WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 12, Issue 2, 367-386. Review Article ISSN 2277– 7105

STUDY OF PHENYTOIN DRUG RELATED WITH PHARMACOVIGILANCE

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Article Received on
24 November 2022,
Revised on 14 Dec. 2022,
Accepted on 04 Jan. 2023
DOI: 10.20959/wjpr20232-26927

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ABSTRACT

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 phenytoin (referred as antiepileptic and anticonvulsant drug) This review is concerned with data collected about toxicology & account of phenytoin.

KEYWORDS: Pharmacovigilance, toxicology, phenytoin, adverse drug reaction, clinical trials.

INTRODUCTION

The practice of monitoring the effects of medical drugs after they have licensed for use, especially in order to identify and evaluate previously unreported adverse reaction. ‘pharmakon’ is a Greek word which medicinal substance & ‘Vigilia’ is a Latin word which denotes to keep watch or to monitor.

According to WHO “The science & activities relating to the detection, assessment, understanding & prevention of adverse effects or any other drug related problem”.

OBJECTIVES

1.Safe use of drugs, patients' safety & ultimately, safeguarding public health, to achieve this goal, national regulators & international organizations should empower healthcare professionals & the public to report more adverse drug reactions.

2. Improve patient care & safety.

3. Improve public health & safety.

4. Encourage safe, rational and appropriate use of drug.

- Types of pharmacovigilance.

There are four important methods in pharmacovigilance such as.

- Passive surveillance
- Active surveillance
- Cohort event monitoring
- Targeted clinical investigation

Passive Surveillance

Spontaneous adverse effects reported by healthcare professionals to companies.

It involves the usage of spontaneous adverse event reports voluntarily sent by healthcare professionals or patients to the marketing authorization holder or regulatory authority.

Here, data related to the adverse reaction are collected in central in a central or regional database. The identity of the reporter remains anonymous, but patient-related details like country; age, gender & preexisting combeites can be recovered from the reporting forms.

Active Surveillance

Toxicity and safety monitoring during process of manufacturing. This method aims to monitor certain specific drug related adverse events & seek to ascertain the number of adverse drug reaction entirely through a pre-planned process. It is commonly known as toxicity monitoring or safety monitoring.

Cohort Event Monitoring

Clinical trials in which people are treated for study.

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. Adverse events of the target drug or the events associated with one or more medicines taken with that drug are monitored.

Targeted clinical investigations

This is performed to identify adverse drug reaction specially on people who have genetic disorder, pregnant women, older people.

These kinds of investigation are performed to identify & characterize the adverse reaction related to a drug among special population like people with some genetic disorder, pregnant women, older people.

Role of Pharmacovigilance

Pharmacovigilance has been widely accepted to possess a significant role in early observation of the risk associated with the drug. All the medicines are tested on a small ratio of the population concerned before it is approved for post marketing surveillance. The pharmacovigilance has been known to possess various roles like, identification, quantification and documentation of drug-related problems; contribution towards reducing the risk of drug-related problems in healthcare systems; and enhancement of knowledge and understanding of factors and mechanisms which are responsible for drug related injuries. However, in order to fulfill various roles of pharmacovigilance, the interactions and influence of many stakeholders in society with decision-making powers has been required, which include, politicians at national, regional and local levels; healthcare administrators; drug regulatory authorities; pharmaceutical companies; healthcare professionals like physicians, dentists, pharmacists and nurses; academic institutions; media representatives; health insurance companies; lawyers; and patient group.

Clinical Trials

Clinical trial is a systemic investigation in human subjects for evaluating the safety & efficacy of any new drug. Clinical trials are conducted only when satisfactory report information has been gathered on the quality pf the non-clinical safety.

Review Steps

Preclinical (animal studies)

An investigational New Drug Application (IDA)

Phase 1 (study)

Phase 2 (study)

Phase 3 (study)

Submission of New Drug Application (NDA) 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 approval”.

Phase 4 (study).

There are 4 phases of biomedical clinical trials.

