



Study Of Pharmacovigilance Related Drug Pantoprazole

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Abstract

Pantoprazole (Protonix) is an irreversible proton pump inhibitor (PPI) that reduces gastric acid secretion. In combination with two antimicrobial agents (most commonly metronidazole, clarithromycin or amoxicillin) for 6-14 days, pantoprazole 40 mg twice daily produced *Helicobacter pylori* eradication rates of 71-93.8% (intent-to-treat [ITT] or modified ITT analysis) in patients without known antibacterial resistance. Pantoprazole-containing triple therapy was at least as effective as omeprazole- and similar in efficacy to lansoprazole-containing triple therapy in large trials. In the treatment of moderate to severe gastro-oesophageal reflux disease (GORD), oral pantoprazole 40 mg/day was as effective as other PPIs (omeprazole, omeprazole multiple unit pellet system, lansoprazole and esomeprazole) and significantly more effective than histamine H₂-antagonists. Pantoprazole 20 mg/day provided effective mucosal healing in patients with GORD and mild oesophagitis. Intravenous pantoprazole 40 mg/day can be used in patients who are unable to take oral medication. Oral pantoprazole 20-40 mg/day for up to 24 months prevented relapse in most patients with healed GORD. According to preliminary data, oral pantoprazole 20 or 40 mg/day was effective at healing and preventing non-steroidal anti-inflammatory drug (NSAID)-related ulcers, and intravenous pantoprazole was at least as effective as intravenous ranitidine in preventing ulcer rebleeding after endoscopic haemostasis. Oral or intravenous pantoprazole up to 240 mg/day maintained target acid output levels in most patients with hypersecretory conditions, including Zollinger-Ellison syndrome. Oral and intravenous pantoprazole appear to be well tolerated in patients with acid-related disorders in short- and long-term trials. Tolerability with oral pantoprazole was similar to that with other PPIs or histamine H₂-antagonists in short-term trials. Formal drug interaction studies have not revealed any clinically significant interactions between pantoprazole and other agents. In conclusion, pantoprazole is an effective agent in the management of acid-related disorders. As a component of triple therapy for *H. pylori* eradication and as monotherapy for the healing of oesophagitis and maintenance of GORD, pantoprazole has shown similar efficacy to other PPIs and greater efficacy than histamine H₂-antagonists. Limited data suggest that it is also effective in

Zollinger-Ellison syndrome and in preventing ulcer rebleeding. Pantoprazole is well tolerated with minimal potential for drug interactions. The availability of pantoprazole as both oral and intravenous formulations provides flexibility when the oral route of administration is not appropriate. Thus, pantoprazole is a valuable alternative to other PPIs in the treatment of acid-related disorders.

- Phases of clinical trials is a systematic investigation in human subjects for evaluating the safety and efficacy any new drug

Clinical trials are conducted only when satisfactory information has been gathered on the quality of the non-clinical safety.

Drug review step:

1. Preclinical (animal testing)
2. An investigational new drug application (IND)
3. Phase 1 study
4. Phase 2 study
5. Phase 3 study

- Submission of new drug application (NDS) is the formal step asking the FDA to consider a drug for marketing approval
- FDA reviewers will approve the application or find it either “approvable” or not approvable

- Phase of clinical trials -

- Phase 1(micro dosing human study undertake before phase 1 trials is also called as phase 0 study
- Very low dose about 1/100th of the estimation human dose and maximum 100g
- The phase 0 is studied that the micro dose pharmacokinetic may be different from that at pharmacological doses
- Phase 2(human pharmacology and safety)
- The first human administration of the drug is carried out by clinical pharmacologist and trained physician in a sitting where all vital functions and emergency facilities are available are available lowest estimation dose (1/100 to 1/10) of the highest dose producing no toxicity in animal
- The importance emphasis in a safety tolerability and function heart rate bronchospasm and kidney /liver damage the side effect is noted and the pharmacodynamic effect in man
- phase 1 (fewer than 100 patients) for several months
- Phase 2 (therapeutic exploration and dose ranging)
- To specific inclusion and exclusive criteria. It is generally carried out at 2-4 centres
- Phase 2 is study mostly controlled and randomised several months to two years
- Phase 3: (therapeutic confirmation/ composition)
- The aim is to established the value of the drug in the relation to existing therapy
- Indication is finalised and guidelines the therapeutic use for formulated an NDA is submitted license authority (FDA) and convinced to give marketing permission (500-3000patients) one to four year required.
- Phase 4: (post marketing surveillance data gathering studies)

- The drug has been marketed for general use practising physician are identified data or collection on structured about efficacy acceptability and ADR
- Further therapeutic trails like children, pregnant woman patient with hepatic disease etc
- Most drug continue their development even after marketing (two years is required)

Function of drug controller general of India (DCGI)and central drugs standard control organization (CDSCO)

Function of DCGI:

- Permission to conduct clinical trials with new drugs /Existing drug/medical devices under drugs category
- Import license/ test license for clinical trials drugs supplies -current with main submission
- Approval for conducting clinical trials with medical devices under drug category
- Permission N.O.C/notification for protocol amendment/ICF amendments /safety reports
- Notification for SAEs observed in ongoing clinical trials

Function of CDSCO:

- Approval of new drug and clinical Trials
- Import registration and licensing
- License approving of blood banks, LVPs, vaccines, R-DNA products and some medical devices (CLAA scheme)
- Amendments to D and C act rule
- Banning of drugs and cosmetics
- Grant of test license NOCs for export
- Testing of new drugs
- Oversight and marker surveillance through inspectorates of central over and above. The state authority

Types of regulatory application

- IND (investigational new drugs application)
- NDA (new drug application)
- ANDA (abbreviated new drug application)
- BLA (biologic license application)

Application of IND

- Investigation IND (traditional)
- Exploratory IND (phase conclusion early in phase 1)
- No therapeutic or diagnostic intense
- Emergency use (use of experimental drug in emergency situation)
- No time for IND
- Treatment IND – for use in serious/life threatening case preclinical final clinical work

Application of NDA –

- Since 1938, every new drug has been the subject of an approved NDA before U.S. commercialization
- The NDA application is the vehicle through which drug sponsors formally propose that the FDA approve a new pharmaceutical for sale and marketing in the U.S.
- The data gathered during the animal studies and human clinical trials of an investigational new drug become part of the NDA

Application of ANDA:

- An abbreviated new drug application contains data which is submitted to FDA of a generic drug product
- Once approved an applicant may manufacture and market the generic drug product to provide a safe effective, lowest cost alternative to the brand name drug is references

A generic drug product is one that is comparable to an innovator drug product in dosage form strength route of administration quality performance characteristics and intended use

☐ Objectives and scope of ICH-Good clinical practice and new drug and clinical trials rule 2019

Objectives:

- Development with consideration of the current good clinical practices of the European union, Japan and USA, plus those of Australia, Canada, Nordica countries and world health organization
- Provide a unified standard for the European union Japan and USA to facilitate the mutual acceptance of clinical data by the regulatory authorities in these jurisdiction
- Protect the patient
- Facilitate the mutual acceptance of clinical data across ICH GCP regions
- Facilate global submissions through mutual acceptance of data.

