WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 2, 247-272. Review Article ISSN 2277– 7105

STUDY OF DICYCLOMINE DRUG RELATED WITH PHARMACOVIGILANCE

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Article Received on
23 Nov. 2022,

Revised on 13 Dec. 2022,
Accepted on 03 Jan. 2023

DOI: 10.20959/wjpr20232-26909

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ABSTRACT

Pharmacovigilance is an important & integral part of clinical research despite its 40 year history pharmacovigilance remains a dynamic Clinical & scientific discipline. The harm be minimized by ensuring can that medicines of good quality, safety & efficacy are used Rationally and that the expectation and concems of the patient are taken into account when therapeutic decision are made. Pharmacovigilance deals with safety & monitoring of drugs for purpose of detection of frequency of adverse drug reaction to improve patients' healthcare & safety. Adverse drug reactions have been large scale problem in developing counties which brings pharmacovigilance as a major field in drug manufacturing & development. Pharmacovigilance is aimed at increasing reporting rates and minimizing adverse drug reactions. As pharmacovigilance is concerned with toxicology studies of drug this study deals with the account of isoniazid (referred as first line anti tubercular drug) This review is concerned with data collected about toxicology & account of isoniazid.

KEYWORDS:

• INTRODUCTION

The wold heath organization (WHO) defines pharmacovigilance as the science & activities relating to the detection evaluation understanding & prevention of adverse reaction to medicines or any other medicine related problems.

- **Clinical research**

>definition clinical research:- clinical research is a branch of health care science that determines the Safety & effectiveness of medication, devices, diagnostic products & treatment. regimen intended for human use.

- **Classification**
- **Pre-clinical trial**

>A laboratory test of a new drug or a new invasive medical device on animal subjects; conducted to gather evidence justifying a clinical trial.

- **Following type of step are performed**
- **Screening test:-** A screening test is done to detect potential health disorders or diseases in people who do not have any symptoms of disease.
- **2) Test is isolated organs bacterial culture etc:-** bacteria culture test, a healthcare provider takes a sample of blood, stool, urine, skin, mucus or spinal fluid.
- **Test on animal models of human disease:-** A useful animal model for disease must be similar in its pathology to disease conditions in humans. Experimental animal models of rheumatoid arthritis and multiple sclerosis are useful for a better understanding of disease mechanisms and for evaluating the therapeutic efficacy of new and emerging drugs.
- **Confirmatory test and analogous activities:-** Compounds found active are taken up for detailed study by more elaborate tests which confirm and characterize the activity.
- **Systemic pharmacology:-** Systemic drug therapy involves treatment that affects the body as a whole or that acts specifically on systems that involve the entire body, such as the cardiovascular, respiratory, gastrointestinal, or nervous systems.
- **Quantitative test:-** A quantitative test is all about objectivity and group behaviour. It doesn't concern the individual thoughts of participants, forsaking the context around the user action.
- **Pharmacokinetics:-** Pharmacokinetics, sometimes described as what the body does to a drug, refers to the movement of drug into, through, and out of the body the time course of its absorption.
- **Toxicity test:-** Animals are useful models to predict the toxicity of chemicals in humans because they have similar cell organelles, cells and organs.

- **Clinical trial**

Clinical trials studies with human subjected to test new drug or combination of drugs new approaches to surgery radiotherapy procedures to improve the diagnosis of disease & the quality of life the patient.

- **the clinical studies me divided into 4 phase**
- **Phase 0**

> A phase 0 study gives no data safety or efficacy, being by definition a does too low to cause any therapeutic effect.

>The drug development companies carry out phase 0 studies to rank drug candidates in order decide which has the bes pk parameters in human to take forward into development.

2) phase 1:- The first studies in human are phase 1 trials. They are performed with small of patients or healthy volunteers & are used to answer question such as what dose of the drug is likely to be effective & what side effect might occur.

3) phase II :- The trials with larger number of patients & focus on how well the treatment or procedure works perhaps in particular situation or groups of patients.

4) phase 3:- The trials enroll large number of patient & used to compare the effectiveness & safety of new drug treatment with that of the, standard existing treatment Information obtained from large. >Phase III trials demonstrates the benefits a new drug over the existing treatment are presented to regulatory authorities in order to obtain to market & Sell the drug.

5) Phase 4:-phase 4 studies may be regulatory authorities or may be undertaken by the sponsoring company for competitive or other resonance.

