in Chewable Tablets, USP)

S BATAANI O I N FATAB S®

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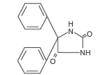
INFATABS® Dilantin®

(Phenytoin Chewable Tablets LISP)

NOT FOR ONCE-A-DAY DOSING

Dilantin is an antiepileptic drug

Dilantin (phenytoin) is related to the barbiturates in chemical structure, but has a five membered ring. The chemical name is 5,5-diphenyl-2,4-imidazolidinedione, having the following structural formula



Each Dilantin Infatab, for oral administration, contains 50 mg phenytoin, USP. Also contains: D&C yellow No. 10, Al lake; FD&C yellow No. 6, Al lake; flavor; saccharin sodium, USP; confectioner's sugar, NF; talc, USP; magnesium stearate, NF; and purified water, USP.

CLINICAL PHARMACOLOGY Mechanism of Action

Phenytoin is an antiepileptic drug which can be useful in the treatment of epilepsy. The Phenytoin is an antiepileptic drug which can be useful in the treatment of epilepsy. 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 posttetanic potentiation at synapses. Loss of posttetanic potentiation prevents cortical seizure foci from detonating adjacent cortical areas. Phenytoin reduces the maximal activity of brain stem centers responsible for the tonic phase of tonic-clonic (grand mal) seizures.

Pharmacokinetics and Drug Metabolism

Clinical studies using Dilantin Instabs have shown an average plasma half-life of 14 hours with a range of 7 to 29 hours. Steady-state therapeutic levels are achieved at least 7 to 10 days (5–7 half-lives) after initiation of therapy with recommended doses of 300 mg/day.

When serum level determinations are necessary, they should be obtained at least 5–7 When serum level determinations are necessary, they should be obtained at least 5–7 half-lives after treatment initiation, dosage change, or addition or subtraction of another drug to the regimen so that equilibrium or steady-state will have been achieved. Trough levels provide information about clinically effective serum level range and confirm patient compliance and are obtained just prior to the patient's next scheduled dose. Peak levels indicate an individual's threshold for emergence of dose-related side effects and are obtained at the time of expected peak concentration. For Dilantin Infatabs, peak levels occur 1½–3 hours after administration.

Optimum control without clinical signs of toxicity occurs more often with serum levels between 10 and 20 mcg/mL, although some mild cases of fonic-clonic (grand mal) epilepsy may be controlled with lower serum levels of phenytoin.

In most patients maintained at a steady dosage, stable phenytoin serum levels are illness being treated.

achieved. There may be wide interpatient variability in phenytoin serum levels with equivalent dosages. Patients with unusually low levels may be noncompliant or hypermetabolizers of phenytoin. Unusually high levels result from liver disease, variant YP2C9 and CYP2C19 alleles, or drug interactions which result in metabolic interference The patient with large variations in phenytoin plasma levels, despite standard doses, presents a difficult clinical problem. Serum level determinations in such patients may be particularly helpful. As phenytoin is highly protein bound, free phenytoin levels may be altered in patients whose protein binding characteristics differ from normal.

Most of the drug is excreted in the bile as inactive metabolites which are then reabsorbed secretion. Because phenytoin is hydroxylated in the liver by an enzyme system which is produce very substantial increases in serum levels, when these are in the upper range. The steady-state level may be disproportionately increased, with resultant intoxication, from an increase in dosage of 10% or more.

Clinical studies show that chewed and unchewed Dilantin Infatabs are bioequivalent, yield approximately equivalent plasma levels, and are more rapidly absorbed than 100-mg Dilantin Kapseals®.

Special Populations

Patients with Renal or Hepatic Disease: Due to an increased fraction of unbound phenytoin in patients with renal or hepatic disease, or in those with hypoalbuminemia, the interpretation of total phenytoin plasma concentrations should be made with caution (see DOSAGE AND ADMINISTRATION). Unbound phenytoin concentrations may be more useful in these patient populations.

Age: Phenytoin clearance tends to decrease with increasing age (20% less in patients over 70 years of age relative to that in patients 20-30 years of age). Phenytoin dosing requirements are highly variable and must be individualized (see DOSAGE AND ADMINISTRATION).

Gender and Race: Gender and race have no significant impact on phenytoin

INDICATIONS AND USAGE

Dilantin Infatabs (Phenytoin Chewable Tablets, USP) are indicated for the control of Dilantin initiators (Prienytoin Chewapie ladolets, USP) are indicated for the control of generalized tonic-clonic (grand mail) and complex partial (psychomotor, temporal lobe) seizures and prevention and treatment of seizures occurring during or following neurosurgery. Phenytoin serum level determinations may be necessary for optimal dosage adjustments (see DOSAGE AND ADMINISTRATION and CLINICAL PHARMACOLOGY sections).

CONTRAINDICATIONS

Phenytoin is contraindicated in those patients with a history of hypersensitivity to phenytoin or its inactive ingredients, or other hydantoins. Coadministration of Dilantin is contraindicated with delayirdine due to potential for loss of virologic response and possible resistance to delayirdine or to the class of non-

WARNINGS

Effects of Abrupt Withdrawal

When, in the judgment of the clinician, the need for dosage reduction, discontinuation, or substitution of alternative antiepileptic medication arises, this should be done gradually. In the event of an allergic or hypersensitivity reaction, more rapid substitution of alternative therapy may be necessary. In this case, alternative therapy should be an anticonvulsant not belonging to the hydantoin chemical class.