Avoid trail duplication (saving time, money, resources)

- Facilitate global submissions through mutual acceptance of data technical requirements for medicinal products containing new collection the information on GCP guidelines (literature survey)
- Describe the principal of GCP
- Study the application of GCP principles
- To study the concept of informed consent
- To recognize the implications of non-Compliance
- To review positive & Negative case studies.
- To discuss the key aspects of GCP such as patient recruitment Consent & data privacy.

Scope:-

- Good clinical practice (GCP): - A standard for the design, conduct, performance monitoring auditing, recording analyses & reporting results are credible accurate of that the rights, integrity of confidentiality of trial Subjects are protected.
- The objective of this guidelines is to outline the mission & the organisation of a Sponsor's auditing department & the principles for planning performing & reporting audits all of which should be Considered when the auditor who belongs to the sponsor performs an audit Clinical trial Sponsor performed by the Sponsor.
- This guideline, is expected to be a basic principle along with international Conference on Harmonization (ICH) Good clinical practice (GCP) for a Sponsor auditor to Conduct an audit in the various situations of each country and sponsor
- Micro-biology and seriology
- Hematocogy and blood.
- Molecular biology and molecular pathology.

➤ New drug and clinical trials rule 2019:

This document summarizes major. Changes affecting ethics committee (EC)after coming into force of the new drug clinical trials rules 2019(new rules) i.e., GSR227(E) by India's ministry of health and family welfare (MOHFW)

EC means, for the purpose of

1. Clinical trials (CT), EC constituted under rule 8 of the new CT rules
 2. Biomedical and health researcher, constituted under rule 16 and registered under rule 17 of new CT rules
- A clinical trial is a systematic study of new drug or investigational new drug in human subjects to generate data to determine the safety, Efficacy or toxicity of a new drug or investigational new drug in a view to discover new module

- For a new molecule to be commercialize it has to undergo various rigorous phase of clinical and pre-clinical studies
- In general, it takes about 10 to 12 years of intense study on the new molecule before the release of the drug into the market
- Clinical studies involve the research to estimate the. Safety and efficacy of the drug in humans
- It is necessary to take their condition consent before the subjecting the group of people's (participants) in clinical studies
- However, the safety of the participants being a major concern the sponsors and investors must follow ethical principles and must implement good clinical practice

1. Protocol designing of clinical trials
2. General and background information
3. Objectives and justification
4. Trial design
5. Selection of withdrawal of subject
6. Ethical considerations
7. Treatment and study design
8. Safety assessment
9. Quality control
10. Record keeping
11. Protocol and amendments

Component:

1. Assessment of efficacy
2. Assessment of safety
3. Statistics
4. Data handling and management
5. Quality control and quality assurance
6. Finance and insurance
7. Publication policy
8. Evaluation
9. Supplementary and appendix

✓ Clinical trials application process (CTA)

Clinical trials application submission- validation of submitted documents- evaluation of the whole clinical trials application-deficiency requirement request on data information missing on submitted file- no finding or missing data – Evaluation report and recommendations -SFDA response – CT application approval or rejection

Concept of pharmacovigilance.

- Definition - The science & activities relating to the detection assessment understanding & prevention of adverse effect or any other drug related problem.
- derived from the Greek word "pharmakos (medicine) & Latin the vigilance, (Watchfulness).

Objectives of pharmacovigilance.

- To monitor adverse drug reaction (ADRS) Indian population.
- To create awareness amongst health care professional about the importance of ADR reporting in India
- monitor benefit risk profit of medicines
- Generate independence evidence. based recommendation on the safety of medicine.
- Support of CDSCO, formulating safety decisions related regulatory medicines.
- communicate findings with all key stakeholders
- A national centre of excellence at global drug safety, monitoring standard.
- To improve patient to improve care public health and safety
- To contribute to the assessment benefit harm, To effectiveness. of medicines.
- To promote understanding education & clinical training.

Type of components of pharmacovigilance -

- four main components of pharmacovigilance
 - I. Adverse event case management including expedited reporting Aggregate reporting
 - II. risk management.
 - III. constitutional objectives of Pharmacovigilance program of India
 - IV. signal intelligence

Objectives

- To monitor adverse drug reaction ADR in Indian population
- To create awareness amongst health the care professionals about importance of ADR reporting of India
- To monitor benefit risk profile of medicine. Generate independent evidence-based recommendation medicine on the safety of medicines
- Support the CDSCO for formulating safety related regulatory decisions for medicines.
- communicate findings with all key create stakeholders.
- Create a national centre of excellence per with global drug safety monitoring standard.

constitution:

- Pharmacovigilance mainly involves monitoring & reporting of adverse reaction associated with use of medicinal products
- Under- reporting of adverse drug reaction a serious issue hampering the dynamics program of pharmacovigilance programme
- Pharmacovigilance is re based shared stakeholders

ADR monitoring centre (AMC)

1. Department of pharmacology therapeutics & toxicology govt. medical college bakhshi Nagar, Jammu
2. Department of Pharmacology of medical PGIMER
3. Department Pharmacology, Lady hard of medical college New Delhi
4. Department Pharmacology Jipmer, Pondicherry.
5. Department of Pharmacy JSS medical college hospital, Karnataka.
6. Department of clinical Pharmacology. Christian medical college Vellore Tamil Nādu.
7. Department of Pharmacology Guwahati Assam Institute of Pharmacology madras
8. Department college. Pharmacology, Santosh medical university Ghaziabad.

*** Components**

1. Adverse event case management including expedited reporting:
 - An adverse event medical occurrence administered & is any upward C patient medical product which does not necessarily have to a causal relationship. with this treatment.
 - An adverse event any can therefore, unfavourable & unintended sign abnormal. Laboratory Finding System or diseases temporarily associated with the used of medical product a considered related 10 this product. not medical
2. Aggregate reporting:
 - Aggregate reporting refers to those reports that focus not 40 much but rather 03 individual Over view cases, assessment of the safety profile & benefit-risk evaluate.
 - Periodic safety update reports. (PSUR) / periodic benefit risk evaluation reports (PBRERS). Periodic adverse (drug) experiences report CUs). Development safety update reports. (DSURS) Integrated summaries of safety Clinical or safety summaries of safety (EU). related parts of clinical study report.

Periodic safety update reports (PSVR)periodic benefit risk evaluation report

- Periodic safely update report is a pharmacovigilance document intended to provide an update of the worldwide safety experience of a medical product to regulatory authority's medical product to regulatory authorities at different time points post authorization
- The objective of present at the PSVR is to present a comprehensive & critical analysis of the risk-benefit. balance of the product taking into account new safety information. On the context of cumulative information on risk and benefit.

Example.

