MercuryPharma

Package leaflet: Information for the patient

Phenytoin Sodium 50mg/ml Solution for Injection

(Phenytoin sodium)

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.
- You may have been given Phenytoin Injection as a single dose to control seizures in an emergency (status epilepticus). In this case, you will only be able to read this leaflet after you have had the product given to you. Your doctor will have considered the important safety information in this leaflet, but your urgent need for treatment may have been more important than some of the normal cautions. Check them now, especially if you are going to continue to be given Phenytoin Injection (or any other form of phenytoin).

The name of your medicine is Phenytoin Sodium 50mg/ml Solution for Injection. It will be referred to as Phenytoin Injection for ease hereafter.

What is in this leaflet

1. WHAT PHENYTOIN INJECTION IS AND WHAT IT IS USED FOR

Phenytoin belongs to a group of drugs known as hydantoins. It is called an anticonvulsant because it works by controlling the overactivity in the brain that can cause epilepsy or seizures (fits).
Phenytoin Injection is used to:
- control epileptic fits involving jerking and spasm of the muscles (known as grand mal fits)
- prevent and treat fits resulting from brain surgery or head injury.

You should consult your doctor if you are unsure why you have been given Phenytoin Injection if you do not feel better or if you feel worse.

2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN PHENYTOIN INJECTION

Do not use Phenytoin Injection:
- if you are allergic to phenytoin or any of the other ingredients of this medicine (listed in section 6) or to any other hydantoin drug (such as ethotoin or methoin)
- if you have a slow heart beat or heart problems that interfere with the rate at which your heart beats
- if you are allergic to other medicines for epilepsy
- if you are also taking delavirdine (used for HIV therapy)
- if you suffer from certain conditions that affect the heart rhythm for example a decreased heart rate (sinus bradycardia), heart block (sinoatrial block or A-V block) or Adams-Stokes syndrome.

Make sure your doctor knows if you suffer from any of the above before you are given the injection.

Warnings and precautions
Talk to your doctor or nurse before you are given Phenytoin Injection if you suffer from or have suffered in the past from any of the following conditions:
- low blood pressure or heart failure
- disease of the liver or kidneys
- diabetes
- porphyria (an inherited condition affecting the nervous system and skin, characterised by abdominal pain, vomiting or muscle weakness)
- if you have drunk a large amount of alcohol recently or if you drink large amounts of alcohol regularly or if you have alcohol dependence
- potentially life-threatening skin rashes (Stevens-Johnson syndrome, toxic epidermal necrolysis) have been reported with the use of Phenytoin sodium, appearing initially as reddish target-like spots or circular patches often with central blisters on the trunk. Additional signs to look for include ulcers in the mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes). These potentially life-threatening skin rashes are often accompanied by flu-like symptoms. The rash may progress to widespread blistering or peeling of the skin. The highest risk for occurrence of serious skin reactions is within the first weeks of treatment
- if you have developed Stevens-Johnson syndrome or toxic epidermal necrolysis with the use of Phenytoin sodium, you must not be re-started on Phenytoin sodium at any time
- heart rhythm problems
- if you develop a rash or these skin symptoms, stop taking Phenytoin Injection, seek immediate advice from a doctor and tell that you are taking this medicine. Consult your doctor before discontinuing Phenytoin Injection. If you suddenly stop using this medicine you may have a seizure.

The risk of these serious skin side effects may be associated with a variant in genes in a subject with Chinese or Thai origin. If you are of such origin and have been tested previously carrying this genetic variant (HLA-B*1502), discuss this with your doctor before using Phenytoin Injection.

Black patients may be at greater risk of liver problems, serious skin reactions and allergic reactions.

If you are taking phenytoin at the same time as you receive radiation therapy to your head and the dose of another medication called corticosteroids is reduced, you may more likely to develop a severe skin rash called erythema multiform or one that causes blistering called Stevens Johnson Syndrome or Toxic Epidermal Necrosis (see Possible Side Effects in section 4).

A small number of people being treated with anti-epileptics such as Phenytoin have had thoughts of harming or killing themselves, if at any time you have these thoughts, immediately contact your doctor.

Tell your doctor if any of these apply to you as special care may be needed. Your doctor will take particular care with this medicine if you are elderly or gravely ill.

Phenytoin may precipitate or aggravate absence seizures and myoclonic seizures (two specific types of epilepsy).