Phase I studies usually test new drugs for the first time in a small group of people to evaluate a safe dosage range and identify side effects.

Phase II studies test treatments that have been found to be safe in phase I but now need a larger group of human subjects to monitor for any adverse effects.

Phase III studies are conducted on larger populations and in different regions and countries and are often the step right before a new treatment is approved.

Phase IV studies take place after country approval and there is a need for further testing in a wide population over a longer timeframe.

Phase 0

Microbiology study

The Micro dosing human studies undertaken before phase 1 trials is also called phase 0 studies. Very low dose, about 1/100th of the estimation human dose & maximum 100 gm. Phase 0 is studied that the micro dose pharmacokinetic may be different from that at pharmacological doses.

Phase 1

Human pharmacology & safety

The first human administration of drug is carried out by clinical pharmacologist and trained physician in a sitting where all vital functions & emergency resuscitative facilities are available lowest estimated dose (1/100 to 1/10) of highest dose producing no toxicity in animals. The importance / emphasis in safety tolerability & function heart rate bronchospasm & kidney/ liver damage. The side effects are noted & pharmacodynamics effect in man.

Fewer than 100 patients are used in this phase.

Phase 2

Therapeutic exploration & dose ranging

This is conducted by physicians when trained clinical investigators & involve 100-500 patients selected according to specific inclusions & exclusions criteria. It is generally carried out at 2-4 centers

Phase 2 is study mostly controlled and randomized.

Phase 3

Therapeutic confirmation / composition

The aim is to establish the value of the drug in relation to existing therapy. Indication are finalized & guidelines the therapeutic use formulated. An NDA is submitted license authority (FDA) & convinced to give marketing permission. About 500 –3000 patients are used in phase 3.

Phase 4

Post marketing surveillance data gathering studies

The drug has been marketed for general use practicing physician are identified data/ collection on structured about efficacy, acceptability & adverse drug reactions. Further therapeutic trials like children, pregnant women, patients having hepatic diseases. Most drug continue their development even after marketing. Approval by FDA & US FDA.

DISCOVERY

In 1908 phenytoin (5,5-diphenylhydantoin) was first synthesized as a barbiturate derivative in Germany by professor Heinrich Biltz (1865-1943) and subsequently resynthesized by an American chemist of the pharmaceutical company Parke-Davis in 1923 in Detroit.

Phenytoin was first made in 1908 by the German chemist and found useful for seizures in 1936.

Phenytoin is available as a generic medication. In 2017, it was the 221st most commonly prescribed medication in the United States, with more than two million prescriptions.

In 1938, outside people including H. Houston Merritt and Tracy Putnam discovered phenytoin's usefulness for controlling seizures, without the sedative effects associated with phenobarbital.

It was approved by the FDA in 1953 for use in seizures.

INTRODUCTION

Phenytoin, formerly known as diphenylhydantoin, is a potent anticonvulsant used to treat and prevent generalized grand mal seizures, complex partial seizures and status epileptics.

Phenytoin (**PHT**), sold under the brand name **Dilantin** among others. is an anti-seizure medication.

It may also be used for certain heart arrhythmias or neuropathic.

It can be taken intravenously or by mouth.

Phenytoin is used to control seizures. It does not treat all types of seizures, and your doctor will determine if it is the right medicine for you.

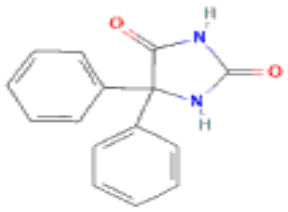
The intravenous form generally begins working within 30 minutes and is effective for roughly 24 hours.

Blood levels can be measured to determine the proper dose.