- **Function of drug controller generate of India do (DCGI)**

The drug controller General of India (DCGI) heads the central drug Standard control organization (CDSOC).

> The DCGI prepares & maintains the national reference standard for drug. In case of any regulates medical dispute with respect to the quality of the drug the DCGJ is the appellate authority.

>The DCGI is also central licensing authority for medical devices fall under the medical device Rules 2017.

- **Central drugs standard control organisation CDSCO**

>Setting standards of drugs.

>Quality control over drug imported. into the country.

> Conducting clinical trials. >Coordinating activities of the state drug control organisation.

>Grand of licences to import drug by Government hospital or medical Institutions for the use of their patients.

- **Type of regulatory application**
- **Investigational New drug [IND]:-** >Submitted by a physician to propose studying. An unapproved drug. An approved product for a new, indication or in a new Population.

a) Pre-clinical testing:- Laboratory test of a new drug or a new medical device usually done on animals subjected to see if the hope it for treatment really works and if it is safe to test on humans.

b) Manufacturing information:- >Manufacturing information manufacturing information provide services to support the manufacturing function. Purchasing may also be manufacturing information system in same business.

c) Clinical trial protocol:- Includes objective, design, methodology population to be studied, statistical consideration, ethical conduct and organisation.

2) New drug application (NDA):- The new drug application is the vehicle in the united state through which drug sponsor formally proposed that the Food and Drug Administration (FDA) have the a approved a new pharmaceutical for sale and marketing.

3) Abbrevated new drug application (ANDA):- An abbrevated new drug application is an application of US generic drug approval for the existing licence medication or approved drug. In since the existence of the DESI programme anabiat FDA two approved ANDAs.

- **good clinical practise**
- **Objective and scope ICH good clinical practise**

>protect the patient.

>To recognise the implication of non-compliance.

>To identify & then to reduce differences in technical requirement for drug development among regulatory agencies.

> Quicker access to patients of safe & effective new medicine.

> Describe the responsibilities & expectation of all participants in the conduct of clinical trials.

> Provide assurance of the safety of the newly developed compound.

> Provide standards on how should be conducted.

>Provide a unified standard for the European union, Japan & USA to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdictions.

>To emphasize the important of ICH GCP compliance when conducting clinical trial.

- **Scope of good clinical practice**

>Basis for the conduct of clinical trials. >Harmonisation between the member states in entire EU.

> All clinical trial, except no interventional trials

> Industry & Academia sponsored trials.

> Protection of human rights.

> Rules for protection of personal data.

>Declaration of Helsinki, version 1996.

>Still in according with ICH-GCP.

- **Protocol designing for clinical trials**

> Title Page [General Information).

> Background Information.

> objective / purpose.

> Study design.

> selection & Exclusion of subject

>Quality Control & Assurance.

>Ethics.

> Publication policy.

>Reference.

- **Clinical trials application process**

> Clinical trial Application CT submission

>CT Application by sponsor/ Academic Investigator / Hospital to CDSCO

>CT dossier & documents sent to NDA

>Review by CDSCO & NDAC Met Meeting of sponsor/ Academic

>Investigator with CDSCO & NDAC

>Approval rejection of CT Application.

- **concept of pharmacovigilance**

>Definition, objective, types & componunt of pharmacovigilance

>Definition:-The practice of monitoring the effect of medical drug after they been licensed for used specially in order to identify & evoluated previously unreported adverse reaction.

- **According to WHO:-** The science & activities relating to the detection, assessment understanding & prevention of adverse effects or any! other drug related problem
- **Pharmakon→ medicinal substance vigila Two watch over Pt.**

- **Objective**

> Improve public health & safety.

>Encourage safe, rational & appropriate use of drug.

> Promote understating education & clinical training in pharmacovigilance.

>Benefit risk analysis.

> Identification of risk factors & possible mechanism underlying adverse effects.

> detection of increase in frequency adverse reaction.

> Early adverse reaction & interaction specially for the newly marketed drug.

- **Types of Pharmacovigilance**

>There are four imp pharmacovigilance such :-

1) Passive surveillance

2) Active Surveillance.

3) Cohort event monitoring.

4) Targeted clinical investigation.