- I. data from clinical & non clinical studied.
- II. Product usage data and drug utilization information
- III. Scientific literature

3. Signal intelligence:

- PV signal intelligence practice. are focused on adopting DPA algorithm to mine DRS data for constituting hypotheses of signal drug AE
- combination that needed further investigation to established evidence-based medicine to confirm refuel casualty associations between those pairs.
- Then regularity actions taken to health. protect they may be taken public health

4. Risk management

- Right management m Pharmacovigilance undertaken to promote used of medicines & safeguard health of patients
- .It is active set performed for identification of risk management following stages

1. Identification & characterization of the safety profile & the medical products.
2. Planning of PV activities to characteristics risk & identify new risk.
3. Planning of PV implantation of risk monitoring of mitigation of these activities effective of these activities
4. Document that have post approval obligation been imposed as a condition of marketing authorization

Types of PVA. Passive Surveillance:

- Passive surveillance involves the usage of spontaneous adverse event report voluntarily sent by healthcare professional or patient to the marketing authorization holder or regulatory authority.
- It identity of The reporter remains anonymous but patient related details like country on gender pre-existing, CO-mobilise can be recovered from the reporting forms.

B. Active surveillance

- This method aims to monitor certain specific drug related adverse event & seek of ascertain the number of adverse drug reaction entirely through a pre-planned process
- It is also known as toxicity monitoring or safety monitoring

C. cohort event monitoring

- In this method the Surveillance study planned prior to beginning the treatment with the medication
- A group of people are exposed to a drug for a defined period and actively followed up during treatment
- Adverse event of the target drug with or one the events associated or more medicines taken with that drug are monitored.

- This kind performed of investigations are to identify ize the adverse to population characters related drug among special like genetic disorder people with & older people. pregnant woman and older people

PROTONIX

(pantoprazole sodium)

Delayed-Release Tablets

only

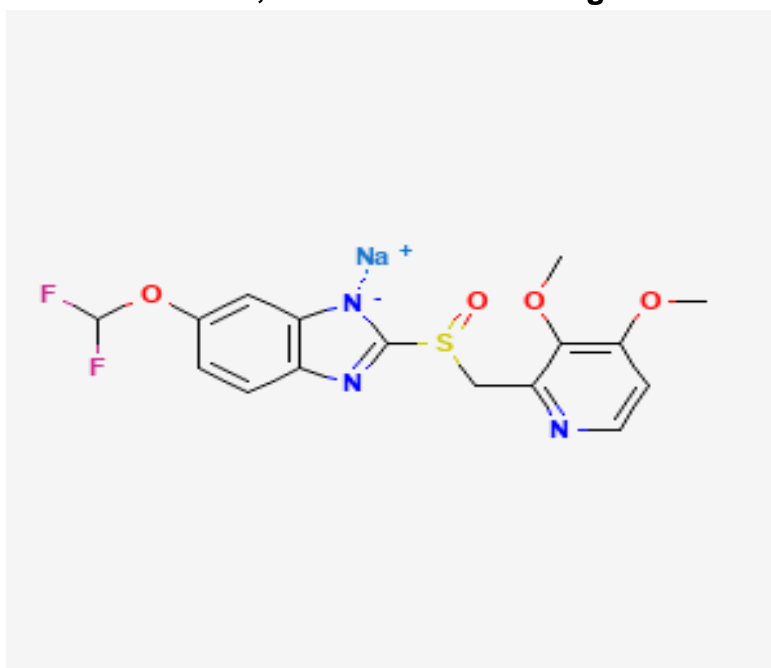
DESCRIPTION

The active ingredient in PROTONIX (pantoprazole sodium) Delayed-Release Tablets is a substituted

benzimidazole, sodium 5-(difluoromethoxy)-2-[[[(3,4-dimethoxy-2-pyridinyl)methyl] sulfinyl]-1H-

benzimidazole sesquihydrate, a compound that inhibits gastric acid secretion. Its empirical formula is

$C_{16}H_{14}F_2N_3NaO_4S \times 1.5 H_2O$, with a molecular weight of 432.4. The structural formula is:



Pantoprazole sodium sesquihydrate is a white to off-white crystalline powder and is racemic. Pantoprazole has weakly basic and acidic properties. Pantoprazole sodium sesquihydrate is freely soluble in water, very slightly soluble in phosphate buffer at pH 7.4, and practically insoluble in n-hexane.

The stability of the compound in aqueous solution is pH-dependent. The rate of degradation increases with decreasing pH. At ambient temperature, the degradation half-life is approximately 2.8 hours at pH 5.0 and approximately 220 hours at pH 7.8.

PROTONIX is supplied as a delayed-release tablet for oral administration, available in 2 strengths. Each delayed-release tablet contains 45.1 mg or 22.6 mg of pantoprazole sodium sesquihydrate

(equivalent to 40 mg or 20 mg pantoprazole, respectively) with the following inactive ingredients: calcium stearate, crospovidone, hypromellose, iron oxide, mannitol, methacrylic

acid copolymer, polysorbate 80, povidone, propylene glycol, sodium carbonate, sodium lauryl sulfate, titanium dioxide, and triethyl citrate.

CLINICAL PHARMACOLOGY

Pharmacokinetics

PROTONIX is prepared as an enteric-coated tablet so that absorption of pantoprazole begins only after the tablet leaves the stomach. Peak serum concentration (C_{max}) and area under the serum concentration time curve (AUC) increase in a manner proportional to oral and intravenous doses from 10 mg to 80 mg. Pantoprazole does not accumulate and its pharmacokinetics are unaltered with multiple daily dosing. Following oral or intravenous administration, the serum concentration of pantoprazole declines

exponentially with a terminal elimination half-life of approximately one hour. In extensive metabolizers (see Metabolism section) with normal liver

an oral dose of the enteric-coated 40 mg pantoprazole tablet, the peak concentration (C_{max}) is 2.5 µg/mL, the time to reach the peak concentration (t_{max}) is 2.5 h and the total area under the plasma concentration versus time curve (AUC) is 4.8 µg·hr/mL. When pantoprazole is given with food, its C_{max} is highly variable and may

increase significantly. Following intravenous administration of pantoprazole to extensive metabolizers, its total clearance is 7.6-14.0 L/h and its apparent volume of distribution is 11.0-23.6L.

Absorption

The absorption of pantoprazole is rapid, with a C_{max} of 2.5 µg/mL that occurs approximately 2.5 hours after single or multiple oral 40-mg doses. Pantoprazole is well absorbed; it undergoes little first-pass metabolism resulting in an absolute bioavailability of approximately 77%. Pantoprazole absorption is not affected by concomitant administration of antacids. Administration of pantoprazole with food may delay its absorption up to 2 hours or longer; however, the C_{max} and the extent of pantoprazole absorption (AUC) are not altered. Thus, pantoprazole may be taken without regard to timing of meals.

Distribution

The apparent volume of distribution of pantoprazole is approximately 11.0-23.6L, distributed mainly in extracellular fluid. The serum protein binding of pantoprazole is about 98%, primarily to albumin.

Metabolism

Pantoprazole is extensively metabolized in the liver through the cytochrome P450 (CYP) system. Pantoprazole metabolism is independent of the route of administration (intravenous or oral). The main metabolic pathway is demethylation, by CYP2C19, with subsequent sulfation; other metabolic pathways include oxidation by CYP3A4. There is no evidence that any of the pantoprazole metabolites have significant pharmacologic activity. CYP2C19 displays a known genetic polymorphism due to its

deficiency in some sub-populations (e.g. 3% of Caucasians and African-Americans and 17-23% of Asians). Although these sub-populations of slow pantoprazole metabolizers have elimination half-life values of 3.5 to 10.0 hours, they still have minimal accumulation (≤ 23%) with once daily dosing.