DESCRIPTION

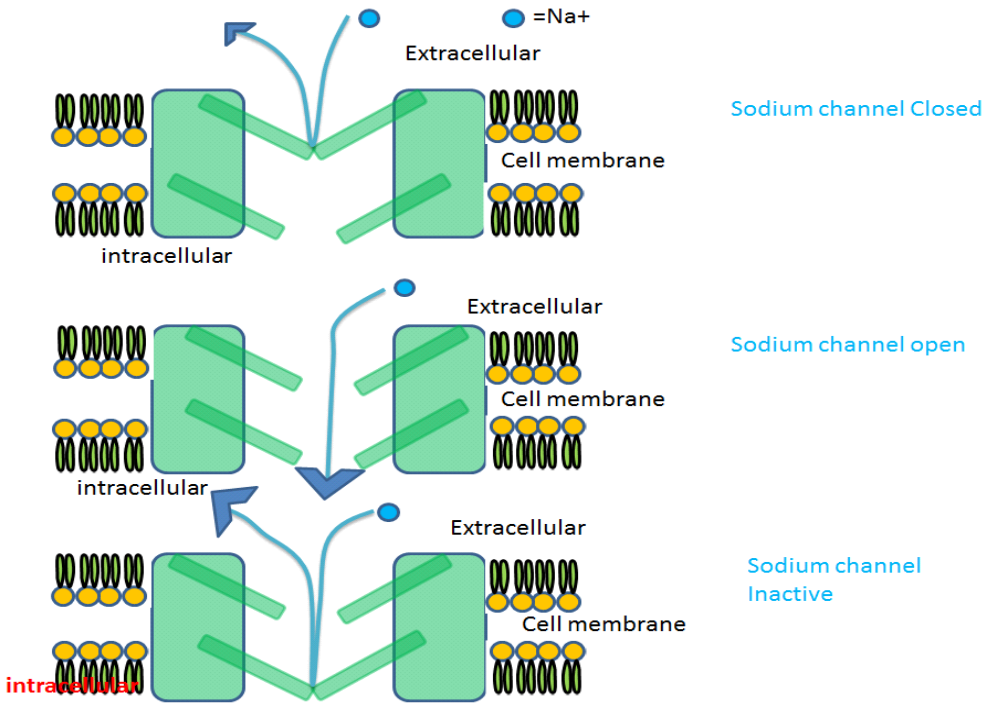
Phenytoin sodium is an antiepileptic drug. Phenytoin sodium is related to the barbiturates in chemical structure, but has a five-membered ring. The chemical name is sodium 5, 5-diphenyl-2,4-imidazolidinedione, having the following structural for.

STRUCTURE: PHYNATOIN



MECHANISM OF ACTION

Phenytoin is believed to protect against seizures by causing voltage dependent block of voltage gated sodium channels. This blocks sustained high frequency repetitive firing of action potentials. This is accomplished by reducing the amplitude of sodium-dependent action potentials through enhancing steady-state inactivation. Sodium channels exist in three main conformations: the resting state, the open state, and the inactive state.



Phenytoin binds preferentially to the inactive form of the sodium channel. Because it takes time for the bound drug to dissociate from the inactive channel, there is a time-dependent block of the channel. Since the fraction of inactive channels is increased by membrane depolarization as well as by repetitive firing, the binding to the inactive state by phenytoin sodium can produce voltage-dependent, use-dependent and time-dependent block of sodium-dependent action potentials.

The primary site of action appears to be the motor cortex where spread of seizure activity is inhibited. Possibly by promoting sodium efflux from neurons, phenytoin tends to stabilize the threshold against hyperexcitability caused by excessive stimulation or environmental changes capable of reducing membrane sodium gradient. This includes the reduction of at synapses which prevents cortical seizure foci from detonating adjacent cortical areas. Phenytoin reduces the maximal activity of brain stem centers responsible for the tonic phase of generalized tonic-clonic seizures.

- **PHARMACOKINETICS**
- **Absorption**

Phenytoin is completely absorbed. Peak plasma concentration is attained approximately 1.5-3 hours, and 4-12 hours after administration of the immediate release formulation and the

extended release formulation, respectively. It should be noted that absorption can be markedly prolonged in situations of acute ingestion.

- **Volume of Distribution**

The volume of distribution of phenytoin is reported to be approximately 0.75 L/kg.

