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NEWSLETTER OF CLINICAL PHARMACY

VOLUME-5, ISSUE-2 NOVEMBER 2022- MAY 2023.

Vision

St.Peter's is committed to generate, disseminate and preserve knowledge and work with pioneers of this knowledge, and to be the most sought after institute globally in the field of pharmaceutical sciences by creating world class pharmacy professionals and researchers.

Mission

To achieve academic excellence with integrity and creating opportunities for leadership and responsibilities through ground breaking performance in the field of Pharmaceutical Sciences by educating students with pharmaceutical needs of the society and to advance the knowledge through research and to serve the profession and community.

FDA APPROVED DRUGS NOVEMBER 2022 – MAY 2023

SL. NO	DRUG NAME	BRAND NAME	INDICATION	ADVERSE REACTION
1.	OXCARBAZEPINE	OXCARBAZEPINE	Treatment of partial seizures	Dizziness, sedation, Abnormal gait, ataxia
2.	IRBESARTAN	IRBESARTAN ANDA	Treatment of hypertension	Fever, dizziness or fainting, signs of bone marrow or blood disorder.
3.	CELECOXIB	CELECOXIB ANDA	Mild to moderate pain, Ankylosing spondylitis, osteoarthritis	Dyspepsia, diarrhea, Abdominal pain, Elevated AST/ALT or BUN
4.	TERIFLUNOMIDE	TERIFLUNOMIDE ANDA	Multiple sclerosis	Pale stools, Dark urine, loss of appetite, yellow eyes or skin, Upper stomach pain
5.	DOXYLAMINE SUCCINATE	UNISOM	Treats Insomnia	Blurred vision, Decreased coordination,
6.	ENOXAPARIN SODIUM	LOVENOX	Deep venous thrombosis, Acute coronary syndrome	Haemorrhage, malena, bleeding gums, hematuria
7.	VORICONAZOLE	VORICONAZOLE	To treat serious fungal or yeast infections	Visual disturbances, fever, rashes, vomitings
8	MIFEPRISTONE	MIFEPREX	Pregnancy termination	Allergic reactions, Heavy vaginal bleeding, high fever
9.	MESALAMINE	MESALAMINE	To treat Ulcerative colitis	Malena, chest pain, chest pain
10.	PEMBROLIZUMAB	KEYTRUDA	Lung cancer, Head and neck cancer, Hodgkinn’s disease	Muscle pain, Rashes, diarrhea, fevrer, cough, loss of appetite

INTRODUCTION

A clinical trial is a systematic process to determine the safety and efficacy of a drug or device in treating, preventing, or diagnosing a disease. It includes various phases:

- **Phase 0:** Micro-dosing studies, previously done in animals, now conducted in humans to assess dose tolerability (pharmacokinetics) before Phase 1.
- **Phase 1:** Non-therapeutic, focusing on safety and dosage in healthy volunteers.
- **Phase 2:** Exploratory, determining the effective dosage and therapeutic effects.
- **Phase 3:** Therapeutic confirmatory, assessing efficacy and safety on a larger scale.
- **Phase 4:** Post-approval, monitoring long-term effects and safety post-marketing.

The details of the clinical trial phases are shown in Table 1

Clinical trial phase	**Type of the study**	**Nature of study**
Phase 0	Exploratory	*Study Type:* Examines extremely low drug concentrations (micro-dosing). *Nature:* Focuses on pharmacokinetics and determining doses for Phase I. Previously in animals, now conducted in humans.
Phase I (Ia, Ib)	Non-Therapeutic Trial	*Participants:* <50 healthy subjects. *Nature:* Establishes safe dose range, MTD, pharmacokinetics, and pharmacodynamics. Typically single-center studies. *Sub-phases:* *Phase Ia:* SAD, MTD; 6-8 groups of 3-6 participants; duration varies. *Phase Ib:* MAD; dose gradually narrowed; 3 groups of 8 participants each
Phase II (IIa, IIb)	Exploratory Trial	*Participants:* 5-100 patients. *Nature:* Examines effective dosage, therapeutic effects, drug regimen, and interactions. Usually multicentric. *Sub-phases:* *Phase IIa:* Decides dosage; 20-30 patients; weeks to months. *Phase IIb:* Studies dose-response, interactions, and placebo comparison.
Phase III	Therapeutic Confirmatory Trial	*Participants:* 300-3000 patients. *Nature:* Pre-marketing, multicentric trial. Evaluates drug efficacy and safety, compares with placebo/standard drug, and notes adverse effects. Initiates NDA with regulatory agencies like the FDA.
Phase IV	Post-Approval Study	*Nature:* Conducted after drug approval and post-marketing.