- **Passive surveillance:-** The identity of the reporter remains anonymous but patient related details like country age gender & pre-existing comorbidities can be recovered from the reporting forms.
- **Active surveillance:-**This method aims to monitor certain Specific drug related adverse events & seek to ascertain the number of adverse day reaction entirely through pre-planned process. It is. commonly known as toxicity monitoring or safety monitoring.
- **cohort event monitoring:-** In this method, the surveillance study is planned prior to beginning the treatment with the medication.>A group of people are exposed to a drug for a defined period & actively Followed up during treatment.

- **Targeted clinical investigations:-** & These kinds of investigations are performed to identify & characterize the adverse reactions related to a day among special population like people with some genetic disorder people, pregnant women and older people.

- **Components of pharmacovigilance**

> Pharmacovigilance delivers four primary capabileties to pharmaceutical companies :-

1) Adverse event case managment including expedited reporting.

2) Aggregate reporting.

3) Signal intelligence.

4) Risk management.

1) Adverse event case managment including expedited reporting

>An any up word medical occurocance in a patient administrated medical product which does not necessarily have a 'Casual relationship with this treatment.

2) Aggregate reporting:- Aggregate reporting refer to the report that focus so much on individual cases but rather on overview assessment the of the safety profile of benefit risk evaluation.

>Example

>periodic safety update reports [PSUR].

>periodic benefit risk evaluation report [PBRER].

>periodic adverse (drug) experience report [US].

>Development safety update research [DSURs].

> Integrated summaries safety [US].

>Clinical summaries of softly [us].

A) Periodic safety update Report [PSUR]:- It is Pu doc. intended to provide an evaluation of risk-benifit balance of medicinal product for submission by markating authorisation holders at defined time points during the post authorisation phase.

> Source of safety information.

> Active surveillance system.

> clinical data trial.

> competent authorities updates & website publication.

> Non -clinical studies update

> Post authorisation use in special population.

- **Table of content in PSUR**

1) Introduction.
2) Worldwide marketing authorisation status.
3) Actions taken in the reporting interval for safety reason
4) changes to reference safety information.
5) data in Summary tabulation.
6) summaries of significant findings from clinical trials during the reporting interval.
7) finding from non-interventional studies.
8) Info. from other sources.
9) Non-clinical trial.
10) Literature.
11) other periodic reports.
12) Signal & risk evaluation.
13) Benefit evaluation.
14) Conclusion.
15) Appendices to PSUR.

B) Periodic benefit risk evaluation reports [PB RERI

> Rason of AE reports.
> Protection of human subjects
> Collection of clean & reproducible data.
> Regulatory perspective.
> Analyze data & determine risk /benifit
> before giving permission to marketed.

C) Development safety Update Research [DSUR]:- This are new internationally harmonized safety documents covering the summary of medicinal products during their development or clinical trial phase.

3) signal intelligence:- pharmacovigilance are signal intelligence practice are focused adapting DPA algorism. SRS data for constituting hypothesis of signal drug - AF Combination that needed further investigation to establish evidence-based medicine to confirm casualties associated between those pairs.

4) Risk managements

> safe of risk management

1) Identify the risk:-

a) Preclinical studies.

b) Harms identified in CT & meta analysis.

c) formal mortality & morbidity studies.

2) Understand the risk

a) Regorous case definition.

b) Case series analysis.

c) clean description in label.

3) Monitor the risk

a) Past markating surveillance.

b) database analyses.

c) Prospective cohort studies & register.

>Risk minimization & communication

1) Communicate the risk

a) advise in label [not enough to communicate specific risk minimization. activities or change behaviour]

b) partnership with regulators.

c) Education of physician patients company staff.

2) Act to reduce the risk.

a) Limited distribution.

b) Limited prescribing rights.

c) contra- indicate for certain groups, indication routes of administration.

d) advice for high risk groups.

>Risk managment leagal framework

1) ICH E2E − PV planning [November 2004].

2) EMA - Guideline on risk managment System for medicinal products for human use. [EMEA / CHMP/ 96268 / 2005].

3) GMP- ANNEX 20 Quality risk management [fed 2008].

- **Constitution and objective of pharmacovigilance program of India [PVPI]**

>objective

1) To create a national wide system for patient safety reporting.
2) To identify & Analyze new signal from the report case.
3) To Analyze the benefit-risk ratio of marketed medications.
4) To generate evidence based information on safety of medicines.
5) To support regulatory agency in the decision making process use the medication.
6) To promote rational use of medicine.

- **Constitution**

>Pharmacovigilance mainly involve monitoring & reporting OF adverse drug reaction assosiated with the use of medicinal products.