- **Protein binding**

Phenytoin is roughly 90% protein bound.

- **Metabolism**

Phenytoin is extensively metabolized and is first transformed into a reactive *arene oxide intermediate*. It is thought that this reactive intermediate is responsible for many undesirable phenytoin adverse effects such as hepatotoxicity, SJS/TEN, and other idiosyncratic reactions. The *arene oxide* is metabolized to either a *hydroxyphenytoin* or *phenytoin dihydrodiol* metabolite, although the former accounts for about 90% of phenytoin metabolism.

- **Route of elimination**

The majority of phenytoin is excreted as inactive metabolites in the bile. An estimated 1-5% of phenytoin is eliminated unchanged in the urine.

- **Half-life**

Oral administration: The half-life of phenytoin ranges from 7 to 42 hours, and is 22 hours on average.

- **Clearance**

Intravenous administration: The half-life of phenytoin ranges from 10-15 hours. The clearance of phenytoin is non-linear. At lower serum concentrations (less than 10 mg/L), elimination is characterized by first order kinetics. As plasma concentrations increase, the kinetics shift gradually towards zero-order, and finally reach zero-order kinetics once the system is saturated.

- **Toxicity**

The experience of phenytoin toxicity is not limited to situations of acute ingestion, but may also occur due to drug interactions or due to physiological circumstances that impact serum

albumin (ie. kidney disease) or drug metabolism. Other changes that may result in phenytoin toxicity include pregnancy, malnutrition and malignancy.[3]

Phenytoin toxicity most often affects the cardiovascular and nervous systems. The most common presentation of toxicity depends on the route of administration. Cardiovascular adverse effects are most commonly linked to intravenous phenytoin administration, whereas neurological adverse effects are more common with oral phenytoin administration.

Neurotoxicity is usually dependent on serum concentrations. When concentrations range from 10-20 mg/L, mild nystagmus and lateral gaze may occur, while more significant nystagmus is associated with concentrations ranging from 20-30 mg/L. At concentrations of 30-40 mg/L, slurred speech, tremor, nausea, vomiting and ataxia have been reported. In more serious cases where serum levels range from 40-50 mg/L patients are at risk of lethargy, confusion and hyperactivity, and at levels beyond 50 mg/L, coma and seizures may occur.

Phenytoin is classified as an antiarrhythmic and can cause SA and AV nodal blocks as well as dysrhythmias due to its effect on voltage-gated sodium channels. Further, since phenytoin is poorly soluble, the parenteral form is administered with propylene glycol, which is a cardiac depressant. The infusion rate of parenteral phenytoin should not exceed 50 mg per minute due to the risk of hypotension, bradycardia, and asystole.

Treatment for phenytoin toxicity is non-specific and centres around supportive care. One dose of activated charcoal may be used to prevent phenytoin absorption in cases of acute ingestion.

Although hemodialysis is moderately effective at removing phenytoin, it is not normally recommended due to the risks associated with the procedure, and the general effectiveness of supportive care.

- **Food Interactions**
- Avoid alcohol. Alcohol may increase or decrease serum levels of phenytoin.
- Take separate from antacids. Take at least 2 hours before or after antacids. Taking this medication with antacids can reduce absorption.
- Take with food. Food reduces irritation and increases bioavailability.