Clinical research design is broadly categorized into two types: **non-interventional (observational)** and **interventional (experimental)** studies.

- **Non-interventional/Observational Studies:**

1) *With Comparator Group:* Analytical studies, such as case-control and cohort studies.
2) *Without Comparator Group:* Descriptive studies.

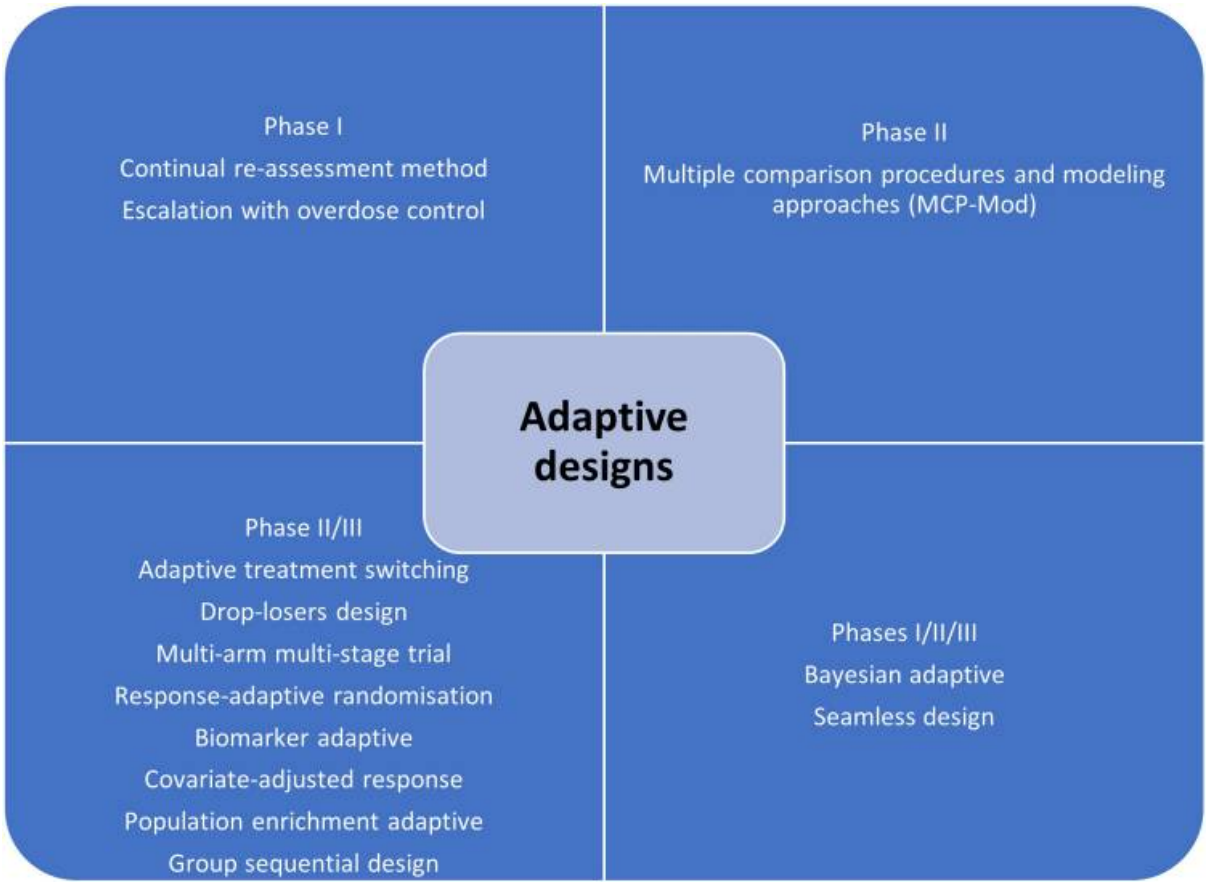
- **Interventional/Experimental Studies:** Can be either *randomized* or *non-randomized*.