(Phenytoin Chewable Tablets, USP)

Suicidal Behavior and Ideation

houghts or behavior in patients taking these drugs for any indication. Patients treated ith any AED for any indication should be monitored for the emergence or worsening f depression, suicidal thoughts or behavior, and/or any unusual changes in mood or

had a median treatment duration of 12 weeks, the estimated incidence rate of suicidal ehavior or ideation among 27,863 AED-treated patients was 0.43%, compared to 0.24% among 16,029 placebo-treated patients, representing an increase of approximately one case of suicidal thinking or behavior for every 530 patients treated. There were four suicides in drug-treated patients in the trials and none in placebo-treated patients, but the number is too small to allow any conclusion about drug effect on suicide. he number is too small to allow any conclusion about drug effect on suicide.

he increased risk of suicidal thoughts or behavior with AEDs was observed as early as one week after startling drug treatment with AEDs and persisted for the duration of treatment assessed. Because most trials included in the analysis did not extend beyond 24 weeks, the risk of suicidal thoughts or behavior beyond 24 weeks could

The risk of suicidal thoughts or behavior was generally consistent among drugs in the data analyzed. The finding of increased risk with AEDs of varying mechanisms of action and across a range of indications suggests that the risk applies to all AEDs used for any indication. The risk did not vary substantially by age (5-100 years) in the clinical

Table 1 shows absolute and relative risk by indication for all evaluated AEDs. Table 1 Risk by indication for antiepileptic drugs in the pooled analysis

Indication	Placebo Patients with Events Per 1000 Patients	Drug Patients with Events Per 1000 Patients	Relative Risk: Incidence of Events in Drug Patients/ Incidence in Placebo Patients	Risk Differen Additional Di Patients with Events Per 1 Patients
Epilepsy	1.0	3.4	3.5	2.4
Psychiatric	5.7	8.5	1.5	2.9
Other	1.0	1 0	1.0	0.0

were similar for the epilepsy and psychiatric indications.

Anyone considering prescribing Dilantin Infatabs or any other AED must balance the risk of suicidal thoughts or behavior with the risk of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behavior. Should suicidal thoughts and behavior emerge during treatment, the prescriber needs to consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

Patients, their caregivers, and families should be informed that AEDs increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of the signs and symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to healthcare providers.

Serious Dermatologic Reactions Serious and sometimes fatal dermatologic reactions, including toxic epidermal serious and sometimes ratal derinationgly features, including toxic epidermal necrolysis (TEN) and Stevens-Johnson syndrome (SJS), have been reported with phenytoin treatment. The onset of symptoms is usually within 28 days, but can occur later. Dilantin should be discontinued at the first sign of a rash, unless the rash is clearly not drug-related. If signs or symptoms suggest SJS/TEN, use of this drug should not be resumed and alternative therapy should be considered. If a rash occurs, the patient should be evaluated for signs and symptoms of Drug Reaction with Eosinophilia and Systemic Symptoms (see DRESS/Multiorgan hypersensitivity below).

Studies in patients of Chinese ancestry have found a strong association between the risk of developing SJS/TEN and the presence of HLA-B*1502, an inherited allelic variant of the HLA B gene, in patients using carbamazepine. Limited evidence suggests that HLA-B*1502 may be a risk factor for the development of SJS/TEN in patients of Asian ancestry taking other antiepileptic drugs associated with SJS/TEN, including phenytoin. Consideration should be given to avoiding phenytoin as an alternative for carbamazepine in patients positive for HLA-B*1502.

In patients positive for HLA-5*1502 genotyping has important limitations and must never substitute for appropriate clinical vigilance and patient management. The role of other possible factors in the development of, and morbidity from, SJS/TEN, such as antieplieptic drug (AED) dose, compliance, concomitant medications, comorbidities, and the level of dermatologic monitoring have not been studied.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), also known as

Phenytoin is not effective for absence (petit mal) seizures. If tonic-clonic (grand mal) pharmacokinetics. Multiorgan hypersensitivity, has been reported in patients taking antiepileptic drugs, Pediatrics: Initially, 5 mg/kg/day in two or three equally divided doses, with subsequent including Dilantin. Some of these events have been fatal or life-threatening. DRESS dosage individualized to a maximum of 300 mg daily. A recommended daily maintenance typically, although not exclusively, presents with fever, rash, and/or lymphadenopathy, dosage is usually 4 to 8 mg/kg. Children over 6 years and adolescents may require the in association with other organ system involvement, such as hepatitis, nephritis, hematological abnormalities, myocarditis, or myositis sometimes resembling an acute viral infection. Eosinophilia is often present. Because this disorder is variable in its expression, other organ systems not noted here may be involved. It is important to note that early manifestations of hypersensitivity, such as fever or lymphadenopathy, may be present even though rash is not evident. If such signs or symptoms are present, the patient should be evaluated immediately. Dilantin should be discontinued if an Iternative etiology for the signs or symptoms cannot be established

Hypersensitivity

Dilantin and other hydantoins are contraindicated in patients who have experienced phenytoin hypersensitivity (see CONTRAINDICATIONS). Additionally, consider alternatives to structurally similar drugs such as carboxamides (e.g., carbamazepine), barbiturates, succlinimides, and oxazolidinediones (e.g., trimethadione) in these same patients. Similarly, if there is a history of hypersensitivity reactions to these structurally similar drugs in the patient or immediate family members, consider alternatives to Dilantin.