- **Brand Name Prescription Products**

NAME	DOSAGE	STRENGTH	ROUTE	LABELLER	MARKETING START	MARKETING END
Dilantin	Capsule	100 mg	Oral	Upjohn Canada Ulc	1951-12-31	Not applicable
Dilantin	Injection	50 mg/1mL	Parenteral	Parke Davis Div Of Pfizer Inc	2011-12-30	2012-01-10
Dilantin	Capsule	30 mg	Oral	Upjohn Canada Ulc	1951-12-31	Not applicable
Dilantin	Injection	50 mg/1mL	Parenteral	Parke Davis Div Of Pfizer Inc	2011-12-30	2012-01-10
Dilantin Infatabs	Tablet	50 mg	Oral	Upjohn Canada Ulc	1952-12-31	Not applicable
Dilantin Inj 50mg/ml	Liquid	250 mg / 5 mL	Intramuscular; Intravenous	Parke Davis Division, Warner Lambert Canada Inc.	1972-12-31	1996-09-10
Dilantin Kapseals	Capsule, extended release	30 mg/1	Oral	PARKE-DAVIS	2008-09-22	2008-09-22
Dilantin-125	Suspension	125 mg/5mL	Oral	Parke-Davis Div of Pfizer Inc	1953-01-06	Not applicable
Dilantin-125	Suspension	125 mg/5mL	Oral	Physicians Total Care, Inc.	1953-01-06	2010-06-30
Dilantin-125 Suspension	Suspension	125 mg / 5 mL	Oral	Upjohn Canada Ulc	1953-12-31	Not applicable

- **Drug Drug interaction**

Amiodarone

Estrogens(hormonal pills)

Fungal infection (ketoconazole, intraconazole)

- **Uses for Phenytoin**

Seizure Disorders

- Management of generalized tonic-clonic (grand mal) seizures.
- Management of partial seizures with complex symptomatology (psychomotor and temporal lobe seizures).
- *Not* recommended for treatment of pure absence (petit mal) seizures since the drug may increase frequency of these seizures, but may be used in conjunction with other anticonvulsants when mixed seizure types are present.
- Seizures Associated with Neurosurgery.
- Prevention and treatment of seizures occurring during and following neurosurgery.

- **Overdose**

Signs and Symptoms

There are marked variations among individuals with respect to phenytoin plasma levels where toxicity may occur. Nystagmus or lateral gaze, usually appears at 20 µg/mL, ataxia at 30 µg/mL, dysarthria and lethargy appear when the plasma concentration is over 40 µg/mL, but as high a concentration as 50 µg/mL has been reported without evidence of toxicity. As much as 25 times thetherapeutic dose has been taken to result in a serum concentration above 100 µg/mL with completerecovery. The lethal dose in children is not known. The lethal dose in adults is estimated to be 2 gto 5 g.

The cardinal initial symptoms are nystagmus, ataxia, dysarthria and CNS depression. Other signs that may be seen are tremor, hyperreflexia, somnolence, drowsiness, lethargy, hallucinations, confusion, mental status changes, slurred speech, blurred vision, nausea, vomiting, choreoathetosis, dyskinesias, hyperglycaemia and mild hypoglycaemia. Severe poisoning may result in respiratory

- **Special precautions for storage**

Capsules: Store at 30°C.

Paediatric Suspension: Store at or below 25°C.

- Contraindication

Phenytoin is contraindicated in those patients who are hypersensitive to phenytoin or other hydantoins.

Selection of drug class

Phenytoin is a medicine used to treat epilepsy.

Selection of drug class for pharmacovigilance study using different criteria. (E.g. availability, selling of drug).

- **Availability**

WHAT IS PHENYTOIN AND HOW DOES IT WORK?

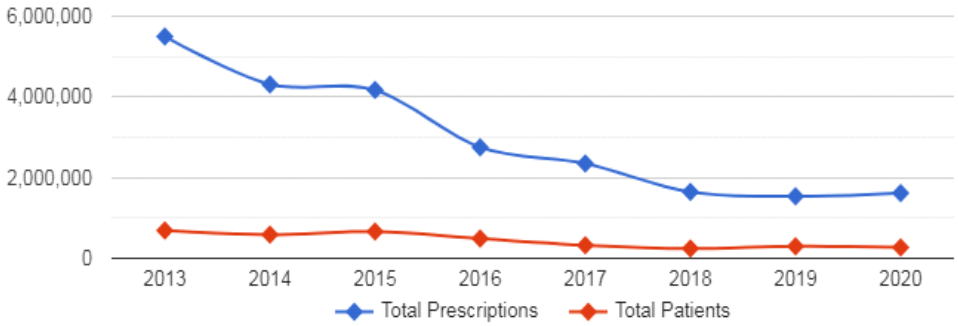
- Phenytoin is used to prevent and control seizures (also called an anticonvulsant or antiepileptic drug). It works by reducing the spread of seizure activity in the brain.
- Phenytoin may also be used to treat certain types of irregular heartbeats.
- Phynatoin is available in form of tablet, capsule, syrup, injection.