>under reaction the reporting of advers drug reaction is a Serious issue hampering the dynamic of pharmacovigilance program.

- **List of National do advers drug Monitoring centre's [AMCs] & their functions**
- **National coordinating centre [NCC]**

1) Dept. of pharmacology. ALL India Institute of medical sciences. New Delhi.

- **ADR monitoring center**

1) Therapeutics & toxicology gout medical Collage, Bakshi nagar, Jammu.
2) Dept. of p'cology, PG IMPR chandigarh.
3) RG kar medical collage, New Delhi Kolkata.
4) Lady Harding medical collage New Delhi.
5) seth hospital as medical collage & KEM hospital, parel, mumbai.
6) School of tropical medicine, chittaranjan Avenar, kolkata.
7) JIPMER Pondicherry. Karnataka.
8) JSS medical college hospital
9) Medical College, Guwahati, Assam.
10) Madras medical college, Chennai.
11) SAINS medical college, vijjain.
12) SMS college for Jaipur.
13) Christian medical college, Vellore. TN.

- **Functions**

1) To optimize safe & effective vibe of medicines in set up.

2) To create awareness amongst heath care professionals about the importance of ADR reporting.

3) To monitor benefit risk profile of medicine.

4) Generate independent evidence based recombination on the safety of medicines.

5) collection of ADR reports.

6) Perform follow up with the complainant to check completeness as per sop's.

7) data entry into vingiflow.

8) Reporting to PVPI NCC through vingiflow with the source data attached to the ADR case.

9) Training/ Feedback to physician through newsletters. circulated by the PVPI NCC.

10) centre coordinator responsible for sending monthly reports to AMC.

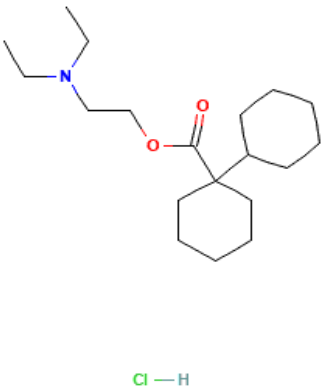
- **International Conference on Harmonization. JCH E2e Guidelines**
- **element of the non-clinical & clinical safety specification**
- **Dicyclomine**

> dicyclomine e also known as dicyclomine sold under the brand name Betyl in the US, medication that is used to treat spasm of the intestines such as occur in irritable bowel syndrome.

> Dicyclomine hydrochloride - 2-[diethylamino] Lethylbicyeclohexy -1 -carboxylate hydrochloride. is an antispasmodic & anticholinergic drugs.

> surfactants are a kind amphiphilic molecule with a polar head hydrophobic tail on one side & a long hydrophobic tail on the other.

- **Structure**



- **dicyclomine molecular weight** - 309.487 g/mol.
- **Molecular formula**-C19, H36C1NO2.
- **Category** -Pregnancy.
- **Synonyms** - Dicyclomine HCl, Dicycloverine Hydrochloride.
- **Brand Name of dicyclomine** – bently R.
- **Drug class:-**anticholinergic.

- **Use**

> Dicyclomine is used to treat a certain type of intentional problem called irritable bowel Syndrome.

> It help to reduce the symptoms of stomach & intestinal cramping.

> this medication works by slowing the natural movements of the gut & by relaxing the muscles in the stomach & intestines.

> Dicyclomine belongs to a class of drugs known as anticholinergics/ antispasmodics.

> This medication must not be used by children younger than 6 months old because of the risk of serious side Effect.

- **Side effect**

> fast -slow heartbeats, pounding heart beats or fluttering in your chest.

> Confusion, agitation, hallucination unusual thoughts or behaviour.

> Problems with memory or speech.

> problems with balance or muscle to muscle movement.

> diarrhea severe constipation or worsening of bowel symptoms.

> trouble swallowing.

- **Common side effect**

> drowsiness, dizziness, weakness, nervousness.

> blurred vision.

> dry mouth.

> nausea.

- **Elimination of half life**

> Dicyclomine is 79.5% eliminated in the urine & 8.4% in the faces.

> The mean plasma elimination half life is approximately 1.8 hours.

- **Discovery & development**

> Dicycloverine was first synthesized chemically in the United states circa 1945 by scientists at willium S.Merrell company.

> It was first marketed in 1952 for gastrointestinal disorders, including colic in infants.