Hepatic Injury

Cases of acute hepatotoxicity, including infrequent cases of acute hepatic failure, have Abrupt withdrawal of phenytoin in epileptic patients may precipitate status epilepticus. been reported with Dilantin. These events may be part of the spectrum of DRESS or

Antiepileptic drugs (AEDs), including Dilantin Infatabs, increase the risk of suicidal Hematopoietic complications, some fatal, have occasionally been reported in association with administration of Dilantin. These have included throm granulocytopenia, agranulocytosis, and pancytopenia with or without bone marrow suppression.

behavior.

There have been a number of reports suggesting a relationship between phenytoin Pooled analyses of 199 placebo-controlled clinical trials (mono- and adjunctive therapy) of 11 different AEDs showed that patients randomized to one of the AEDs had hyperplasia, pseudolymphoma, bymphoma, and Hodgkin's disease, approximately twice the risk (adjusted Relative Risk 1.8, 95% CI:1.2, 2.7) of suicidal Although a cause and effect relationship has not been established, the occurrence of lymphadenopathy indicates the need to differentiate such a condition from other types of lymph node pathology. Lymph node involvement may occur with or without symptoms and signs of DRESS.

Effects on Vitamin D and Bone

The chronic use of phenytoin in patients with epilepsy has been associated with decreased bone mineral density (osteopenia, osteoporosis, and osteomalacia) and bone fractures. Phenytoin induces hepatic metabolizing enzymes. This may enhance the metabolism of vitamin D and decrease vitamin D levels, which may lead to vitamin D deficiency, hypocalcemia, and hypophosphatemia. Consideration should be giver to screening with bone-related laboratory and radiological tests as appropriate and initiating treatment plans according to established guidelines.

Effects of Alcohol Use on Phenytoin Serum Levels Exacerbation of Pornbyria

In view of isolated reports associating phenytoin with exacerbation of porphyria, caution should be exercised in using this medication in patients suffering from this disease.

Risks to Mother. An increase in seizure frequency may occur during pregnancy because of altered phenytoin pharmacokinetics. Periodic measurement of plasma phenytoin concentrations may be valuable in the management of pregnant women as a guide to appropriate adjustment of dosage (see PRECAUTIONS, Laboratory Tests). However, postpartum restoration of the original dosage will probably be

Risks to the Fetus. If this drug is used during pregnancy, or if the patient becomes pregnant while taking the drug, the patient should be apprised of the potential harm to the fetus.

Prenatal exposure to phenytoin may increase the risks for congenital malformations and Prenatal exposure to phenytoin may increase the risks for congenital malformations and other adverse developmental outcomes. Increased frequencies of major malformations (such as ordacial clefts and cardiac defects), minor anomalies (dysmorphic facial features, nall and digit hypoplasia), growth abnormalities (including microcephaly), and mental deficiency have been reported among children born to epileptic women who took phenytoin alone or in combination with other antiepileptic drugs during pregnancy. There have also been several reported cases of malignancies, including neuroblastoma, in children whose mothers received phenytoin during pregnancy. The overall incidence of malformations for children of epileptic women treated with antiepileptic drugs (phenytoin and/or others) during pregnancy is about 10%, or two- to three-fold that in the general population. However, the relative contributions of antiepileptic drugs and other factors associated with epilepsy to this increased risk are uncertain and in most cases it has not been possible to attribute specific developmental abnormalities to particular antiepileptic drugs. particular antiepileptic drugs.

Patients should consult with their physicians to weigh the risks and benefits of phenytoin during pregnancy.

Postpartum Period. A potentially life-threatening bleeding disorder related to decreased levels of vitamin K-dependent clotting factors may occur in newborns exposed to phenytoin in utero. This drug-induced condition can be prevented with vitamin K administration to the mother before delivery and to the neonate after birth. Preclinical:

administration of phenytoin doses of 75 mg/kg or higher (approximately 120% of the maximum human loading dose or higher on a mg/m² basis) to pregnant rabbits.

General: The liver is the chief site of biotransformation of phenytoin: patients with impaired liver function, elderly patients, or those who are gravely ill may show early signs of toxicity.

A small percentage of individuals who have been treated with phenytoin have been shown to metabolize the drug slowly. Slow metabolism may be due to limited enzyme availability and lack of induction; it appears to be genetically determined. If early signs of dose-related CNS toxicity develop, plasma levels should be checked immediately.

Hyperglycemia, resulting from the drug's inhibitory effects on insulin release, has been reported. Phenytoin may also raise the serum glucose level in diabetic patients. Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS)/Multiorgan hypersensitivity

Phenytoin is not indicated for seizures due to hypoglycemic or other metabolic causes. Appropriate diagnostic procedures should be performed as indicated.

and absence (petit may isecures are present, combined origit inerapy is needed. Serum levels of phenytoin sustained above the optimal range may produce confusional states referred to as "delirium," "psychosis," or "encephalopathy," or rarely irreversible cerebellar dysfunction. Accordingly, at the first sign of acute toxicity, plasma levels are recommended. Dose reduction of phenytoin therapy is indicated if plasma levels are excessive; if symptoms persist, termination is recommended. (See WARNINGS section.)