- Phenytoin is available under the following different brand names: Dilantin , Dilantin 125, and Phenytek.

- **Phenytoin Summary for 2020**

Top drug rank	#260 (11)
Estimated number of prescriptions in the United States (2020)	1,616,629
Estimated number of patients in the United States (2020)	270,818
Average total drug cost (USD)	
Per prescription	$65.26
Per day of therapy	$1.12/day
Average out-of-pocket cost (USD)	
Per prescription	$22.19
Per day of therapy	$0.45/day

Total Prescriptions and Patients per Year (2013 - 2020)



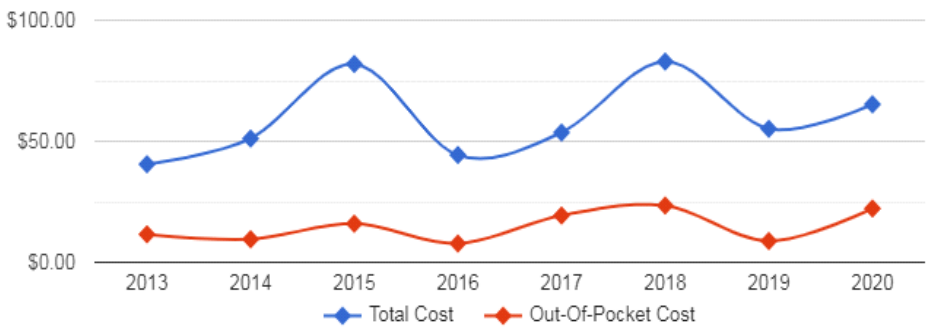
Year	Total Prescriptions	Total Patients
2013	5,495,874	692,160
2014	4,310,313	586,611
2015	4,171,794	663,577
2016	2,751,980	490,763
2017	2,348,515	321,383
2018	1,643,497	240,541
2019	1,536,389	298,537
2020	1,616,629	270,818

- **Rank of Top Drugs over Time**

"Rank" refers to the frequency that a given medication is prescribed within a calendar year compared to all other medications. A rank of "4" would indicate that the medication was the fourth most commonly prescribed medication.

Year	Rank	Change
2013	131	6
2014	156	25
2015	157	1
2016	200	43
Year	**Rank**	**Change**
2017	226	26
2018	272	46
2019	271	1
2020	260	11

- **Cost per Prescription Fill (USD)**



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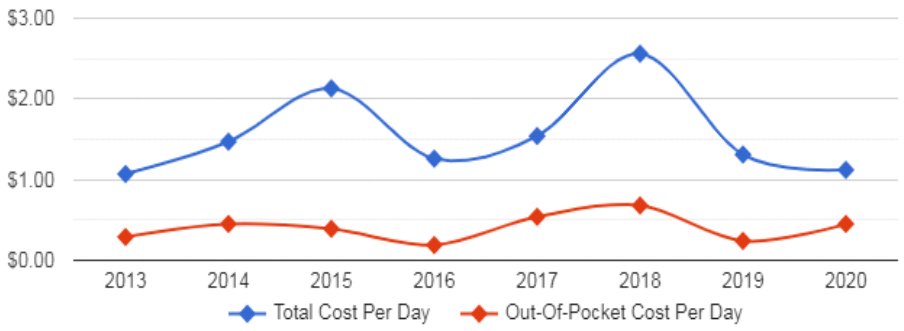
Year	Total Cost	Out-Of-Pocket Cost
2013	$40.49	$11.60
2014	$51.16	$9.55
2015	$81.89	$15.98
2016	$44.29	$7.77
2017	$53.63	$19.37
2018	$82.95	$23.43
2019	$55.16	$8.80
2020	$65.26	$22.19