> the INN Name " dicycloverine was recommended in 1959.

> In the mid-1980s several governments restricted its use in infants due to report of convulsions, difficult in breathing. irritability & restlessness in infants given the drug.

> the US market for the drug at that time was around $8 million. Doc had 60 % of itt & Rugby had 40%.

> The next year Hoechst Marion Roussel which by that time had acquired the business granted a license to **Endo pharmaceutical.**

- **Development**

> Accuracy of the developed method was determined by method of standard additions.

> known amount of DIC, [0,15, 30, 45 µg/ml], MEF[0,1.25, 2.5, 5 µg ml] & PCM [0, 2.5, 5, 75 µg/ml] were sample added to pre quantified sample solution & the amount OF DIC, MEF & PCM were estimated by-measuring the peak areas & by fitting these Values to the straight line equation of calibration curve.

> the limit of detection [LOD] is defined as the lowest concentration of an analyte that can reliably b reliably be differentiated from background levels.

> Limit of quantification [LOD] of an individual analytical procedure is the lowest amount of analyte that can be quantitatively determined suitable precision & accuracy.

> Robustness was studied by evaluating, variation the effect of small but deliberate Variation in the chromatographic.

> The condition studied were flow rate & percentage of organic phase

> system suitability test of the chromatography system was performed before validation" method.

> Area retention time [RT], asymmetry factor. & theoretical plates for the five Suitability injection were determined.

- **Pre clinical research**

> Pre clinical trials are laboratory. test of a new drug substance of medical devices usually done on animal subjects to whether the treatment really works. & if it is safe to test on human.

> the main goals of pre-clinical studies are to determine a product's ultimate safety profile.

> Products may include new medical devices. drugs gene therapy solutions etc.

- **The types of studies included in pre-clinical tril**
- **Screening test:**-medical histories & demographic data, including name, sex, age, race, body weight, height, body build.

2) Tests on isolated organs, bacterial cultures

> These also preliminary tests to detect specific activity such as.

> Anti-histaminic.

> Anti- secretory.

> vasodilator.

> Antibacterial.

3) Tests on animal models of human disease. > Transtating computational system of molecular [[x] to phenotypic [Y] association from animal models to human provides a powerful Frameworks for translating.

4) General observation test:- > Hypothesis Generating descriptive statistics 6) Toxic Exploratory observation.

5) Confirmatory tests & analogous activities:- compounds founds active taken up for detailed study by more elaborate tests which confirm & characterize the activity.

6) systemic pharmacology. Irrespective of the primary action of the drug its effect on major organ systems, such as nervous, cardio- vascular, respiratory renal are worked out.

7) Quantitative test: The dose response relationship, maximal. effects & comparative efficacy with existing drug is carried out.

- **Clinical research**

> Because clinical trails are conducted under widely varying condition, advers reaction rates observed in the clinical trials of a drug contact be directly compared to rates in the clinical trials of and their drug & may not reflect the rates. observed in practice.

> The data described below reflect expoure in controlled Clinical trail involving over 100 patients tarted for functional bowel/imitable tow bowel syndrome with dicyclomine hydrochloride at initial does of 160 mg daily.

> In these trick most of the side effect were typically anticholinergic in nature reaction and were reported by 61% of the patient.

> 9% patient were discontinued from bently because of one or more of these side effect with 2% In 41% of the Patients with side effect, side effect disappeared or were tolerated at the 160mg daily dose without reduction.

- **Phases**

1) Phase 1:- 20-100 usually healthy volunteer.

donation:- many months.

Goal-safety:- specially**.**

2) Phase 2:- Patients up to many hundreds (1-400].

durations :- many safety but month to 2 years.

Goal:- short term safety but mainly effectiveness definition of" effective dosage.

3) Phase 3:- Patients many hundreds to thousands many.

Duration:- 1-4 years

Goal:- Safety, effectiveness Comparative, dosage, increase the 'n' apply for registration.

3) Phase 4:- Patients many mon thousands.

Duration:- Many years.

Goal:- Pharmacosurvellance expand indication create experience.

- **Past marketing monitaring**

> have been identified during post approval use of bently. because these reaction are reported voluntarily form a population of uncertain size, it is not always possible. to reliaby estimate their frequency or establish a causal relationship to drug exposure.

>cardiac disorders & palpitations.

>Eye disorders:- Cycloplegia, mydriasis.