Other medicines and Phenytoin Injection
Tell your doctor if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription.
This will allow your doctor to decide whether it is safe for you to be given phenytoin.

Some medicines can affect the way Phenytoin Injection works or Phenytoin Injection itself can reduce the effectiveness of other medicines taken at the same time. These include:
- medicines used for epilepsy or fits (e.g. carbamazepine, lamotrigine, phenobarbital, sodium valproate and valproic acid, topiramate, oxcarbazepine, succinimides including ethosuximide and vigabatrin)
- corticosteroids e.g. prednisolone (used in numerous situations to aid the body's healing process)
- medicines used to treat fungal infections (e.g. amphotericin B, fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole and miconazole)
- medicines used to treat skin diseases (e.g. methoxsalen)
- medicines used for tuberculosis and other infections (e.g. chloramphenicol, isoniazid, rifampicin, sulphonamides, sulfadiazine, sulfamethizole, sulfamethoxazole-trimethoprim, sulfaphenazole, sulfisoxazole, doxycycline and ciprofloxacin)
- medicines used for asthma and bronchitis (e.g. theophylline)
- medicines used for diabetes (e.g. tolbutamide)
- medicines used for high blood pressure (e.g. calcium channel blockers like diltiazem, felodipine)
- medicines used for pain and inflammation (e.g. phenylbutazone, salicylates, including aspirin and steroids)
- medicines used for stomach ulcers and heartburn (e.g. omeprazole, sucralfate, the medicines known as H_2 antagonists e.g. cimetidine, ranitidine, famotidine and some antacids)
- medicines used for sleeplessness, depression and psychiatric disorders (e.g. chlordiazepoxide, clozapine, diazepam, disulfiram, lithium, methadone, fluoxetine, fluvoxamine, sertraline, haloperidol, levodopa, paroxetine, methylphenidate, phenothiazines, quetiapine, trazodone, reserpine, tricyclic antidepressants and viloxazine)
- medicines used for cancer (e.g. antineoplastic agents like teniposide, fluorouracil, capecitabine, bleomycin, carboplatin, cisplatin, doxorubicin and methotrexate)
- medicines used for organ and tissue transplants, to prevent rejection (e.g.ciclosporin, tacrolimus)
- medicines used for heart and circulation problems (e.g. dicoumarol, amiodarone,digitoxin, digoxin, nisoldipine, disopyramide, mexiletine, furosemide and quinidine , reserpine, warfarin and calcium channel blockers including diltiazem and nifedipine)
- hormone replacement therapies (oestrogens) and oral contraceptives (the birth control pill)
- medicines used to lower high blood cholesterol and triglycerides (e.g. atorvastatin, fluvastatin, simvastatin)
- medicines used in the treatment of HIV infection (e.g. delavirdine, efavirenz, fosamprenavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir)
- medicines used to expel parasitic worms from the body (e.g. albendazole, praziquantel)
- medicines used to treat thyroid disorders (e.g. thyroxine)
- some medicines used in operations, e.g. halothane, methadone (an anaesthetic) and neuromuscular blockers (used to relax muscles e.g. pancuronium, vecuronium, rocuronium and cisatracurium)
- some products available without a prescription (e.g. folic acid, vitamin D) Blood test may be necessary every six months to monitor the amount of folic acid in the blood
- the herbal remedy St. John's wort (*Hypericum perforatum*) should not be taken at the same time as this medicine. If you have already taken St. John's wort, consult your doctor before stopping St. John's wort preparations
- anticoagulants, e.g. warfarin (as its effect may be enhanced by phenytoin)
- Phenytoin injection may also interfere with certain laboratory tests that you may be given.

Phenytoin Injection with food, drink and alcohol
Speak to your doctor before being given this medicine if you have recently had a drink of alcohol.
Drinking a lot of alcohol can also affect the concentration of Phenytoin in your blood.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before taking this medicine.
If you do get pregnant while you are taking Phenytoin Injection, you must tell your doctor straight away. It is important that your epilepsy remains well controlled, but, as with other anti-epilepsy treatments, there is a risk of harm to the foetus.
Make sure you are very clear about the risks and benefits of taking Phenytoin Injection.
Do not stop taking Phenytoin Injection until you have seen your doctor as it is important to control your fits. If given during pregnancy phenytoin may affect the baby but your doctor may decide that it is very important that you continue with phenytoin. He or she will explain the risks to you.
As phenytoin is released into breast milk, you should not breast-feed if you are being given this medicine.

continued overleaf

Driving and using machines
Phenytoin Injection may cause dizziness or drowsiness. If you experience these symptoms, do not drive or use any tools or machinery.
Ask your doctor for advice before taking any medicine.