Information for Patients: Inform patients of the availability of a Medication Guide, and instruct them to read the Medication Guide prior to taking Dilantin. Instruct patients to take Dilantin only as

atients taking phenytoin should be advised of the importance of adhering strictly to the prescribed dosage regimen, and of informing the physician of any clinical condition in which it is not possible to take the drug orally as prescribed, e.g., surgery, etc.

Patients should be made aware of the early toxic signs and symptoms of potential hematologic, dermatologic, hypersensitivity, or hepatic reactions. These symptoms may include, but are not limited to, fever, sore throat, rash, ulcers in the mouth, easy but he has been supported by the description of the second state. may include, but are not limited to, lever, sore throat, rash, utcers in the indum, easy bruising, lymphadenopathy and petechial or purpuric hemorrhage, and in the case of liver reactions, anorexia, nausea/vomiting, or jaundice. The patient should be advised that, because these signs and symptoms may signal a serious reaction, that they must report any occurrence immediately to a physician. In addition, the patient should be advised that these signs and symptoms should be reported even if mild or when occurring after addition. occurring after extended use.

Patients should also be cautioned on the use of other drugs or alcoholic beverages without first seeking the physician's advice. The importance of good dental hygiene should be stressed in order to minimize the

MEDICATION GUIDE

DILANTIN (Dr lan' tin) (Phenytoin)

Chewable Tablets, Extended Oral Capsules

Read this Medication Guide before you start taking DILANTIN and each time you get a refill. There may be new information. This information does not take the place of talking to your healthcare provider about your medical condition or treatment. If you have any questions about DILANTIN, ask your healthcare provider or pharmacist.

What is the most important information I should know about DILANTIN?

Do not stop taking DILANTIN without first talking to your healthcare provider Stopping DILANTIN suddenly can cause serious problems.

DILANTIN can cause serious side effects including:

1. Like other antiepileptic drugs, DILANTIN may cause 3. suicidal thoughts or actions in a very small number of 4. neonle, about 1 in 500.

Call a healthcare provider right away if you have any of these symptoms, especially if they are new, worse, or worry you:

- thoughts about suicide or dying
- · attempts to commit suicide
- new or worse depression
- new or worse anxiety
- feeling agitated or restless panic attacks
- trouble sleeping (insomnia)
- · new or worse irritability
- acting aggressive, being angry, or violent
- acting on dangerous impulses
- an extreme increase activity and talking (mania)

 other unusual changes in behavior or mood How can I watch for early symptoms of suicidal thoughts and actions?

- Pay attention to any changes, especially sudden changes. in mood, behaviors, thoughts, or feelings.
- scheduled Call your healthcare provider between visits as needed, especially

if you are worried about symptoms. Do not stop taking DILANTIN without first talking to a healthcare provider.

 Stopping DILANTIN suddenly can cause serious problems. Stopping a seizure medicine suddenly in a patient who has epilepsy can cause seizures that will not stop (status epilepticus).

Suicidal thoughts or actions can be caused by things other than medicines. If you have suicidal thoughts or actions, your healthcare provider may check for other causes.

- 2. Dilantin may harm your unborn baby.
- If you take DILANTIN during pregnancy, your baby is at Before you take DILANTIN, tell your healthcare provider if you: risk for serious birth defects.
- Birth defects may occur even in children born to women who are not taking any medicines and do not have other
- If you take DILANTIN during pregnancy, your baby is also at risk for bleeding problems right after birth. Your healthcare provider may give you and your baby medicine to prevent this.

 All women of child-bearing age should talk to their healthcare provider about using other possible treatments instead of DILANTIN. If the decision is made to use DILANTIN, you should use effective birth control (contraception) unless you are planning to become pregnant.

- Tell your healthcare provider right away if you become pregnant while taking DILANTIN. You and your healthcare provider should decide if you will take DILANTIN while you are pregnant.
- Pregnancy Registry: If you become pregnant while taking DILANTIN, talk to your healthcare provider about registering with the North American Antiepileptic Drug Pregnancy Registry. You can enroll in this registry by calling 1-888-233-2334. The purpose of this registry is to collect information about the safety of antiepileptic drugs during pregnancy.
- Swollen glands (lymph nodes)
- Allergic reactions or serious problems which may affect organs and other parts of your body like the liver or blood cells. You may or may not have a rash with these types of reactions. Symptoms can include any of the following:
- swelling of your face, eyes, lips, or tongue
- trouble swallowing or breathing
- a skin rash
- fever, swollen glands (lymph nodes), or sore throat that do not go away or come and go
- painful sores in the mouth or around your eyes
- yellowing of your skin or eves
- bruising or bleeding
- severe fatigue or weakness
- severe muscle pain
- frequent infections or an infection that does not go away
- loss of appetite (anorexia)
- nausea or vomiting

Call your healthcare provider right away if you have any of the symptoms listed above.