ELIMINATION

After a single oral or intravenous dose of ¹⁴C-labeled pantoprazole to healthy, normal metabolizer volunteers, approximately 71% of the dose was excreted in the urine with 18% excreted in the feces through biliary excretion. There was no renal excretion of unchanged pantoprazole.

SPECIAL POPULATION

Geriatric

Only slight to moderate increases in pantoprazole AUC (43%) and C_{max} (26%) were found in elderly volunteers (64 to 76 years of age) after repeated oral administration, compared with younger subjects. No dosage adjustment is recommended based on age.

Pediatric

The pharmacokinetics of pantoprazole have not been investigated in patients <18 years of age.

Gender

There is a modest increase in pantoprazole AUC and C_{max} in women compared to men. However, weight-normalized clearance values are similar in women and men. No dosage adjustment is needed based on gender (Also see Use in Women).

Renal Impairment

In patients with severe renal impairment, pharmacokinetic parameters for pantoprazole were similar to those of healthy subjects. No dosage adjustment is necessary in patients with renal impairment or in patients undergoing hemodialysis.

Hepatic impairment

In patients with mild to severe hepatic impairment, maximum pantoprazole concentrations increased only slightly (1.5-fold) relative to healthy subjects. Although serum half-life values increased to 7-9 hours and AUC values increased by 5- to 7-fold in hepatic-impaired patients, these increases were no greater than those observed in slow CYP2C19 metabolizers, where no dosage frequency adjustment is warranted. These pharmacokinetic changes in hepatic-impaired patients result in minimal drug accumulation following once daily multiple-dose administration. No dosage adjustment is needed in patients with mild to severe hepatic impairment. Doses higher than 40 mg/day have not been studied in hepatically-impaired patients.

DRUG-DRUG INTERACTION

Pantoprazole is metabolized mainly by CYP2C19 and to minor extents by CYP3A4, 2D6 and 2C9. In in vivo drug-drug interaction studies with CYP2C19 substrates (diazepam [also a CYP3A4 substrate] and phenytoin [also a CYP3A4 inducer]), nifedipine, midazolam, and clarithromycin (CYP3A4 substrates), metoprolol (a CYP2D6 substrate), diclofenac, naproxen, and piroxicam (CYP2C9 substrates) and theophylline (a CYP1A2 substrate) in healthy subjects, the pharmacokinetics of pantoprazole were not significantly altered. It is, therefore, expected that other drugs metabolized by CYP2C19, 3A4, 2D6, 2C9 and 1A2 would not significantly affect the pharmacokinetics of pantoprazole. In vivo studies also suggest that pantoprazole does not significantly affect the kinetics of other drugs (cisapride, theophylline, diazepam [and its active metabolite, desmethyldiazepam], phenytoin, warfarin, metoprolol, nifedipine, carbamazepine, midazolam, clarithromycin, naproxen,

piroxicam, and oral contraceptives [levonorgestrel/ethinyl estradiol]) metabolized by CYP2C19, 3A4, 2C9, 2D6 and 1A2. Therefore, it is expected that pantoprazole would not significantly affect the pharmacokinetics of other drugs metabolized by these isozymes. Dosage adjustment of such drugs is not necessary when they are co-administered with pantoprazole. In other in vivo studies, digoxin, ethanol, glyburide, antipyrine, caffeine, metronidazole, and amoxicillin had no clinically relevant interactions with pantoprazole. Although no significant drug-drug interactions have been observed in clinical studies, the potential for significant drug-drug interactions with more than once daily dosing with high doses of pantoprazole has not been studied in poor metabolizers or individuals who are hepatically impaired.

Pharmacodynamics

Mechanism of action

Pantoprazole is a proton pump inhibitor (PPI) that suppresses the final step in gastric acid production by covalently binding to the (H⁺,K⁺)-ATPase enzyme system at the secretory surface of the gastric parietal cell. This effect leads to inhibition of both basal and stimulated gastric acid secretion irrespective of the stimulus. The binding to the (H⁺,K⁺)-ATPase results in a duration of antisecretory effect that persists longer than 24 hours for all doses tested.

Antisecretory Activity

Under maximal acid stimulatory conditions using pentagastrin, a dose-dependent decrease in gastric acid output occurs after a single dose of oral (20-80 mg) or a single dose of intravenous (20-120 mg) pantoprazole in healthy volunteers. Pantoprazole given once daily results in increasing inhibition of gastric acid secretion. Following the initial oral dose of 40 mg pantoprazole, a 51% mean inhibition was achieved by 2.5 hours. With once a day dosing for 7 days the mean inhibition was increased to 85%. Pantoprazole suppressed acid secretion in excess of 95% in half of the subjects. Acid secretion had returned to normal within a week after the last dose of pantoprazole; there was no evidence of rebound hypersecretion.

In a series of dose-response studies pantoprazole, at oral doses ranging from 20 to 120 mg, caused dose-related increases in median basal gastric pH and in the percent of time gastric pH was > 3 and >4. Treatment with 40 mg of pantoprazole produced optimal increases in gastric pH which were significantly greater than the 20-mg dose. Doses higher than 40 mg (60, 80, 120 mg) did not result in further significant increases in median gastric pH. The effects of pantoprazole on median pH from one double-blind crossover study are shown below.

MEDIA PH ON DAY

Time	Placebo	20mg	40mg	80mg
8am- 8am (24 hours)	1.3	2.9*	3.8*#	3.9*#
8am- 10pm (Daytime)	1.6	3.2*	4.4*#	4.8*#
10pm- 8am (Night time)	1.2	2.1*	3.0*	2.6*

* Significantly different from placebo

Significantly different from 20 mg

CLINICAL TRIALS -

PROTONIX Delayed-Release Tablets were used in all clinical trials.

Erosive Esophagitis (EE) Associated with Gastroesophageal Reflux Disease (GERD)

A U.S. multicenter double-blind, placebo-controlled study of PROTONIX 10 mg, 20 mg, or 40 mg once daily was conducted in 603 patients with reflux symptoms and endoscopically diagnosed EE of grade 2 or above (Hetzel-Dent scale). In this study, approximately 25% of enrolled patients had severe EE of grade 3 and 10% had grade 4. The percentages of patients healed (per protocol, n=541) in this study were as follows:

PROTONIX

WEEK	10MG QD (n=153)	20 MG QD (n=158)	40 MG QD (n=162)	(n=68)
4	44.6%	58.4%*#	75%*#	14.3%
8	66.0%	83.5%*#	92.6%*#	39.7%

+

(p < 0.001) PROTONIX versus placebo.

* (p < 0.05) versus 10 mg, or 20 mg PROTONIX

In this study, all PROTONIX treatment groups had significantly greater healing rates than the placebo group. This was true regardless of H. pylori status for the 40-mg and 20-mg PROTONIX treatment groups. The 40-mg dose of PROTONIX resulted in healing rates significantly greater than those found with either the 20- or 10-mg dose.

A significantly greater proportion of patients taking PROTONIX 40 mg experienced complete relief of daytime and nighttime heartburn and the absence of regurgitation starting from the

first day of treatment compared with placebo. Patients taking PROTONIX consumed significantly fewer antacid tablets per day than those taking placebo.