Clinical trial designs are of several types that include parallel design, crossover design, factorial design, randomized withdrawal approach, adaptive design, superiority design, and non-inferiority design. The advantages and disadvantages of clinical trial designs are depicted in Table 2

Clinical trial designs, their advantages, and disadvantages

Trial design type	Type of the study	Nature of study	Advantages/disadvantages
Parallel	Randomized	This is the most frequent design wherein each arm of the study group is allocated a particular treatment (placebo (an inert substance)/therapeutic drug)	The placebo arm does not receive the trial drug, so may not get the benefit of it
Crossover	Randomized	The patient in this trial gets each drug and the patients serve as a control themselves	Avoids participant bias in treatment and requires a small sample size. This design is not suitable for research on acute diseases.
Factorial	Non-randomized	Two or more interventions on the participants and the study can provide information on the interactions between the drugs	The study design is complex
Randomized withdrawal approach	Randomized	This study evaluates the time/duration of the drug therapy	The study uses a placebo to understand the efficacy of a drug in treating the disease
Matched pairs	Post-approval study	Recruit patients with the same characteristics	Less variability

Clinical trial designs can be improved to maintain or enhance the study's validity. Adaptive designs allow researchers to make adjustments during the trial without compromising the integrity and validity of the results. This flexibility benefits trial conduction and data collection. However, despite these advantages, adaptive designs haven't gained universal acceptance among clinical researchers, likely due to low familiarity with these designs in the research community. Adaptive designs have been applied across various phases of clinical trials and for different clinical conditions.



Principles of Clinical Trials/Research:

Clinical trials are conducted to expand knowledge, test hypotheses, and perform public health research. This involves data collection and analysis to draw conclusions. Clinical trials can be categorized into **analytical, observational,** and **experimental** research, and further classified into **non-directed data capture, directed data capture,** and **drug trials**. They can be **prospective** or **retrospective** and may include **case-control** or **cohort** studies.

Clinical trials aim to find treatments, prevent diseases, observe conditions, or diagnose medical issues. Among the various types, **observational research**—particularly using cross-sectional study designs—is the most common. This approach is used to analyze the presence

or absence of a disease, potential risk factors, and prevalence and incidence rates in a defined population.

Clinical trials can be **therapeutic** or **non-therapeutic**:
Therapeutic Trials: Use drugs that may benefit the patient.
Non-Therapeutic Trials: Participants do not directly benefit from the drug, but these trials contribute to broader knowledge and future improvements.

Planning a Clinical Trial/Research:

The planning process for a clinical trial involves several key steps:

1. **Protocol Development:** This is the blueprint of the trial, outlining objectives, design, methodology, statistical considerations, and organization. The protocol serves as a comprehensive guide for conducting the trial.
2. **Case Record/Report Form (CRF) Design:** The CRF is a critical document that captures data from each subject. It must be carefully designed to align with the protocol, ensuring that data collection is accurate and comprehensive. CRFs can be printed, optical, or electronic, as per the International Council for Harmonisation (ICH) guidelines.
3. **Institutional Review Boards (IRBs):** These boards review and approve the trial protocol to ensure ethical standards are met, protecting the rights and welfare of participants.
4. **Data Management:** This involves organizing and maintaining the trial data. The clinical data management section is responsible for the collection, processing, and distribution of data. Proper data management is crucial for the integrity and success of the trial.
5. **Site Monitoring:** Regular monitoring of clinical trial sites ensures compliance with the protocol, good clinical practice (GCP), and regulatory requirements. Monitoring helps identify and address issues early in the process.
6. **Project Management:** The project manager plays a vital role in planning, organizing, and controlling the trial. They ensure that timelines are met, resources are allocated effectively, and the trial progresses smoothly.
7. **Critical Steps in Planning:**
    - **Idea Generation & Literature Review:** Identify a research problem and review existing literature.
    - **Hypothesis Formulation & Synopsis Writing:** Develop a hypothesis and a brief overview of the study.
    - **Investigator Identification & Protocol Writing:** Select investigators and draft a detailed protocol.
    - **Funding & Ethics:** Secure funding and establish ethics boards to oversee the trial.
    - **Manuals & Training:** Prepare procedure manuals and provide training to investigators.
    - **Trial Initiation:** Recruit participants and commence the trial.
8. **Key Considerations Before Trial Initiation:**
    - **Need for the Trial:** Determine if the trial is necessary and justified.
    - **Study Design & Methodology:** Ensure the design and methods are robust to produce reliable results.

9. **Quality Assurance:** Implement measures to ensure data quality, minimize bias, and control confounding factors.
10. **Effective Management:** Managing human and financial resources efficiently is essential. The trial manager's role is critical, requiring skills in communication, leadership, and strategic planning.