- **Cost per Day of Therapy (USD/day)**



Year	Total Cost Per Day	Out-Of-Pocket Cost Per Day
2013	$1.07	$0.29
2014	$1.47	$0.45
2015	$2.13	$0.39
2016	$1.26	$0.19
2017	$1.54	$0.54
2018	$2.56	$0.68
2019	$1.31	$0.24
2020	$1.12	$0.45

- **Distribution of Dispensed Dosage Forms (2020)**

Dosage Form	Strength	% of Dispensed Products
Tablet/capsule	100 mg	68.5%
Tablet/capsule	50 mg	26.5%
Other, unspecified, or misc.		5.0%

- **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.

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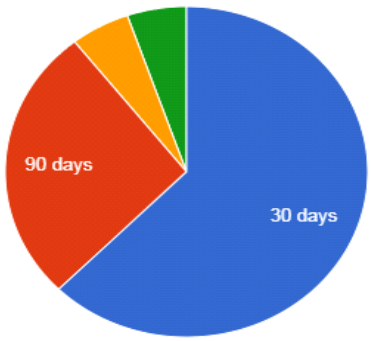

- **Side effects of phenytoin**
- **Common side effects**

These common side effects of phenytoin may happen in more than 1 in 100 people. They're usually mild and go away by themselves. There are things you can do to help cope with them:

Headaches

Feeling drowsy, sleepy or dizzy

Feeling nervous, unsteady or shaky

Feeling or being sick (nausea or vomiting)

Constipation

Sore or swollen gums

Some side effects of phenytoin wear off once your body gets used to the medicine, but it can take several weeks or months. Talk to your doctor or pharmacist if these side effects bother you or do not go away.

- **Serious side effects**

Skin rashes

It's common to get a skin rash with phenytoin. Most skin rashes are not serious.

Stevens-Johnson syndrome is a rare side effect of phenytoin.

It causes flu-like symptoms, followed by a red or purple rash that spreads and forms blisters. The affected skin eventually dies and peels off.

It's more likely to happen in the first 8 weeks of starting phenytoin, or when the dose is increased too quickly.

It can also happen if phenytoin is stopped suddenly for a few days and then restarted at the same dose as before, without reducing the dose and then increasing it slowly again.

Stevens-Johnson syndrome is more common in.

- children
- people who have developed a rash before with a different epilepsy medicine
- people who are allergic to an antibiotic called trimethop
- people also taking a medicine called sodium valproate

To help reduce the chance of you getting a rash that could be confused with Stevens-Johnson syndrome, it's best to not try any new medicines or food during the first 3 months of treatment with phenytoin.

It's also best to not start phenytoin within 2 weeks of a viral infection, vaccination or rash caused by something else.

Other serious side effects

Very few people taking phenytoin have serious problems.

Tell your doctor or contact 111 now if you have a serious side effect, including:

- unexpected bruising or bleeding, a high temperature or sore throat – these could be signs of a blood disorder
- a high temperature, swollen glands or a skin rash, sometimes with yellowing of the whites of your eyes or your skin (this may be less noticeable on brown or black skin),

particularly in the first 2 months of treatment – these may be signs of a hypersensitivity reaction, which is more likely to happen if you're of Black African or African-Caribbean origin or have a weakened immune system.

Serious allergic reaction

In rare cases, it's possible to have a serious allergic reaction (anaphylaxis) to phenytoin.

- Long-term side effects

  Taking phenytoin for a long time can:

- decrease the amount of vitamin D in your blood and might lead to osteoporosis and osteopenia, increasing your risk of breaking a bone. If the amount of vitamin D in your blood is low, your doctor will give you vitamin D supplements
- cause nerve damage (peripheral neuropathy), which can lead to symptoms such as numbness and tingling in hands or feet
- make the skin on your face look and feel coarse and become slightly hairy
- affect your ability to think clearly

- Other side effects

These are not all the side effects of phenytoin. For a full list, see the leaflet inside your medicines packet.