What is DILANTIN?

• Keep all follow-up visits with your healthcare provider as DILANTIN is a prescription medicine used to treat tonic-clonic (grand mal), complex partial (psychomotor or temporal lobe) seizures, and to prevent and treat seizures that happen during or after brain surgery.

Who should not take DILANTIN?

Do not take DILANTIN if you:

- are allergic to phenytoin or any of the ingredients in DILANTIN. See the end of this leaflet for a complete list of ingredients in DILANTIN.
- have had an allergic reaction to CEREBYX (fosphenytoin). PEGANONE (ethotoin), or MESANTOIN (mephenytoin).
- take delavirdine

What should I tell my healthcare provider before taking DILANTIN?

- have or had liver disease have or had porphyria
- have or had diabetes
- have or have had depression, mood problems, or suicidal thoughts or behavior
- are pregnant or plan to become pregnant.
- if you become pregnant while taking DILANTIN, the level

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Swollen glands (lymph nodes)

Allergic reactions or serious problems which may affect organs and other parts of your body like the liver or blood cells. You may or may not have a rash with these types of reactions. Symptoms can include any of the following:

- swelling of your face, eyes, lips, or tongue
- trouble swallowing or breathing
- a skin rash
- fever, swollen glands (lymph nodes), or sore throat that do not go away or come and go
- painful sores in the mouth or around your eyes
- yellowing of your skin or eyes bruising or bleeding
- severe fatigue or weakness
- severe muscle pain frequent infections or an infection that does not go away

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thoughts or behavior are pregnant or plan to become pregnant.

• if you become pregnant while taking DILANTIN, the level

have or have had depression, mood problems, or suicidal

Reference ID: 3462008

pass into breast milk. You and your healthcare provider How should I store DILANTIN? should decide if you will take DILANTIN or breastfeed. You should not do both.

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Taking DILANTIN with certain other medicines can cause side

Keep DILANTIN and all medicines out of the reach of children. medicines without talking to your healthcare provider.

to your healthcare provider and pharmacist when you get a new those listed in a Medication Guide. Do not use DILANTIN for a medicine

How should I take DILANTIN?

- Take DILANTIN exactly as prescribed. Your healthcare
 This Medication Guide summarizes the most important this management of the summarizes of the most important the summarizes of the summarize provider will tell you how much DILANTIN to take.
- healthcare provider
- DILANTIN can cause overgrowth of your gums. Brushing For more information about DILANTIN, visit http://www.pfizer.com and flossing your teeth and seeing a dentist regularly or call 1-800-438-1985. while taking DILANTIN can help prevent this.
- If you take too much DILANTIN, call your healthcare provider or local Poison Control Center right away.
- Do not stop taking DILANTIN without first talking to your Each tablet is a yellow triangular scored chewable tablet. healthcare provider. Stopping DILANTIN suddenly can Active ingredient: 50 mg phenytoin, USP cause serious problems.

What should I avoid while taking DILANTIN?

Do not drink alcohol while you take DILANTIN without first magnesium stearate, and purified water. talking to your healthcare provider. Drinking alcohol while taking Extended Oral Capsule DILANTIN may change your blood levels of DILANTIN which can Dilantin 100mg: Each capsule contains a white powder. The cause serious problems.

activities until you know how DILANTIN affects you. DILANTIN black ink. can slow your thinking and motor skills.

What are the possible side effects of DILANTIN?

See "What is the most important information I should know talc, and magnesium stearate. The capsule body contains about DILANTIN?"

DILANTIN may cause other serious side effects including:

 Softening of your bones (osteopenia, osteoporosis, osteomalacia). This can cause broken bones.

Call your healthcare provider right away, if you have any o the symptoms listed above.

The most common side effects of DILANTIN include:

- problems with walking and coordination
- slurred speech
- confusion dizziness
- trouble sleeping
- nervousness
- tremor headache
- nausea
- vomiting
- constipation
- rash

These are not all the possible side effects of DILANTIN. For more information, ask your healthcare provider or pharmacist.

of DILANTIN in your blood may decrease, causing your Tell your healthcare provider if you have any side effect that

Call your doctor for medical advice about side effects. You • are breast feeding or plan to breastfeed. DILANTIN can may report side effects to FDA at 1-800-FDA-1088.

- Store DILANTIN INFATABS at room temperature between 68°F to 77°F (20°C to 25°C). Protect from moisture.
- Store DILANTIN Capsules at room temperature between 68°F to 77°F (20°C to 25°C) in tight, light-resistant containers. Protect from moisture.

General information about DILANTIN

Know the medicines you take. Keep a list of them and show it Medicines are sometimes prescribed for purposes other than condition for which it was not prescribed. Do not give DILANTIN to other people, even if they have the same symptoms that you have. It may harm them.

information about DILANTIN. If you would like more information, • Your healthcare provider may change your dose. Do not talk with your healthcare provider. You can ask your healthcare change your dose of DILANTIN without talking to your provider or pharmacist for information about DILANTIN that was written for healthcare professionals.

What are the ingredients in DILANTIN?