These steps and considerations are essential for conducting a successful clinical trial, ensuring that the study produces high-quality, reliable results. The practical aspects of clinical trial operations involve several crucial steps and considerations to ensure successful outcomes. Here's a summary of key elements:

1. **Planning and Proposal**:
    - **Letter of Intent**: Shows researcher interest in the study.
    - **Proposal**: Includes the study design, objectives, and methodology.
    - **Timeline**: Sets out the schedule for each phase of the trial.
    - **Protocol and Documents**: Includes case record forms, procedures, and guidelines.
    - **Budget and Funding**: Defines the financial requirements and sources.
2. **Regulatory and Ethical Approval**:
    - **IRB Approval**: Ensures the study meets ethical standards and protects participants' rights.
3. **Execution**:
    - **Conduct and Supervision**: Includes managing day-to-day operations, ensuring protocol adherence, and monitoring progress.
    - **Data Collection and Review**: Accurate data recording, analysis, and interpretation.
4. **Quality Assurance**:
    - **ICH and GCP Guidelines**: Ensure data quality and adherence to procedures.
    - **Audit Team**: Independently reviews and verifies compliance and data integrity.
5. **Recruitment and Participation**:
    - **Recruitment Challenges**: Identifying and overcoming barriers to participant enrollment.
    - **Participant Management**: Ensuring participant engagement and adherence.
6. **Cost and Resource Management**:
    - **Financial Costs**: Clinical trials can be expensive, with significant costs involved.
    - **Resource Allocation**: Requires careful planning and coordination, especially for multi-center trials.
7. **Collaboration and Transparency**:
    - **Stakeholder Collaboration**: Effective communication and cooperation among all parties involved.
    - **Cost Transparency**: Clear reporting and management of financial aspects.

These elements highlight the complexity and multi-faceted nature of clinical trial operations, emphasizing the need for meticulous planning, regulatory compliance, and efficient management to achieve successful research outcomes

Clinical trial applications, monitoring, and audit

Audits are a crucial component of clinical trials, ensuring compliance, integrity, and quality throughout the research process. Here's a detailed overview of clinical trial applications, monitoring, and audit:

Clinical Trial Applications

1. **Application Submission**:
    - **Regulatory Authorities**: Submit the clinical trial application to relevant bodies such as the FDA, EMA, or national regulatory agencies.
    - **Institutional Review Boards (IRBs)**: Obtain IRB approval to ensure the study meets ethical standards.
2. **Documentation**:
    - **Protocol**: Detailed plan of the trial, including objectives, design, and methodology.
    - **Investigator's Brochure**: Information on the investigational drug, including preclinical and clinical data.
    - **Informed Consent Forms**: Ensure participants are fully informed and consent voluntarily.

Monitoring

1. **Site Monitoring**:
    - **Regular Visits**: Conducted by Clinical Research Associates (CRAs) to ensure adherence to the protocol and regulatory requirements.
    - **Data Verification**: Compare source documents to Case Report Forms (CRFs) to ensure accuracy.
2. **Participant Management**:
    - **Enrollment**: Ensure participants meet inclusion criteria and are properly informed.
    - **Safety Monitoring**: Track and report adverse events and ensure participant safety.
3. **Data Collection and Management**:
    - **Data Integrity**: Implement procedures for accurate and reliable data collection.
    - **Data Security**: Ensure data is securely stored and protected against unauthorized access.

Audit

1. **Purpose and Scope**:
    - **Compliance Check**: Verify adherence to protocol, Good Clinical Practice (GCP) guidelines, and regulatory requirements.
    - **Quality Assurance**: Ensure all procedures and documentation meet predefined standards.
2. **Auditor Responsibilities**:
    - **Independence**: Auditors must be independent, not involved with sponsors, CROs, or trial site personnel.
    - **Personnel Qualifications**: Verify that the trial is conducted by qualified and trained staff.

    - **Document Verification**: Check the availability and correctness of key documents, including the investigational brochure, informed consent forms, CRFs, and regulatory approvals.
3. **Data Management**:
    - **Systems Evaluation**: Assess data management systems, including software and backup procedures.
    - **Contingency Plans**: Ensure there are contingency plans for data recovery and alternative recording methods.
    - **Security**: Evaluate data security measures and personnel training in data entry and analysis.
4. **Institutional Review Committees**:
    - **Functioning**: Verify the composition and functioning of ethics committees to ensure proper review and oversight.
5. **Audit Process**:
    - **Planning**: Develop an audit plan outlining objectives, scope, and procedures.
    - **Execution**: Conduct the audit according to the plan, collecting evidence and evaluating compliance.