PROTONIX 40 mg and 20 mg once daily were also compared with nizatidine 150 mg twice daily in a U.S. multicenter, double-blind study of 243 patients with reflux symptoms and endoscopically diagnosed EE of grade 2 or above. The percentages of patients healed (per protocol, n=212) were as follows:

Erosive Esophagitis Healing Rates (per protocol)

PROTONIX			
WEEK	20 MG QD (n=72)	40 MG QD (n=70)	150MG QD (n=70)
4	61.4%	64.0%	22.2%
8	79.2%	82.9%	41.4%

($p < 0.001$) PROTONIX versus nizatidine.

Once daily treatment with PROTONIX 40 or 20 mg resulted in significantly superior rates of healing at both 4 and 8 weeks compared with twice daily treatment with 150 mg of nizatidine. For the 40 mg treatment group, significantly greater healing rates compared to nizatidine were achieved regardless of the H. pylori status.

A significantly greater proportion of the patients in the PROTONIX treatment groups experienced complete relief of nighttime heartburn and regurgitation starting on the first day and of daytime heartburn on the second day compared with those taking nizatidine 150 mg twice daily. Patients taking PROTONIX consumed significantly fewer antacid tablets per day than those taking nizatidine.

Long-Term Maintenance of Healing of Erosive Esophagitis

Two independent, multicenter, randomized, double-blind, comparator-controlled trials of identical design were conducted in GERD patients with endoscopically-confirmed healed erosive esophagitis to demonstrate efficacy of PROTONIX in long-term maintenance of healing. The two U.S. studies enrolled 386 and 404 patients, respectively, to receive either 10 mg, 20 mg, or 40 mg of PROTONIX (pantoprazole sodium) Delayed-Release Tablets once daily or 150 mg of ranitidine twice daily. As demonstrated in the table below, PROTONIX 40 mg and 20 mg were significantly superior to ranitidine at every time point with respect to the maintenance of healing. In addition, PROTONIX 40 mg was superior to all other treatments studied.

Long-Term Maintenance of Healing of Erosive Gastroesophageal Reflux Disease (GERD Maintenance): Percentage of Patients Who Remained Healed

	PROTONIX 20 MG QD	PROTONIX 40MG QD	RANITIDIN E 150MG BID
STUDY 1	n=75	n=74	n=75
Month 1	91*	99*	68
Month 3	82*	93*#	54
Month 6	76*	90*#	44
Month12	70*	86*#	35
Study 2	n=74	n=88	n=84
Month 1	89*	92*#	62
Month3	78*	91*#	47
Month6	72*	88*#	39
Month12	72*	83*	38

* (p <0.05 vs ranitidine)

(p < 0.05 vs PROTONIX 20 mg)

PROTONIX 40 mg was superior to ranitidine in reducing the number of daytime and nighttime heartburn episodes from the first through the twelfth month of treatment. PROTONIX 20 mg, administered once daily, was also effective in reducing episodes of daytime and nighttime heartburn in one trial.

Number of Episodes of Heartburn (mean ± SD)

		PROTONIX 40 MG QD	Ranitidine 150 MG BID
Month 1	Daytime	5.1 ± 1.6*	18.3 ± 1.6
	Nighttime	3.9 ± 1.1*	11.9 ± 1.1
Month12	Daytime	2.9 ± 1.5*	17.5 ± 1.5
	Nighttime	2.5 ± 1.2*	13.8 ± 1.3

* (p < 0.001 vs ranitidine, combined data from the 2 U.S. studies)

Pathological Hypersecretory Conditions Including Zollinger-Ellison Syndrome

In a multicenter, open-label trial of 35 patients with pathological hypersecretory conditions, such as Zollinger-Ellison syndrome with or without multiple endocrine neoplasia-type I, PROTONIX

successfully controlled gastric acid secretion. Doses ranging from 80 mg daily to 240 mg daily maintained gastric acid output below 10mEq/h in patients without prior acid-reducing surgery and

below 5 mEq/h in patients with prior acid-reducing surgery.

Doses were initially titrated to the individual patient needs, and adjusted in some patients based on the clinical response with time. (See DOSAGE AND ADMINISTRATION.) PROTONIX was well

tolerated at these dose levels for prolonged periods (greater than 2 years in some patients).

Pantoprazole

Pharmaceutical Formulations Available on the Market

PPIs are administered by two different routes: oral or intravenous. Currently man-ufactured dosage forms for oral administration include enteric-coated capsules, enteric coated tablets, multiple-unit pellet system (MUPS), and suspensions with microparticulated. For intravenous administration, PPIs are available as lyophilized powders

for reconstitution]. There are a large number of

manufactured brand and generic products. The list

of products available in US and EU, together with a brief characteristic, is presented in Table.

Delayed-Release Tablets -

Most proton pump inhibitors are available as delayed-release tablets. To protect the API from degradation, the tablet has to be coated with enteric polymers. The most commonly used polymers are methacrylate derivatives, such as a methacrylic acid copoly-mer with ethyl acrylate [90–119]. Another way to produce delayed-release tablets is the multiple-unit pellet system (MUPS), featuring enteric-coated pellets

compressed into a tablet and coated with an

immediate-release polymer. After administration, the MUMPS

The tablet disintegrates in gastric fluids into smaller enteric-coated subunits, which are later dissolved in the small intestine. Advantages of MUPS tablets over capsules include lower manufacturing costs, smaller size, and lower risk of sticking to the esophagus during administration, due to the lack of gelatin.

Examples of MUPS tablets containing PPIs are Losec MUPS or Nexium [97,114]. A slight modification of MUPS is the modified-release orodispersible tablets (ODTs).

In addition modified-release pellets, they

contain disintegrants, such as microcrystalline cellulose, which allow the tablet to disintegrate quickly in the mouth.

Examples of ODT formulations include Zoton FasTab, Prevacid, and Mezzopram. Contrary to conventional delayed-release tablets, MUPS tablets can be easily dispersed in water or other vehicles before administration, ensuring better patient compliance.

Delayed-Release Capsules

PPIs are also available in the form of hard gelatin capsules that contain pellets or granules coated with an enteric polymer. A particular example of a formulation is Dexilant capsules, which contain double-delayed-release pellets. In this case, the first

The peak of the maximum plasma concentration dexlansoprazole occurs two hours, while the second 4 to 5 h after administration. Unless otherwise indicated by the manufacturer, the contents of the capsules in the form of granules or pellets can be discharged and suspended in water or applesauce to facilitate administration.

Oral Suspensions

Oral suspensions are a convenient form of the drug for children, patients with swallowing problems, and those requiring enteral feeding. Formulations with PPIs usually contain enteric coated granules or pellets in sachets (Protonix). Some formulations additionally contain placebo pellets (Prilosec) or have powdered form (Zegerid). Oral suspensions of proton pump inhibitors are prepared ex tempore. Depending on the manufacturer's recommendations, they can be administered with applesauce or fruit juice. A study by Bladh et al. assessed the stability of esomeprazole magnesium manufactured in the form of sachets containing pellets intended to form oral suspension in water, apple sauce, and apple or orange juice.