Phenytoin Injection contains ethanol and sodium
This medicinal product contains less than 1 mmol sodium (23mg) per dose, i.e. essentially 'sodium- free'.
This medicinal product contains 10 % vol ethanol (alcohol), i.e. up to 395.75 mg per dose, equivalent to 7.9ml beer, 3.2ml wine per dose.
Harmful for those suffering from alcoholism. To be taken into account in pregnant or breast-feeding women, children and high-risk groups such as patients with liver disease or epilepsy.

3. HOW PHENYTOIN INJECTION IS GIVEN TO YOU

Phenytoin Injection is given by a doctor or nurse. It may be given as an injection slowly into a muscle or a large vein. Alternatively, it may be diluted and given as a drip or infusion into one of your large veins (intravenously). When given as an intravenous infusion, Phenytoin Injection must be diluted with normal saline. Intramuscular or intravenous Phenytoin Injection should not be added to dextrose or dextrose-containing solutions as this could interfere with the dose of this medicine.
The correct dose will be calculated by your doctor according to your body weight and will be written as the equivalent dose of phenytoin sodium (PE). The dose will be as mg per dose if given as an injection or mg per ml of solution if given as an infusion (drip). A repeat injection may be given after 30 minutes if necessary.
During your treatment your doctor may monitor your blood levels of phenytoin by taking regular blood samples. Sometimes it is necessary to give Phenytoin Injection into your muscle if you cannot continue to take it by mouth. This is not normally continued for longer than one week. When switching from oral Phenytoin to intramuscular injection, the dose needs to be increased by approximately 50%. When switching back to oral Phenytoin, the dose should be reduced to half the original oral dose for the same period of time that the intramuscular injection was given. This is because phenytoin continues to be released from your muscles for some time after the injections have been given.
The recommended dose is as follows:

Adults
Severe epileptic seizure or fits (Status Epilepticus)
A dose of 10 to 15 mg per kg of body weight is given intravenously at a rate not exceeding 50 mg per minute in adults. This is followed by more Phenytoin Injection given every 6 to 8 hours either by injection or by mouth.
If Phenytoin Injection does not stop your seizures, other treatments will be tried.

Neurosurgery
A dose of 100 to 200 mg may be given into your muscle (intramuscularly) approximately every 4 hours during surgery and for two to three days afterwards to prevent seizures. This dosage may then be reduced to a maintenance dose of 300 mg daily and adjusted according to your blood levels.

Elderly
Lower or less frequent dosing may be needed in some elderly patients due to decreased clearance of Phenytoin Injection. Your doctor may not need to change your dose, but side effects can occur more often in the elderly.

Kidney or liver problems
Make sure your doctor knows if you have liver or kidney problems as you may need your dose adjusted.

Use in children and adolescents
No dosage adjustment is required, but children tend to breakdown the medicine faster than adults and this may mean that your doctor has to change the number or timing of the Phenytoin Injection doses.

Use in neonates (Very young babies)
The starting dose is usually 15 to 20 mg per kg of baby weight. Intravenous Phenytoin Injection should not be given to neonates at a rate faster than 1 to 3 mg per kg body weight per minute. Intravenous Phenytoin Injection is more reliably absorbed than oral Phenytoin in very young babies.

If you think you have been given more Phenytoin Injection than you should have
Tell your doctor immediately.
Phenytoin Injection is dangerous in overdose. The initial signs are nystagmus (condition of involuntary eye movement), diplopia (double vision), ataxia (the loss of full control of bodily movements) and dysarthria (motor speech disorder). Other signs are tremor, hyperflexia (muscle spasms), lethargy, nausea, vomiting. The patient may become comatose and hypotensive. Death is due to respiratory and circulatory depression.

If you think you have missed a dose of Phenytoin Injection
If you think that you may have missed a dose, tell your doctor immediately.
If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side-effects, although not everybody gets them.