Inactive ingredients: D & C vellow No. 10. A1 lake, FD&C vellow No. 6, flavor, saccharin sodium, confectioner's sugar, talc,

medium orange cap has "PD" imprinted in black ink and the Do not drive, operate heavy machinery, or do other dangerous white, opaque body has "DILANTIN" over "100 mg" printed in

Active ingredient: 100 mg phenytoin sodium

Inactive ingredients: lactose monohydrate, confectioner's sugar, titanium dioxide and gelatin. The capsule cap contains FD&C red No. 28, FD&C yellow No. 6, and gelatin.

Dilantin 30mg: Each capsule contains a white powder. The small pale pink opaque cap has "PD" imprinted in black ink and the white, opaque body has "Dilantin 30 mg" printed in black ink.

Active ingredient: 30 mg phenytoin sodium

Inactive ingredients: lactose monohydrate, confectioner's sugar, talc, and magnesium stearate. The capsule shell cap and body contain Titanium Dioxide (cap and body); gelatin (cap and body); D&C yellow No. 10 (cap); FD&C red No. 3 (cap).

This Medication Guide has been approved by the U.S. Food and Drug Administration.



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Revised September 2013

PAA042242S

of DILANTIN in your blood may decrease, causing your Tell your healthcare provider if you have any side effect that seizures to become worse. Your healthcare provider may bothers you or that does not go away. change your dose of DILANTIN.

• are breast feeding or plan to breastfeed. DILANTIN can may report side effects to FDA at 1-800-FDA-1088. pass into breast milk. You and your healthcare provider How should I store DILANTIN? should decide if you will take DILANTIN or breastfeed. You should not do both

Tell your healthcare provider about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Taking DILANTIN with certain other medicines can cause side

Keep DILANTIN and all medicines out of the reach of children. medicines without talking to your healthcare provider.

to your healthcare provider and pharmacist when you get a new those listed in a Medication Guide. Do not use DILANTIN for a

How should I take DILANTIN?

- Take DILANTIN exactly as prescribed. Your healthcare
 This Medication Guide summarizes the most important than the summarizes of the summarize provider will tell you how much DILANTIN to take.
- healthcare provider
- DILANTIN can cause overgrowth of your gums. Brushing For more information about DILANTIN, visit http://www.pfizer.com and flossing your teeth and seeing a dentist regularly or call 1-800-438-1985. while taking DILANTIN can help prevent this.
- If you take too much DILANTIN, call your healthcare provider or local Poison Control Center right away.
- healthcare provider. Stopping DILANTIN suddenly can Active ingredient: 50 mg phenytoin, USP cause serious problems.

What should I avoid while taking DILANTIN?

Do not drink alcohol while you take DILANTIN without first talking to your healthcare provider. Drinking alcohol while taking Extended Oral Capsule DILANTIN may change your blood levels of DILANTIN which can Dilantin 100mg: Each capsule contains a white powder. The cause serious problems.

activities until you know how DILANTIN affects you. DILANTIN black ink. can slow your thinking and motor skills.

What are the possible side effects of DILANTIN?

about DILANTIN?"

DILANTIN may cause other serious side effects including:

 Softening of your bones (osteopenia, osteoporosis, osteomalacia). This can cause broken bones.

Call your healthcare provider right away, if you have any of the symptoms listed above.

The most common side effects of DILANTIN include:

- problems with walking and coordination
- slurred speech
- confusion
- dizziness
- trouble sleeping nervousness
- tremor
- headache
- nausea
- vomiting constipation
- rash

These are not all the possible side effects of DILANTIN. For more information, ask your healthcare provider or pharmacist

Call your doctor for medical advice about side effects. You

- Store DILANTIN INFATABS at room temperature between 68°F to 77°F (20°C to 25°C). Protect from moisture.
- Store DILANTIN Capsules at room temperature between 68°F to 77°F (20°C to 25°C) in tight, light-resistant containers. Protect from moisture

General information about DILANTIN

Know the medicines you take. Keep a list of them and show it Medicines are sometimes prescribed for purposes other than condition for which it was not prescribed. Do not give DILANTIN to other people, even if they have the same symptoms that you

information about DILANTIN. If you would like more information, Your healthcare provider may change your dose. Do not talk with your healthcare provider. You can ask your healthcare change your dose of DILANTIN without talking to your provider or pharmacist for information about DILANTIN that was written for healthcare professionals.

What are the ingredients in DILANTIN?

• Do not stop taking DILANTIN without first talking to your Each tablet is a yellow triangular scored chewable tablet.

Inactive ingredients: D & C vellow No. 10. A1 lake. FD&C vellow No. 6, flavor, saccharin sodium, confectioner's sugar, talc, magnesium stearate, and purified water.

medium orange cap has "PD" imprinted in black ink and the Do not drive, operate heavy machinery, or do other dangerous white, opaque body has "DILANTIN" over "100 mg" printed in

Active ingredient: 100 mg phenytoin sodium

Inactive ingredients: lactose monohydrate, confectioner's sugar, See "What is the most important information I should know talc, and magnesium stearate. The capsule body contains titanium dioxide and gelatin. The capsule cap contains FD&C red No. 28, FD&C yellow No. 6, and gelatin.

> Dilantin 30mg: Each capsule contains a white powder. The small pale pink opaque cap has "PD" imprinted in black ink and the white, opaque body has "Dilantin 30 mg" printed in black ink.