Pregnancy, breastfeeding and fertility while taking phenytoin.

- **Phenytoin and pregnancy**

Phenytoin has been linked to an increased risk of problems for your baby if you take it during pregnancy.

You'll usually only be advised to take it if your doctor thinks the benefits of the medicine outweigh the risks.

If you take phenytoin for epilepsy, it's important that this is controlled during pregnancy, as seizures can harm you and your baby. If you become pregnant, keep taking phenytoin, but talk to your doctor straight away. It's likely that you will need to be seen in a specialist epilepsy clinic, and they may want to change your medicine.

If you're trying to get pregnant or have become pregnant while taking phenytoin, it's recommended you take a high dose of folic acid (5mg a day). You can get this from your doctor or midwife.

Ideally, it's best to take high dose folic acid for 3 months before you start trying to get pregnant and for the first 12 weeks of pregnancy. Do not worry if you have not taken it before you get pregnant, but start taking it as soon as possible once you know that you are pregnant. It helps your baby to grow normally.

Your baby may need extra monitoring for a few days after they're born. This is because they can sometimes have withdrawal symptoms from phenytoin.

- **Phenytoin and breastfeeding**

If your doctor or health visitor says your baby is healthy, you can take phenytoin while you're breastfeeding.

Phenytoin passes into breast milk in small amounts. Most babies do not get any side effects, but some babies might be more sleepy or not feed as well.

Taking other medicines while you're taking phenytoin might increase the chance of your baby getting these side effects, although this is still rare.

It's important to keep taking phenytoin to keep you well. Do not stop taking it without talking to your doctor. Breastfeeding will also benefit both you and your baby.

If you notice that your baby is not feeding as well as usual, seems unusually sleepy or irritable, or has a rash, or you have any other concerns about them, talk to your pharmacist, midwife, health visitor or doctor as soon as possible.

- **Phenytoin and fertility**

There's no good evidence to suggest that taking phenytoin causes fertility problems in men or women.

However, speak to your doctor if you're female and trying to get pregnant. They may want to review your treatment.

- **Patient Interview**

Interview of patients for under -standing & identification of Adr.

- **Hospital name:- matoshri Ayurvedic hospital & research center.**
- **Patient name :- pankaj pawar**
- **Age :- 24 .**
- **Gender:- male.**
- **Disease:- seizures**

Drug :- Dilantin 30 mg

- **Drug ADR**
- Headaches
- Feeling drowsy, sleepy or dizzy
- Feeling nervous, unsteady or shaky
- Feeling or being sick (nausea or vomiting)
- Constipation
- Sore or swollen gums

- **Routes of Administration**
- Oral route of administration
- Parenteral route of administration

- **Adverse drug reaction monitoring form**

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			12. Relevant tests/ laboratory data with dates
1. Patient Initials _____	2. Age at time of Event or Date of Birth _____	3. M ☐ F ☐ Other ☐ 4. Weight_____Kgs	
B. SUSPECTED ADVERSE REACTION			13. Relevant medical/ medication history (e.g. allergies, race, pregnancy, smoking, alcohol use, hepatic/renal dysfunction etc.)
5. Date of reaction started (dd/mm/yyyy)			
6. Date of recovery (dd/mm/yyyy)			
7. Describe reaction or problem			14. Seriousness of the reaction: No ☐ if Yes ☐ (please tick anyone) ☐ Death (dd/mm/yyyy) ☐ Congenital-anomaly ☐ Life threatening ☐ Required intervention to Prevent permanent impairment/damage ☐ Hospitalization/Prolonged ☐ 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

Phenytoin is the most effective drug against epilepsy. It is used as a antiepileptic and anti convulsant drug. This paper deals with pharmacokinetic and pharmacodynamic activities of drug. During the study of phenytoin enormous information regarding it has been collected in this review is as clinical trials for phenytoin and detailed information of pharmacovigilance.

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