This suspension was found to remain stable after preparation in the pH range of 3.4 -- 5.0 for 60 min. The time needed to disperse pellets in water was 2 min, while in juices it was ca. 15 min. After the pellets were dispersed in apple or orange juice, their stability was above 98%. During delivery of the suspension through the feeding tube, more than 96% of the drug substance was delivered. The formulation was bioequivalent to tablets and capsules containing the same drug substance. Johnson et al. also tested the stability of enteral pellets containing esomeprazole in 100 mL of water, milk (1.5% fat), cultured milk, yogurt and apple or orange juices. After 30 min of incubation, dissolution studies were performed in hydrochloric acid and phosphate buffer. The loss of esomeprazole was less than 2% in all the media tested except milk (with 1.5% fat).

In hospital pharmacies, suspensions containing PPIs are also prepared by dissolving the formulations in a solution of 8.4% sodium bicarbonate, or alternatively in ready-to-use compounding media, e.g., Alka's SyrSpend SF. Polonini et al. [157] demonstrated that such a medium can be used to prepare suspensions containing omeprazole, pantoprazole, esomeprazole, and lansoprazole. It is a dry compounding base in the form of a powder ready for reconstitution, containing modified food starch, calcium carbonate, and sucralose. The vehicle is characterized by its taste-masking effect, lack of preservatives and sodium addition, as well as high microbiological stability.

In addition, oral liquids can be prepared by crushing tablets and suspending them in vehicles mentioned above. This method was described by Dentinger et al. in a study on the stability of pantoprazole in oral liquid suspensions. The researchers found

that the oral liquid prepared extemporaneously from pantoprazole tablets in an 8.4% sodium bicarbonate solution was stable in dark glass bottles for 62 days under refrigeration conditions .

Melkoumov et al. investigated the stability of lansoprazole micro-granules (Prevacid FasTab) after suspending them in the Ora-Blend® vehicle. Ora-Blend® is a flavored colloidal medium with slightly acidic pH. It was found that the extemporaneous formulation with lansoprazole remained stable for 3 days at 4.5–5.5 °C . Ferron et al. reported the results of an open-label, randomized, two-period crossover study comparing the bioavailability of pantoprazole administered as a suspension in 8.4% sodium bicarbonate solution and as delayed-release tablets. It was observed that the bioavailability of pantoprazole from suspension was lower, although both formulations reached similar maximum concentration.

Powders for Injections or Infusions

Due to the poor solubility of PPIs, their salts are used to formulate intravenous dosage forms. Examples include sodium salts of omeprazole, esomeprazole, and pantoprazole. They are marketed as lyophilized powders for infusions or injections . In the manufacturing process, the alkaline aqueous solution of PPI is adjusted to pH 11 with sodium hydroxide. Subsequently, the solution is filtered and then dispensed into 5 or 10 mL vials and freeze-dried under aseptic conditions. The recommended solvents for reconstitution are 0.9% sodium chloride or a 5% dextrose solution. The least commonly used is the lactated Ringer's solution (e.g., Nexium I.V.). The pH of the reconstituted solution for infusion is usually around 10 . Omeprazole sodium is also available as a combination product for injection. The product contains a vial with lyophilized omeprazole powder and a separate solvent ampoule. The solvent is composed of water, macrogol 400 and citric acid. The pH of the solution after reconstitution is around 8.6 [161]. Reconstituted solutions are stable for a short period of time, usually 6 to 12 h at room temperature, and must not be stored. Pantoprazole in injection solutions has been reported to be three times more stable than omeprazole

The stability of esomeprazole sodium at concentrations of 0.4 and 0.8 mg/mL was investigated in three injection solutions: 0.9% sodium chloride, 5% dextrose and lactated Ringer's solutions. It was stable in all of them for 48 h at room temperature and 120 h under refrigeration

In the case of infusion solutions, Carpenter et al. found that omeprazole and pantoprazole can be stored for up to 48 h at room temperature without significant loss of drug substance (less than 6%). The powder for infusion reconstituted with a 5% dextrose solution is less stable than with a 0.9% sodium chloride solution . Johnson proved that a solution of pantoprazole sodium in 0.9% sodium chloride stored in polypropylene syringes remained stable for 96 h, both at room temperature and in the refrigerator. After three days of storage at room temperature, the solution turned a slight yellow-orange color, but HPLC analysis showed no unacceptable changes in drug substance content. However, due to the high risk of potential interaction, reconstituted solutions of PPIs cannot be administered with parenteral nutrition or mixed with other infusion solutions

**Examples of proton pump inhibitors
(pantoprazole) currently marketed in the US and EEA (European Economic Area)/UK**

Pantoprazole Sodium Sesquihydrate	Dosage (Mg)	Drug form	Brand name	Additional comments
	20,40	DR tablets	Controloc (Pantoprazole sodium Takeda) Controloc Control 20	<ul style="list-style-type: none"> • Contains 20 mg/40 mg of pantoprazole as pantoprazole sodium, • EC polymer: Methacrylic acid-ethyl acrylate copolymer (1:1), • Controloc Control is an OTC drug
	40	Oral suspension DR	Protonix Pantoprazole SUN Pharma	<ul style="list-style-type: none"> • Granules should be sprinkled in one teaspoon applesauce or apple juice only, • EC polymer: methacrylic acid copolymer, • Can be administered via NG/gastric tube
	40	Powder solution for Injection	Protium I.V. Pantoprazole 40 mg Zentiva	<ul style="list-style-type: none"> • Zentiva • One vial contains 40 mg of pantoprazole in form of pantoprazole sodium, • Contains sodium hydroxide for pH

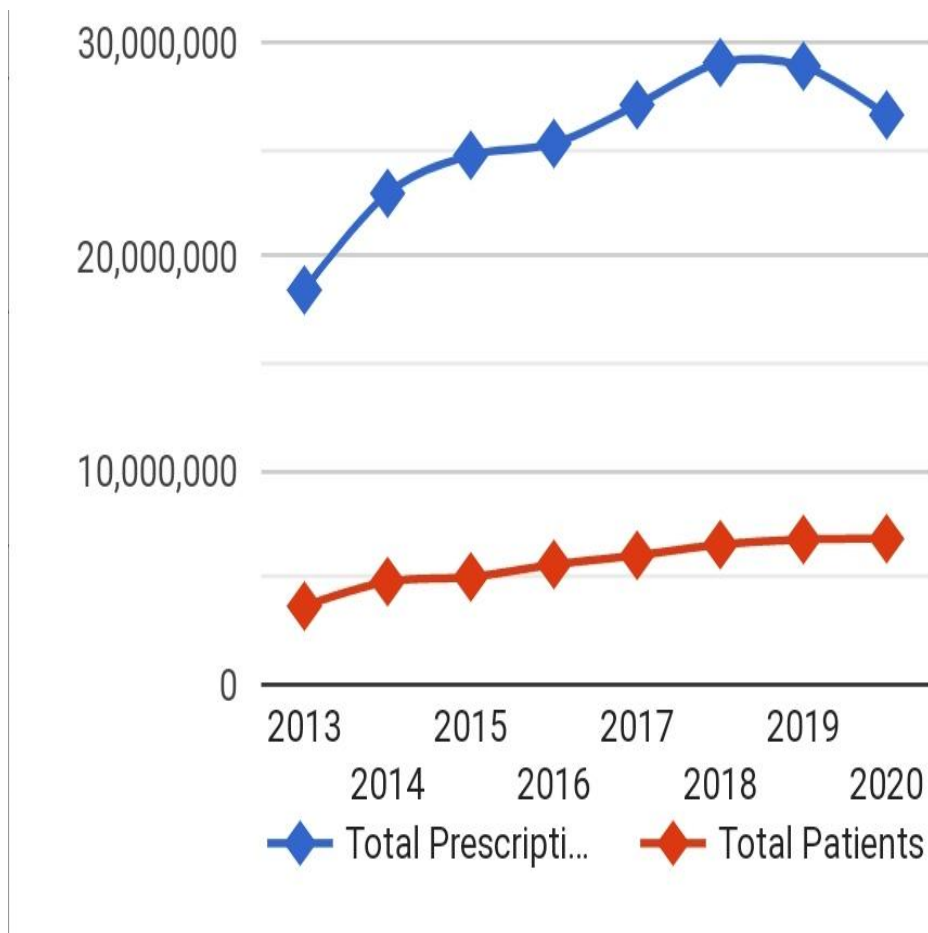
				stabilization, • Can be reconstituted with 0.9% NaCl or 5% glucose solution
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Drug Usage Statistics, United States, 2013 - 2020