>Immune system disorders:- drug hypersensitivity including face oedema.

>Gastrointestinal disorder:- abdominal distension, abdominal pain:

> General disorder & administration site Condition:- fatigue, malaise

>Nervous system disorder:- dizziness, headache.

> Respiratory, thoracic & meditational disorder:- dyspoea, nasal congestion.

- **Investigator**

An individual who conducts a clinical investigation or in the event of an investigation Conducted by a team of individuals is the responsible leader of team.

- **Co-Investigators**

>A member of the research team designated & supervised by the protocol Investigation to perform critical study related & to make important study-related procedure decisions sub-investigator as those individuals authorized to make medical judgments & decisions regarding study.

- **Investigators Responsibilities**

> should be qualified by education, training & experience to assume responsibility for the proper conduct of trial permit monitoring & auditing by sponsor & inspection by regulatory authority.

- **Institutional Review Based [JRB] ethics Committee**

> An institutional review bound [IRB] also called independent ethics committee, ethical review board or research ethics board.

> In the united states ethics committee that reviews proposed & angoing research involving human subjected.

> the institutional review board (IRB] exists to protect the rights & safety of human research.

- **Investigational of New drug [IND]**
- > Investigational New drug (IND) program is the means by which a pharmaceutical Company human obtains permission to start clinical trials & ship a experimental drug across state lines before a marketing application for the drug has been approved.

> In investigational new drug [IND] application is to provide the data showing that it is resonable to being beg in tests of a new drug on human.

- **Non Clinical trials**

>Provide evidence that drug is reasonably safe to conduct the proposed clinical investigation.

> Provide understanding of drug's mechanism of action.

>Information the design of early stage clinical trials.

> Guide patient eligibility criteria & safety monitoring procedures.

- **Human clinical trials**

A) Pharmacokinetics

>**absorption**:- the bioavailability of dicyclomine has not been determined through it is likely "well absorbed as the primary of elimination in the urine

>**Metabolism** :- The metabolism of dicyclomine has not been well researched.

>Excretion:- & 50-70 excreted in urine in 24 hr.

B) Toxicity:-Patient experiencing vomiting may present with headache, nausea, an overdose blurred vision, dilated pupils, dizziness, do mouth, difficulty, swallowing CNS stimulation. as well as hot, dry skin.

C) Pharmacodynamics

>drug Dicyclomine is an anticholinergic used to relax the smooth muscles of the intestines.

>It is duration of action is not especially long as it is usually taken u times daily with individual doses of 10 20- mg orally or 10- 20mg by intramuscular injection.

D) Mechanism of action:- Dicyclomine achieves its action partially through direct antimuscurinic activity of the M1 M3 & M2 receptors, & partially through antagonism of bradykinin & histamine.

E) Dose

>**Adult:-** 10-20 mg/day - 80mg/day.

>**Children:-** 10 mg/ day - 40 mg/day.

- **design & conduct of observational studies**

>Carefully designed & conducted pharmacpidemiological studies specifically observational studies are important took in pharmacovigilance.

>In observational studies the investigator observe & evaluates results of ongoing medical care without controlling the therapy beyond normal medical practice.

>Before the observational study that is part of a pharmacovigilance plan commences a protocol should. "be Finalised.

>It is recommended that the protocol be discussed. with the regulatory authorities before the study starts.

>In also suggested that should be terminated early be discussed with regulatory authoritices in advance.

>A study report after completion & interim reports if appropriate should be submitted to the authorities according to the milestones within the pharmacovigilance plans.

>study protocols should as minimum include the study the study aims & objects methods to be used on the plan for analysis.

>The final study repost accurately & completely present the study object method result and the principle investigator, interpretation of the finding.

>It is recommend that the sponsor follow good epidemiological practice for observational studies and also internationally accepted guidelines such as the guidelines.

- **Selection of a drug class for pharmacovigilance study using different criteria, [e.g commmercial availability selling of drug etc]**
- **Commercial availability**

>Fresenius kabi is pleased to announce the "availability critical fre of this latest addition to our care port folio, representing another important & affordable therapy option. for clinicians & the patients they treat. said John ducker president & CEO of Fresenius kabi USA.

>Fresenius kabi is a global health com that specializes in medicines For infusion & technologies for infusion and clinical nutrition.

>To learn more about Fresenius kabi, including it's expanding Us centers for pharmaceutic research manufacturing & distribution.