Active ingredient: 30 mg phenytoin sodium

Inactive ingredients: lactose monohydrate, confectioner's sugar, talc, and magnesium stearate. The capsule shell cap and body contain Titanium Dioxide (cap and body); gelatin (cap and body); D&C yellow No. 10 (cap); FD&C red No. 3 (cap).

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Patients, their caregivers, and families should be counseled that AEDs, including Dilantin Infatabs, may increase the risk of suicidal thoughts and behavior and should be advised of the need to be alert for the emergence or worsening of symptoms of depression, any unusual changes in mood or behavior, or the emergence of suicidal thoughts, behavior, or thoughts about self-harm. Behaviors of concern should be reported immediately to bettlemen a revider a revider of coarsening of facial features. Systemic lugus

Patients should be encouraged to enroll in the North American Antiepileptic Drug (NAAED) Pregnancy Registry if they become pregnant. This registry is collecting information about the safety of antiepileptic drugs during pregnancy. To enroll, patients can call the toll free number 1-888-233-2334 (see PRECAUTIONS: Pregnancy section).

Laboratory Tests: Phenytoin serum level determinations may be precessored. (NAAED) Pregnancy Registry if they become pregnant. This registry is collecting information about the safety of antiepileptic drugs during pregnancy. To enroll, patients can call the toll free number 1-888-233-2334 (see PRECAUTIONS: Pregnancy section).

Laboratory Tests: Phenytoin serum level determinations may be necessary to achieve optimal dosage adjustments. Phenytoin doses are usually selected to attain therapeutic plasma total phenytoin concentrations of 10 to 20 mcg/mL (unbound phenytoin concentrations of 10 to 20 mcg/mL (unbound phenytoin doses are usually selected to attain therapeutic plasma total phenytoin concentrations of 10 to 20 mcg/mL (unbound phenytoin doses are usually selected to attain therapeutic plasma total phenytoin concentrations of 10 to 20 mcg/mL (unbound phenytoin doses are usually selected to attain therapeutic plasma total phenytoin concentrations of 10 to 20 mcg/mL (unbound phenytoin doses are usually selected to attain therapeutic plasma total phenytoin concentrations of 10 to 20 mcg/mL (unbound phenytoin doses are usually selected to attain therapeutic plasma total phenytoin concentrations of 10 to 20 mcg/mL (unbound phenytoin doses are usually selected to attain therapeutic plasma total phenytoin developed the provided provided the provided provided the provided provided

prug Interactions: Phenytoin is extensively bound to serum plasma proteins and is prone to competitive displacement. Phenytoin is metabolized by hepatic cytochrome P450 enzymes CYP2C9 and CYP2C19, and is particularly susceptible to inhibitory drug interactions because it is subject to saturable metabolism. Inhibition of metabolism and enhance the risk of drug toxicity. Phenytoin is a potent inducer of hepatic drug-metabolizing enzymes. Serum level determinations for phenytoin concentrations and enhance determinations for phenytoin are especially helpful when possible drug interactions are suspected.

The most commonly occurring drug interactions are listed below:

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- rugs that arrect pnenytoin concentrations:

 Drugs that may increase phenytoin serum levels, include: acute alcohol intake, amiodarone, anti-epileptic agents (ethosuximide, felbamate, oxcarbazepine, methsuximide, topiramate), azoles (filuconazole, ketoconazole, itraconazole), capecitabine, chloramphenicol, chlordiazeppoxide, diazepam, disulfiram, estrogens, fluorouracil, fluoxetine, fluvastatin, fluvoxamine, H-antagonists (e.g. cimetidine), halothane, isoniazidi, methylohenidate, omeprazole, phenothiazines, salicylates, sertraline, succinimides, sulfonamides

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 Ned vithout for without bone marrow suppression. While the margine is acute alcohol intake, amiodarone, anti-epileptic agents, acute alcohol intake, amiodarone, anti-epileptic acute alcohol intake, and acute alcohol intake, and acute alcohol inta (e.g., sulfamethizole, sulfaphenazole, sulfadiazine, sulfamethoxazole-trimethoprim), ticlopidine, tolbutamide, trazodone, and warfarin.
- combination (e.g., bleomycin, carboplatin, cisplatin, doxorubicin, methotrexate), carbamazepine, chronic alcohol abuse, folic acid, fosamprenavir, nelfinavir, reserpine, ritonavir, St. John's Wort, sucralfate and vigabatrin.
- Drugs that may either increase or decrease phenytoin serum levels, include:
- Drugs affected by phenytoin:
- Drugs whose efficacy is impaired by phenytoin include: azoles, (fluconazole, ketoconazole, itraconazole, voriconazole, posaconazole), corticosteroids, doxycycline, estrogens, furosemide, irinotecan, oral contraceptives, paclitaxel, paroxetine, quinidine, rifampin, sertraline, teniposide, theophylline, and vitamin D.
- Increased and decreased PT/INR responses have been reported when phenytoin is

- blockade than expected, and infusion rate requirements may be higher.

agents may require adjustment of the close of the interpretation o

Drug/Laboratory Test Interactions: Phenytoin may decrease serum concentrations of T4. It may also produce lower than normal values for dexamethasone or metyrapone tests. Phenytoin may cause increased serum levels of glucose, alkaline phosphatase, and gamma glutamyl transpeptidase (GGT). Care should be taken when using immunoanalytical methods to measure plasma Dilantin Infatabs are supplied as:

Carcinogenesis: See WARNINGS section for information on carcinogenesis.