Pantoprazole Summary for 2020

Top drug rank	#20 (ⓧ 4)
Estimated number of prescriptions in the United States (2020)	26,604,040
Estimated number of patients in the United States (2020)	6,814,036
<hr/>	
Average total drug cost (USD)	
Per prescription	\$37.11
Per day of therapy	\$0.77/day
Average out-of-pocket cost (USD)	
Per prescription	\$7.14
Per day of therapy	\$0.14/day

Total Prescriptions and Patients Per Year (2013 - 2020)



- **Drug Cost Over Time (2013 - 2020)**

Cost Per Prescription Fill

Average cost per filled prescription regardless of how many days of therapy the prescription is filled for (e.g. 10 days, 30 days, 90 days, etc).

Cost per Day of Therapy

The average cost per prescription is divided by the days of therapy. For example, a 10-day antibiotic course costing \$30 would be \$3 per day. Similarly, a 30-day supply of an oral antihypertensive costing \$30 would be \$1 per day.

Total cost:

The average total cost of the medication including the out-of-pocket cost (see below) plus the amount paid by other parties (Medicare, Medicaid, private insurance, Veterans Administration, TRICARE, other state/federal sources, Worker's compensation, and other miscellaneous sources)

Out-of-pocket cost:

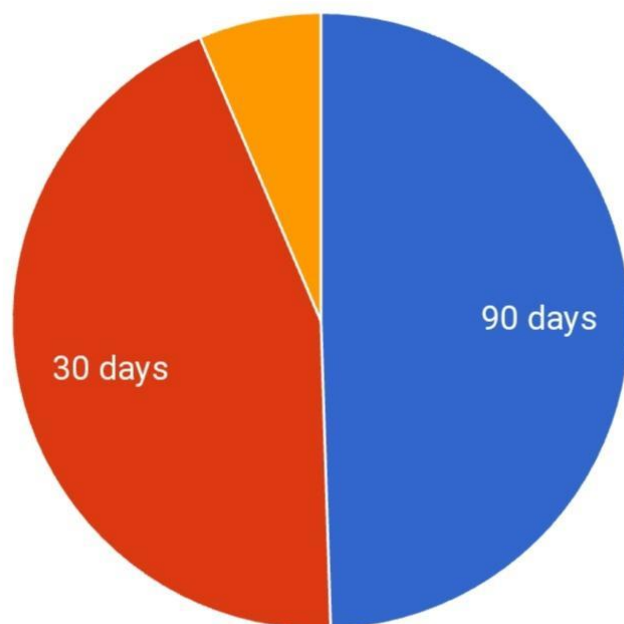
The average payment made by the patient which may include deductibles, coinsurance, copayments, or the cash price paid without insurance coverage.

Distribution of Dispensed Dosage Forms (2020)

Dosage Form	Strength	% of Dispensed Products
Tablet/capsule	40 mg	89.9%
Tablet/capsule	20 mg	9.7%
<i>Other, unspecified, or misc.</i>		0.4%

Distribution of Days Supplied (2020)

"Days supply" is defined as the number of days that a prescription should last. For example, a prescription of 60 tablets that is taken twice daily has a day supply of 30 days.



Related Drugs

Drug Name	Total Prescriptions (2020)
Omeprazole	56,300,064
Pantoprazole (<i>this drug</i>)	26,604,041
Esomeprazole	5,204,951
Lansoprazole	2,623,739
Dexlansoprazole	1,576,634
Esomeprazole; Naproxen	306,557

Therapeutic Classes

- Gastrointestinal Agen
- Proton Pump Inhibitors

Drug Synonyms

Drug synonyms are used during the sanitation and standardization process of "cleaning" the original data source (MEPS). Occassionally, brand names may be listed below that are no longer on the market or are very infrequently used.

Brand Name Synonyms

- Protonix
- Protonix IV

- **FDA Approval Information**

Established Pharmacologic Class (EPC):	<u>Proton Pump Inhibitor</u>
Initial FDA approval date:	2/2/2000
First FDA applicant:	Rx
First dosage form:	Tablet, Delayed Release (oral)

ADVERSE REACTIONS -

Worldwide, more than 11,100 patients have been treated with pantoprazole in clinical trials involving various dosages and duration of treatment. In general, pantoprazole has been well tolerated in both short-term and long-term trials.

In two U.S. controlled clinical trials involving PROTONIX 10-, 20-, or 40-mg doses for up to 8 weeks, there were no dose-related effects on the incidence of adverse events. The following adverse events considered by investigators to be possibly, probably or definitely related to drug occurred in 1% or more in the individual studies of GERD patients on therapy with PROTONIX.

Most Frequent Adverse Events Reported as Drug Related in Short-term Domestic Trials:

Study Event	% Incidence			
	Study 300-US		Study 301-US	
	PROTONIX (n = 521)	Placebo (n = 82)	PROTONIX (n = 161)	Nizatidine (n = 82)
Headache	6	6	9	13
Diarrhea	4	1	6	6
Flatulence	2	2	4	0
Abdominal pain	1	2	4	4
Rash	<1	0	2	0
Eructation	1	1	0	0
Insomnia	<1	2	1	1
Hyperglycemia	1	0	<1	0

Note: Only adverse events with an incidence greater than or equal to the comparators are shown. In international short-term double-blind or open-label, clinical trials involving 20 to 80 mg per day, the following adverse events were reported to occur in 1% or more of 2805 GERD patients receiving pantoprazole for up to 8 weeks.

Adverse Events in GERD Patients in Short-term International Trials

Study Event	% Incidence			
	Pantoprazole Total (N=2805)	Ranitidine 300 mg (N=594)	Omeprazole 20 mg (N=474)	Famotidine 40 mg (N=239)
Headache	2	3	2	1
Diarrhea	2	2	2	<1
Abdominal Pain	1	1	<1	<1

Note: Only adverse events with an incidence greater than or equal to the comparators are shown.