- **Seling of drug**

> Retail price of the said product was notified on 6th fed 2018 vide 5 No 6 of the notification at Rs 1.88 per tablet excluding GST.

>Normally working based whick sheet as per instructions based on which. price, is to be fixed displayed on the website to invite objection if way before announcement of price.

- **Dicyclomine- price list of Brand**
- **Brand name:**-clomin

Manufacturers:-core healthcare Ltd.

Generic:- dicyclomine

Type:- drop

Price:- 11 rupees

Unit:- 10 ml /ml**, Quantity:-** 10 ml

- **Brand name:-** clomin

Manufacturers:- core healthcare Ltd

Generic:- dicyclomine

Type:- Injection

Price:- 2.75 rupees

Unit:- 20 mg

Quantity:- 2 ml

- **Brand name:-** coligon

Manufacturers:- fourrts (India) laboratories Pvt.Ltd.

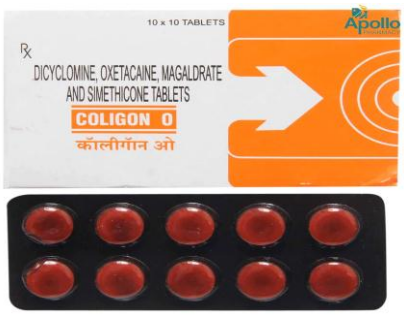
Generic:- dicyclomine

Type:- Capsule/Tablet

Price:- 8.50 rupees

Unit:- 20 mg

Quantity:- 10



- **Brand name:**-Cyclozobin

Manufacturers:- Nicholas India Ltd.

Generic:- dicyclomine

Type:- Capsule/Tablet

Price:-3.50 rupees

Unit:- 10 mg / ml

Quantity:- 1 ml

- **Brand name:-** Dicoli Inj.

Manufacturers:- kontest chemical Ltd.

Generic:- dicyclomine

Type:- Capsule /Tablet

Price:- 7.60 rupees

Unit:- 10 mg/ ml

Quantity:- 2ml

- **Brand name:**-Dicyclomine

Manufacturers:-core healthcare

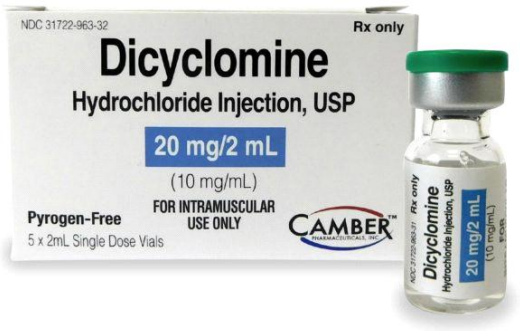
Type:-Injection

Price:-2.25 rupees

Unit:-20 mg

Quantity:-2 ml

- **Identification of most widely prescribed drug from a selected class (consumption report] by approaching pharmacy stores, company, representative & phrama companies web portals**



Before taking this medicine:-You should not use dicyclomine if you are allergic to it or if you have.

> glaucoma.

> bladder obstruction or other urination problem.

> blockage in your digestive tract (stomach or intestine).

> serious heart condition & active bleeding.

- **Not approved for use by anyone younger than 18 year old.**
- **Tell your doctor if you have ever had.**

> heart problem or high blood pressure.

> Liver or kidney disease.

>**older adult may be more sensitive to the effect of dicyclomine.**

- **How should take dicyclomine**

>Follow all direction on your prescription label and read all medication guide's or instructions sheet.

>your doctor may occasionally Change your dose use the medication exactly as direct.

>dicyclomine oral is taken by mouth.

>dicyclomine injection is given in a muscle if you are Anabel to take the medication by mouth.

>call your doctor if your symptoms do not improve after 2 year.

>short at room Temperature away from moisture and heat.

- **What happen if miss a dose**

>skip the missed dose and use your next dose at the regular time do not you two dosed at one time.

- **What happen if overdose**

>seek emergency medical attention or call the poison help line at 1-800-222-1222.

>overdose can cause nausea, vomiting, weakness or loss of movement in any part of your body.

- **What should avoid while taking dicyclomine**

>avoid driving activity until you know how dicyclomine oral.

>avoid using an antacid, Antacid can make it harder for your body to absorb dicyclomine oral.

- **Side effect**

>get emergency medical help if you have sings of an allergic reaction:-difficult breathing, swelling of your face, lips or tongue.