Pregnancy Category D: See WARNINGS section.

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To provide information regarding the effects of in utero exposure to Dilantin Infatabs, physicians are advised to recommend that pregnant patients taking Dilantin Infatabs enroll in the NAAED Pregnancy Registry. This can be done by calling the toll free number 1-888-233-2334, and must be done by patients themselves. Information on the registry can also be found at the website https://www.aedpregnancyregistry.org/. Nursing Mothers: Infant breast-feeding is not recommended for women taking this drug because phenytoin appears to be secreted in low concentrations in human milk.

Pediatric Use: See DOSAGE AND ADMINISTRATION section **Geriatric Use:** Phenytoin clearance tends to decrease with increasing age (see CLINICAL PHARMACOLOGY: Special Populations).

(Phenytoin Chewable Tablets LISP)

The most commonly occurring drug interactions are listed below:

Note: The list is not intended to be inclusive or comprehensive. Individual drug package inserts should be consulted.

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**Program of the list of the lis

The lethal dose in pediatric patients is not known. The lethal dose in adults is estimated ticlopidine, tolbutamide, trazodone, and warfarin.

Drugs that may decrease phenytoin levels, include: anticancer drugs usually in combination (e.g., bleomycin, carboplatin, cisplatin, doxorubicin, methotrexate), and the combination (e.g., bleomycin, carboplatin, cisplatin, doxorubicin, methotrexate), and the combination (e.g., bleomycin, carboplatin, cisplatin, doxorubicin, methotrexate).

Administration of phenytoin with preparations that increase gastric pH (e.g., supplements or antacids containing calcium carbonate, aluminum hydroxide, and magnesium hydroxide) may affect the absorption of phenytoin. In most cases where interactions were seen, the effect is a decrease in phenytoin levels when the drugs are taken at the same time. When possible, phenytoin and these products should not be taken at the same time of day.

The addition or withdrawal of these agents in patients on phenytoin therapy may require an adjustment of the phenytoin dose to achieve optimal clinical outcome.

In acute overdosage the possibility of other CNS depressants, including alcohol, should be borne in mind.

Drugs that should not be coadministered with phenytoin: Delavirdine (see CONTRAINDICATIONS).

Drugs that should not be coadministered with phenytoin: Delavirdine (see CONTRAINDICATIONS).

When given in equal doses, Dilantin Infatabs yield higher plasma levels than Dilantin Kapseals®. For this reason serum concentrations should be monitored and care should be taken when switching a patient from the sodium salt to the free acid form.

of phenytoin is used in Dilantin-125 Suspension and Dilantin Infatabs. Because there is approximately an 8% increase in drug content with the free acid form over that of the applickmately an 6% includes in drug chilent with the free action from the star of the sodium salt, dosage adjustments and serum level monitoring may be necessary when switching from a product formulated with the free acid to a product formulated with the sodium salt and vice versa.

saquinavir), anti-epileptic agents (felbamate, topiramate, oxcarbazepine, quetiapine), atorvastatin, cyclosporine, digoxin, fluvastatin, folic acid, mexiletine, nisoldipine, praziquantel, and simvastatin. Phenytoin when given with fosamprenavir alone may decrease the concentration of amprenavir, the active metabolite. Phenytoin when given with the combination of fosamprenavir and ritonavir may increase the concentration of amprenavir and ritonavir may increase the concentration of the neuromuscular blocking action of the nondecedarian

Install please the concentration of ahipteriaxin.

Instal

N 0071-0007-24-Bottle of 100. N 0071-0007-40-Unit dose (10/10's

Store at room temperature between 68°F to 77°F (20°C to 25°C).



Concentrations of 1 to 2 mog/mL).

A predominantly sensory peripheral polyneuropathy has been observed in patients

Phenytoin is extensively bound to serum plasma proteins and is receiving long-term phenytoin therapy.

There are marked variations among individuals with respect to phenytoin plasma levels

The adequacy of the respiratory and circulatory systems should be carefully observed Drugs that may either increase or decrease phenytoin serum levels, include: phenobarbital, sodium valproate, and valproate serum levels is unpredictable.

and appropriate supportive measures employed. Hemodialysis can be considered since on phenytoin is not completely bound to plasma proteins. Total exchange transfusion has been used in the treatment of severe intoxication in pediatric patients.

DOSAGE AND ADMINISTRATION

Dilantin® Kapseals® is formulated with the sodium salt of phenytoin. The free acid form

Dosing in Special Populations The addition or withdrawal of phenytoin during concomitant therapy with these agents may require adjustment of the dose of these agents to achieve optimal clinical outcome.

Dusting in special repurations

Patients with Renal or Hepatic Disease: Due to an increased fraction of unbound phenytoin in patients with renal or hepatic disease, or in those with hypoalbuminemia, the interpretation of total phenytoin plasma concentrations should be made with caution.

Reference ID: 3462008

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/s/
CHI-ANN Y WU 02/27/2014 For Wm. Peter Rickman