Important: If you experience any of the following serious side effects contact your doctor <u>immediately.</u>
- sudden wheeziness, difficulty in breathing, swelling of eyelids, face or lips, rash or itching (especially affecting the whole body). There is a higher incidence of this in black patients
- if you experience skin discolouration, swelling and pain where the injection was given which then starts to spread down your arm to your hands and fingers. This may mean you have a condition known as Purple Glove Syndrome. In most cases this will improve on its own but in some cases it can be serious and require urgent medical treatment
- if you develop potentially life-threatening skin rashes that causes blistering (this can affect the mouth and tongue). These may be signs of a condition known as Stevens Johnson Syndrome or toxic epidermal necrolysis (TEN). These have been reported very rarely
- if you notice bruising, fever, you are looking pale or you have a severe sore throat. These may be the first signs of an abnormality of the blood, including decrease in the number of red blood cells, white cells or platelets. Your doctor may take regular blood samples to test for these effects
- skin rash, fever, swollen glands, increase in a type of white blood cell (eosinophilia) and inflammation of internal organs (liver, lungs, heart, kidneys and large intestine), you may also experience pain and inflammation of the joints, these may be signs of a hypersensitivity reaction (e.g. drug reaction or rash with Eosinophilia and Systemic Symptoms (DRESS)) or be related to a condition called systemic lupus erythematosus (SLE)
- if you experience confusion or have a severe mental illness, as this may be a sign that you have high amounts of phenytoin in your blood. On rare occasions, when the amount of the phenytoin in the blood remains high, irreversible brain injury has occurred. Your doctor may test your blood to see how much phenytoin is in the blood and may change your dose.

Other side effects that may occur are as below:
Not known: frequency cannot be estimated from the available data
- **effects on your nervous system:** unusual eye movements, unsteadiness, difficulty in controlling movements, shaking, abnormal or uncoordinated movements, slurred speech, confusion, pins and needles or numbness, drowsiness, dizziness, vertigo, sleeplessness, nervousness, twitching muscles, headaches and change in taste
- **effects on your skin:** skin rash including measles-like rash which is usually mild
- **effects on your stomach and intestines:** feeling sick, being sick and constipation
- **effects on your blood and lymph system:** swelling of the lymph glands
- **effects on your liver and kidney:** inflammation of the kidneys and liver, liver damage or liver failure which can lead to death (seen as yellowing of the skin and whites of the eye), abnormal liver function
- **effects on your reproductive system and breasts:** changes in the shape of the penis, painful erection
- **effects on your hands, face and body:** changes in the hands with difficulty in straightening the fingers, changes in facial features, enlarged lips or gums, increased or abnormal body or facial hair
- **effects on medical tests:** abnormal thyroid function tests
- **effects on your respiratory system:** problems breathing including complete stopping of breathing, inflammation of the lining of the lung
- **effects on your immune system:** problems with the body's defense against infection, inflammation of the wall of the arteries
- **effect on your heart and circulation:** low blood pressure, enlargement of blood vessels. Your blood pressure may also be lowered and experience heart rhythm problems when Phenytoin Injection is injected into your vein too quickly
- **effects on your bones:** there have been reports of bone disorders including osteopenia and osteoporosis (thinning of the bone) and fractures. Check with your doctor if you are on long-term antiepileptic medication, have a history of osteoporosis or take steroids
- **effects on injection site:** Intramuscular phenytoin administration may cause pain, tenderness, dying or sloughing of skin cells and formation of an infection at the injection site.

Please see your doctor if you notice any of these side effects and they cause you concern or if you notice any side effects not listed in this leaflet.

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects, you can help to provide more information on the safety of this medicine.

5. HOW TO STORE PHENYTOIN INJECTION

Keep this medicine out of the sight and reach of children.
This medicine should not be used after the expiry date which is stated on the ampoule (a small bottle) label and carton, after EXP. The expiry date refers to the last day of that month.
The ampoules should be protected from light and stored at a temperature not greater than 30°C.
If only part of the contents of an ampoule is used, the remaining solution should be discarded.
Solutions in which a haziness or precipitate develops should not be used.
The solution should not be mixed with any other drugs.
Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Phenytoin Injection contains
The active substance is phenytoin sodium. Each 1ml of this solution contains 50mg of phenytoin sodium.
The other ingredients are propylene glycol BP, ethanol BP and sodium hydroxide BP (as a 10% w/v solution) in water for injections BP.
What Phenytoin Injection looks like and contents of pack
Phenytoin Injection is a clear, colourless, particle-free solution. Each carton contains ten 5ml ampoules of Phenytoin Injection.
Marketing Authorisation Holder
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