- **dicyclomine may cause serious side effects**

>fast or slow heart beat's.

>confusion, agitation or behavior.

>problem with memory or speech.

>problem balance or muscle movement.

- **Dicyclomine dosing information**

>usual adult dose for irritable bowel syndrome

>oral

>initial dose:- 20 mg orally four time a day.

>maintenance dose :- up to 40 mg orally four time a day after one week with initial dose.

>use:-treatment of patient with functional bowel / irritable bowel syndrome.

- **Pharma companies web portal**

>dicyclomine manufacturers

1) Olon from ltaly.

2) PCAS from France**.**

3) unnati pharmaceutical pvt. Ltd. From India.

4) Indoco remedies from India.

- **Identification of adverse effects of a dicyclomine drug**
- **Identification of adverse effects of a selected. doug dicyclomine drug using different search engines [eg Medscape.com, drug.com, xxlist.com etc].**

- **Side Effects**

>Dizziness, drowsiness, light headedness, workers. by eyes dry mouth, condipation & abdominal blapting may occury. If any of these offeds last of get acorse, tell your doctor or pharmacist promptly.

> To relieve dry mouth, chew gum, drink, water or use a saliva substitutle to relieve dry eyes, consult your pharmacist For andificial trans or other eye lubricanta.

> Tell your doctor right away if you have any serious side effects, including decreased sweating, dry / hot/ flushed skin, fast/ irregular, mental/ mood changes, difficulty urinating, decreased sexual ability.

>Get medical help right away if you have any very serious side effects, including eye pain swelling/redness, vision change.

>This not a complete lot of possible side effect If you notice other effects not listed above, contad doctor or pharmacist.

>In call your doctor for medical advice side effects you may report side effects to heath at 1-866-234-2345.

Version-1.2

SUSPECTED ADVERSE DRUG REACTION REPORTING FORM

For VOLUNTARY reporting of Adverse Drug Reactions by Healthcare Professionals

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

FOR AMC/NCC USE ONLY

AMC Report No. :

Report Type ☐ Initial ☐ Follow up

Worldwide Unique No. :

A. PATIENT INFORMATION

1. Patient Initials _____

2. Age at time of Event or Date of Birth _____

3. M ☐ F ☐ Other ☐

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. Relevant medical/ medication history (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/renal dysfunction etc.)

14. Seriousness of the reaction: No ☐ if Yes ☐ (please tick anyone)

☐ Death (dd/mm/yyyy) ☐ Congenital-anomaly
☐ Life threatening ☐ Required intervention to Prevent permanent
☐ Hospitalization/Prolonged impairment/damage
☐ Disability ☐ Other (specify)

15. Outcomes

☐ Recovered ☐ Recovering ☐ Not recovered
☐ Fatal ☐ Recovered with sequelae ☐ Unknown

C. SUSPECTED MEDICATION(S)

S.No	8. Name (Brand/Generic)	Manufacturer (if known)	Batch No. / Lot No.	Exp. Date (if known)	Dose used	Route used	Frequency (OD, BD etc.)	Therapy dates		Indication	Causality Assessment
								Date started	Date stopped		
i											
ii											
iii											
Iv											

S.No as per C	9. Action Taken (please tick)						10. Reaction reappeared after reintroduction (please tick)			
	Drug withdrawn	Dose increased	Dose reduced	Dose not changed	Not applicable	Unknown	Yes	No	Effect unknown	Dose (if reintroduced)
i										
ii										
iii										
iv										

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

S.No	Name (Brand/Generic)	Dose used	Route used	Frequency (OD, BD, etc.)	Therapy dates		Indication
					Date started	Date stopped	
i							
ii							
iii							

Additional Information:

D. REPORTER DETAILS

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

17. Date of this report (dd/mm/yyyy):

Confidentiality: The patient's identity is held in strict confidence and protected to the fullest extent. Programme staff is not expected to and will not disclose the reporter's identity in response to a request from the public. Submission of a report does not constitute an admission that medical personnel or manufacturer or the product caused or contributed to the reaction.

CONCLUSION

Dicyclomine is the most effective drug against gastric irritation. It is shows antimuscarinic activity. This paper deals with pharmacokinetic and pharmacodynamic activities of drug. During the study of dicyclomine enormous information regarding it has been collected in this review is as clinical trials for dicyclomine and detailed information of pharmacovigilance.

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