In addition, in these short- and long-term domestic and international trials, the following treatment-emergent events, regardless of causality, occurred at a rate of $\geq 1\%$ in pantoprazole-treated patients: anxiety, arthralgia, asthenia, back pain, bronchitis, chest pain, constipation, cough increased, dizziness, dyspepsia, dyspnea, flu syndrome, gastroenteritis, gastrointestinal disorder, hyperlipemia, hypertonia, infection, liver function tests abnormal, migraine, nausea, neck pain, pain, pharyngitis, rectal disorder, rhinitis, SGPT increased, sinusitis, upper respiratory tract infection, urinary frequency, urinary tract infection, and vomiting.

ADVERSE EFFECTS -

BODY AS A WHOLE:

abscess, allergic reaction, chills, cyst, face edema, fever, generalized edema, heat stroke, hernia, laboratory test abnormal, malaise, moniliasis, neoplasm, non-specified drug reaction, photosensitivity reaction

CARDIOVASCULAR SYSTEM:

abnormal electrocardiogram, angina pectoris, arrhythmia, atrial fibrillation/flutter, cardiovascular disorder, chest pain substernal, congestive heart failure, hemorrhage, hypertension, hypotension, myocardial infarction, myocardial ischemia, palpitation, retinal vascular disorder, syncope, tachycardia, thrombophlebitis, thrombosis, vasodilatation.

DIGESTIVE SYSTEM:

anorexia, aphthous stomatitis, cardiospasm, colitis, dry mouth, duodenitis, dysphagia, enteritis, esophageal hemorrhage, esophagitis, gastrointestinal carcinoma, gastrointestinal hemorrhage, gastrointestinal moniliasis, gingivitis, glossitis, halitosis, hematemesis, increased appetite, melena, mouth ulceration, oral moniliasis, periodontal abscess, periodontitis, rectal hemorrhage, stomach ulcer, stomatitis, stools abnormal, tongue discoloration, ulcerative colitis.

HEPATO-BILIARY SYSTEM:

biliary pain, hyperbilirubinemia, cholecystitis, cholelithiasis, cholestatic jaundice, hepatitis, alkaline phosphatase increased, gamma glutamyl transpeptidase increased, SGOT increased.

HEMIC AND LYMPHATIC SYSTEM:

anemia, ecchymosis, eosinophilia, hypochromic anemia, iron deficiency anemia, leukocytosis, leukopenia, thrombocytopenia.

MUSCULOSKELETAL SYSTEM:

arthritis, arthrosis, bone disorder, bone pain, bursitis, joint disorder, leg cramps, neck rigidity, myalgia, tenosynovitis.

NERVOUS SYSTEM:

abnormal dreams, confusion, convulsion, depression, dry mouth, dysarthria, emotional lability, hallucinations, hyperkinesia, hypesthesia, libido decreased, nervousness, neuralgia, neuritis, neuropathy, paresthesia, reflexes decreased, sleep disorder, somnolence, thinking abnormal, tremor, vertigo.

RESPIRATORY SYSTEM:

asthma, epistaxis, hiccup, laryngitis, lung disorder, pneumonia, voice alteration.

SKIN AND APPENDAGES:

acne, alopecia, contact dermatitis, dry skin, eczema, fungal dermatitis, hemorrhage, herpes simplex, herpes zoster, lichenoid dermatitis, maculopapular rash, pruritus, skin disorder, skin ulcer, sweating, urticaria.

Adverse Drug Reaction (ADR) Monitoring Form :-

- **Preparation of ADR monitoring form as per guidelines given by AMCs (e.g. Indian Pharmacopoeia Commission)**
- **Adverse drug reactions monitoring form:-**

Sr .no	Indian pharmacopoeia commission	For AMC/NCC Use only
	Report type clinical follow up -	AMC report no -

		World wide unique no -
A	Patient information	12- Relevant test/laboratory date with date
1	Patient initial	13- Relevant medical history e.g- pregnancy allergy
2	Age at time event	
3	M-. F-. Other -	

a	Weigh. <u> </u> Kg/s	
B	Suspect adverse reactions	14- serious relations
5-	Date of started	<ul style="list-style-type: none"> ● Death. ● Congited
6-	Date of recovery	<ul style="list-style-type: none"> ● Life threatening
7-	D described reaction problem	<ul style="list-style-type: none"> ● Disability
		15- outcome <ul style="list-style-type: none"> ● Recover ● Rp covering

Suspected medication:-

S r. n	Name Brand generic	Manufactu rers	Batch no	Exp date	Dose used	Freque ncy	Route used	Indicat ion casual ty assess ment
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1								
2								
3								

2:- concentration comitant medical products including medication and herbal remedies with date (exclude those and treatment)

Additional information :-	D. Reporter details 16- name and professional adrss- Pin-. E-mail - Help no- (with STD code)- Occupation -. Sign-. 17- date this report -
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Hospital Visits :-**Common side effects:-**

These common side effects of pantoprazole happen in more than 1 in 100 people. There are things you can do to help cope with them.

- Headaches
- Feeling sick (nausea)
- Being sick (vomiting) or diarrhoea
- Stomach pain
- Constipation
- Farting (flatulence)

If this advice does not help and any of these side effects continue to bother you, tell your doctor or pharmacist.

Serious side effects:-

- your skin becomes more yellow (although this may be less obvious on brown or black skin), your pee becomes darker and you feel more tired – these can be signs of liver problems
- In some cases joint pain along with the red rash especially part of body

Serious allergic reaction:-

- In rare cases, it's possible to have a serious allergic reaction (anaphylaxis) to pantoprazole.
- These are reported adverse effects which commonly found in patients during the near hospital visit

Case Report-

Pantoprazole-Induced Delirium: Review of a Case and Associated Literature

1. Case Report Introduction-

Proton pump inhibitors (PPIs) are frequently prescribed antiulcer agents in the hospital. One of the most commonly used PPIs is pantoprazole. PPIs are generally considered safer and more effective than H₂ blockers as antiulcer agents [1, 2]. A study showed reduced incidence of antiulcer drug-associated delirium when medications were switched from H₂ blockers to proton pump inhibitors [3]. While there is plenty of literature supporting the use of pantoprazole as an effective antiulcer agent, only one case of delirium associated with PPIs, omeprazole, has been reported [4]. There are three reports of central nervous system dysregulation reported on omeprazole [5]. There is no reported case of pantoprazole-associated delirium in the literature. In our report, we present a case of a 93-year-old woman with no known past psychiatric history and medical history of hypertension and arthritis, who developed symptoms of delirium including visual hallucinations while on pantoprazole.

Patient interview :-

Interview of patients for understanding & identification of Adr.
Hospital name:- matoshri Ayurvedic hospital & research center.

Patient name :-

Age :- 20.

Gender:- male.

Disease:- gastro-oesophageal reflux disease (GORD)

Drug :- pantoprazole

Drug ADR:-

Nausea.

Anxiety.

Swelling.

Ulceration of stomach.

Nausea

Vomitting

Dosage :- pantoprazole tablet.

Pantoprazole:- 40 mg.

Routes of administration:-

Oral route of administration.

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