Clinical trial data analysis, regulatory audits, and project management

Clinical Trial Data Management Systems (CDMS)

1. **Study Management**:
    - **Study Design**: Define objectives, enrolment criteria, and termination criteria.
    - **Site and Staff Management**: Coordinate site activities and manage study personnel.
    - **Subject Management**: Track participant enrolment and progress.
    - **Contracts and Documentation**: Manage contracts, regulatory documents, and trial-related paperwork.
    - **Data Management**: Includes data entry, validation, and integration from various sources.
    - **Patient Diaries**: Integration for capturing participant-reported outcomes.
    - **Medical Coding**: Standardize terminology for medications and adverse events.
    - **Monitoring and Reporting**: Oversee trial progress, monitor adverse events, and ensure compliance.
    - **Supplier and Lab Data Management**: Handle external suppliers and lab data integration.
    - **External Interfaces**: Manage data exchange with external systems.
    - **Randomization**: Implement randomization procedures if applicable.
2. **Data Analysis**:
    - **Error Minimization**: Ensure accuracy through mechanisms like double data entry.
    - **Medical Coding**: Use standardized coding for medications and adverse events.
    - **Data Storage**: Secure and manage data within the CDMS.
3. **Project Planning and Timelines**:

    - **Preparation Timelines**: Set deadlines for protocol preparation, CRF design, and project planning.
    - **Enrollment and Data Recording**: Define timelines for participant recruitment and data collection.
    - **Finalization Timelines**: Include deadlines for the last subject's CRF and the locked period after the last entry.
    - **Data Collection Methods**: Plan for data collection modes and transportation methods for CRFs, patient diaries, and adverse event records.
4. **Standard Operating Procedures (SOPs) and Quality Control (QC)**:
    - **SOP Preparation**: Develop SOPs for all trial procedures.
    - **QC Procedures**: Define types and timing of quality control measures.
    - **Project Review**: Assess budget, resources, and process quality.
    - **Measurement and Control**: Monitor turnaround times, address training issues, and manage CRF collection and delivery.

Clinical Quality Assurance (CQA) Audit

1. **Audit Planning**:
    - **Detailed Plan**: Develop a comprehensive audit plan outlining objectives, scope, and methods.
    - **Points of Improvement**: Identify areas needing improvement based on previous audits or quality issues.
2. **Conducting Audits**:
    - **SOP and Compliance Verification**: Ensure adherence to SOPs and regulatory requirements.
    - **Generating Results**: Produce meaningful audit findings that contribute to quality improvement.
    - **Promoting Improvement**: Use audit results to enhance clinical trial processes and practices.
3. **Components of CQA Audit**:
    - **Documentation Review**: Assess protocol adherence, informed consent, and data accuracy.
    - **Process Evaluation**: Evaluate trial processes, data management, and reporting mechanisms.
    - **Regulatory Compliance**: Verify compliance with GCP guidelines and regulatory standards.

Ethics and concerns in clinical trial/research

Key Ethical Principles in Clinical Trials

1. **Informed Consent**:
    - Participants must be fully informed about the study, including its purpose, procedures, risks, and benefits, and must voluntarily agree to participate.
2. **Respect for Autonomy**:
    - Participants have the right to make informed decisions about their involvement and to withdraw from the study at any time.
3. **Beneficence**:

    - Researchers must aim to maximize benefits and minimize harm to participants.
4. **Justice**:
    - Fair selection of participants and equitable distribution of research benefits and burdens.
5. **Integrity and Transparency**:
    - Researchers should maintain honesty and transparency in reporting results and conducting the study.

Modern Ethical Oversight

- **Ethics Committees and IRBs**: Continually review and monitor research to ensure compliance with ethical standards.
- **Regulatory Bodies**: Ensure adherence to ethical guidelines and legal requirements.

These ethical frameworks and guidelines collectively ensure that clinical research is conducted with respect for participants, scientific rigor, and societal benefit.

CONCLUSION –

Clinical research and clinical trials are important from the public health perspective. Clinical research facilitates scientists, public health administrations, and people to increase their understanding and improve preparedness concerning the diseases prevalent in different geographical regions of the world. Moreover, clinical research helps in mitigating health-related problems as evidenced by the current Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) pandemic and other emerging and re-emerging microbial infections. Clinical trials are crucial to the development of drugs, devices, and vaccines. Therefore, scientists are required to be up to date with the process and procedures of clinical research and trials as discussed comprehensively in this review.

