. Did the patient have a similar reaction to the same or similar drugs in any previous exposure?	+1	0	0
10. Was the adverse event confirmed by any objective evidence?	+1	0	0

Scoring

>9 = definite ADR 5–8 = probable ADR
1–4 = possible ADR 0 = doubtful ADR

Journal WATCH

CONCLUSION:

Amoxicillin's pharmacovigilance research showed that the medication is typically well-tolerated and safe. But the study also found that using amoxicillin can result in several adverse drug reactions (ADRs), such as hepatotoxicity, allergic responses, and gastrointestinal problems. The Naranjo scale evaluation showed that most reported adverse drug reactions (ADRs) were either likely (scoring 5-8) or plausible (scoring 2-4) amoxicillin-induced ADRs. For patient safety, the results of the research emphasize how crucial it is to keep an eye on amoxicillin use and report any potential adverse drug reactions. When using amoxicillin, healthcare providers should be aware of the possible dangers and take the appropriate steps to reduce them. Future research should concentrate on identifying the processes and risk factors that underlie amoxicillin-induced adverse drug reactions (ADRs) and creating plans to control and avoid them. All things considered, this study adds to the body of information already available on the safety profile of amoxicillin and highlights the necessity of ongoing pharmacovigilance initiatives to guarantee the safe use of this often-prescribed antibiotic.

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