PRODUCT MONOGRAPH OF VOGLIBOSE

Chemical Formula – C10H21N7

Mol. Wt. - 267

Chemical Name – 3,4 – di deoxy – 4 – [(2 – hydroxy -1-hydroxymethyl) ethyl] amino]-2-C-(hydroxymethyl) – D – epi - inositol

Synonyms – Glustat , Basen

Description

Voglibose was first discovered in 1981, and first launched in Japan in 1994 under the trade name BASEN.

To improve postprandial hyperglycaemia in DM condition.

Voglibose is a valiolamine derivative.

Class – alpha glycosidase inhibitor.

Major drugs belong to this class are Acarbose, Miglitol, Voglibose, of which voglibose is newest.

Mechanism of Action

The anti-hypoglycaemic action of voglibose results from a reversible inhibition of membrane bound intestines α glycosidase hydrolize enzymes which hydrolize oligosaccharides and disaccharides to glucose and other monosaccharides in the brush border of the small intestine.

Pharmacokinetics -

Extent of Absorption - Slow and poorly absorbed, dose – dependent.

Unchanged form - < 6%

Bioavailability - < 6%

Clearance - mainly renal

Half life - 4.08 hrs.

Protein binding - low to high, species dependent, saturable

Distribution - low tissue affinity

Metabolism - little metabolism occurs

Excretion - Almost completely by fecal

renal < 5%

SIDE EFFECTS - Abdominal pain, diarrhoea, flatulence (gas), skin reactions, heartburn, nausea, and vomiting

Indication - Prescribed only for diabetes mellitus and also reduces macro vascular complications caused by DM.

Contraindications - Inflammatory bowel disease

Gastrointestinal obstruction

Hernia

Severe ketosis

Diabetic hypersensitivity

Pregnancy & Lactation

Not to be used as single therapy in IDDM (type 1)

Adverse reactions – Abdominal distension.

Dosage -

Dose – 0.2 – 0.3 mg 3 times/ day each immediately before each meal.

Do not chew, break, or crush tablet; swallow it as whole with water

Route of Administration – Oral

Dose adjustment – is necessary and used with caution in patients with Kidney impairment/disease, in liver problems also.

Missed Dose – If dose is forgotten, take it as soon as possible. If its time for next dose, just take one dose, avoid taking two doses at same time because of potential adverse effects.

Overdose – Can be accidental, chances of getting harmful effects on body functions, lead to some medical emergency.

Precautions – Avoid excess dosage.

- if allergic to any medications, inform to doctor as product contain some inactive ingredients which causes serious allergic reactions.

- Inform doctor, if you are having any medical history of intestinal obstruction, digestive disorders, Inflammatory disease, ulcers, ketosis, diabetic hypersensitivity.

Warnings – Pregnant women should avoid taking unless it is absolutely appropriate & only if recommended by the doctor.

- Breast feeding women should also avoid taking this medication as it can pass into breast milk.

Storage – Store below room temperature below 30 0C

- Keep out of children's reach.

Drug Interactions -

Food-drug interactions – Avoid alcohol consumption while taking voglibose as it increases side effects.

Drug-disease interactions – Voglibose should not be taken in patients with diabetic ketoacidosis, IBD, Intestinal ulcers, intestinal obstructions, and chronic disorders of digestion or absorption as it may deteriorate conditions as a result of increased gas formation in intestine.

Drug-drug interactions – interact with

Blood thinners - Voglibose / Acarbose interact with warfarin sodium result in increased risk of bleeding.

DEPARTMENTAL ACTIVITIES:

Our Institution St Peter's Institute of Pharmaceutical Sciences in association with ISPOR India Telangana chapter and IPA hanumakonda conducted 2 days " Advanced learning module on Oncology."

Speaker of the session: Dr. Manthan Merja, Surgical Oncologist, SAL Hospital. Gujarat Cancer and Research Institute.

Dr. Avinash Khadela, Clinical Oncologist, Assistant Professor at L.M College of Pharmacy

On march 4 th 2023, our Institution conducted “Scientific poster presentation session” for Pharm D Students. Students competitively, enthusiastically presented posters, explored and expressed there knowledge. Best posters were awarded and appreciated.

Our institution conducted “workshop on handling instuments in laboratory” explained by our faculty Mr. Sandeep, Ms. Anusha on Kymograph, Organbath, Actophotometer,Coating machine and blender.