

## **Package leaflet: Information for the patient**

### **Phenytoin 250 mg/5 ml solution for injection or infusion**

Phenytoin sodium

**Read all of this leaflet carefully before you are given 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, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. 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).

#### **What is in this leaflet:**

1. What Phenytoin injection is and what it is used for
2. What you need to know before you are given Phenytoin injection
3. How Phenytoin injection is given
4. Possible side effects
5. How to store Phenytoin injection
6. Contents of the pack and other information

#### **1. What Phenytoin injection is and what it is used for**

This medicine is a solution for injection or infusion containing phenytoin, which belongs to a group of medicines called antiepileptic medicines.

Phenytoin injection can be used to treat severe epileptic seizures or fits (status epilepticus). It can also be used to control or prevent seizures during or after brain surgery and/or severe head injury. Phenytoin injection is also used to control or prevent seizures for short periods of time when antiepileptic medicinal products cannot be taken by mouth.

Phenytoin injection can also be used to treat specific heart rhythm problems (cardiac arrhythmias) when these are caused by the medicine digoxin, or when these do not respond well to treatment with other medicines, or when other treatments cannot be used.

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 take Phenytoin injection**

- If you are allergic (hypersensitive) to phenytoin, or any of the other ingredients of this medicine (listed in section 6).
- If you are allergic to other medicines for epilepsy.
- 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- Stoke Syndrome.

- If you are taking medicines for HIV infection such as delavridine.

### **Warnings and precautions**

Talk to your doctor, pharmacist 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
- Liver disease where the dosage may need to be adjusted
- Kidney disease
- Diabetes
- Porphyria (an inherited disease that affects haemoglobin biosynthesis)
- Heart rhythm problems (Phenytoin injection can treat some rhythm problems, but can make others worse)
- Alcohol dependence.

You should be administered Phenytoin injection with caution if you suffer from kidney or liver problems.

A small number of people being treated with antiepileptics such as phenytoin sodium have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor.

Potentially life-threatening skin rashes (Stevens Johnson syndrome, toxic epidermal necrolysis) have been reported with the use of phenytoin, 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 injection, you must not be re-started on phenytoin injection at any time.

If you develop a rash or these skin symptoms, stop taking Phenytoin injection, seek urgent advice from a doctor and tell him that you are taking this medicine. Consult your doctor before discontinuing Phenytoin injection. If you suddenly stop taking this medicine you may have a seizure.

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).

### **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.

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 heart and circulation problems (e.g. dicoumarol, amiodarone, reserpine, digitoxin, digoxin, mexiletine, nisoldipine, furosemide, quinidine, warfarin and calcium channel blockers including diltiazem and nifedipine)
- Medicines used for epilepsy (e.g. carbamazepine, lamotrigine, phenobarbital, sodium valproate, valproic acid, oxcarbazepine, topiramate, succinimides including ethosuximide, and vigabatrin)
- Medicines used to treat fungal infections (e.g. amphotericin B, fluconazole, itraconazole, ketoconazole, posaconazole, voriconazole, miconazole)

- Medicines used for tuberculosis and other infections (e.g. chloramphenicol, isoniazid, rifampicin, sulfonamides, sulfadiazine, sulfamethizole, sulfamethoxazole-trimethoprim, sulfaphenazole, sulfisoxazole, doxycycline, ciprofloxacin)
- Medicines used for stomach ulcers (e.g. omeprazole, sucralfate and the medicines known as H2 antagonists including cimetidine, ranitidine, famotidine and some antacids)
- Medicines used for asthma and bronchitis (e.g. theophylline)
- Medicines used for pain and inflammation (e.g. phenylbutazone, propoxyphene, salicylates including aspirin and steroids)
- Medicines used for sleeplessness, depression and psychiatric disorders (e.g. chlordiazepoxide, clozapine, diazepam, disulfiram, fluoxetine, methylphenidate, paroxetine, phenothiazines, quetiapine, trazodone, tricyclic antidepressants, fluvoxamine, sertraline and viloxazine)
- Medicines used for diabetes (e.g. tolbutamide)
- Some hormone replacement therapies (oestrogens), oral contraceptives (the birth control pill)
- Medicines used for organ and tissue transplants, to prevent rejection (e.g. ciclosporin, tacrolimus)
- Medicines used for cancer (e.g. antineoplastic agents including teniposide, fluorouracil, capecitabine, bleomycin, carboplatin, cisplatin, doxorubicin, methotrexate)
- 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)
- Muscle relaxants used for surgery (neuromuscular blockers), some anaesthetic medicines (halothane) and methadone
- Some products available without a prescription (folic acid, vitamin D).

Your doctor may need to test the amount of phenytoin in your blood to help decide if any of these medicinal products are affecting your treatment.

The herbal preparation St John's wort (*Hypericum perforatum*) should **not** be taken at the same time as this medicine. If you already take St John's wort, consult your doctor before stopping the St John's wort preparation.

Phenytoin injection may also interfere with certain laboratory tests that you may be given.

### **Phenytoin injection with drinking alcohol**

Drinking a lot of alcohol can also affect the concentration of phenytoin in your blood.

### **Pregnancy and Breast-feeding**

If you are or think you may be pregnant or are planning to become pregnant, whilst having phenytoin, your doctor will decide if you should continue with this medicine or whether another would be more suitable during your pregnancy.

Do not stop taking phenytoin 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. . Make sure you are very clear about the risks and benefits of taking Epanutin RMP.  
As phenytoin is released into breast milk, you should not breast-feed if you are taking this medicine.

### **Children**

Phenytoin is used for newborns, infants and children.

Ask your doctor or pharmacist for advice before taking any medicine.

### **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 and contact your doctor.

### **Phenytoin injection contains ethanol, sodium and propylene glycol**

This medicinal product contains 10 vol % ethanol (alcohol), i.e. up to 406 mg per ampoule, equivalent to 10 ml beer, 4.17 ml wine per ampoule.

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.

This medicinal product contains less than 1 mmol sodium (23 mg) per ampoule, i.e. essentially 'sodium-free'.

This medicinal product contains propylene glycol which may cause alcohol-like symptoms.

## **3. How Phenytoin injection is given**

You will be in hospital when you are given Phenytoin injection.

Phenytoin injection will be either injected into one of your large veins (intravenously) or into your muscle (intramuscularly). When given intravenously, Phenytoin injection must be diluted.

The dose and concentration of the solution of Phenytoin injection you are given will be decided by your doctor 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).

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.

### **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 given every 6 to 8 hours either by injection or by mouth.

If phenytoin does not stop your seizures, other treatments will be tried.

#### **Cardiac arrhythmias (variations to normal heartbeat)**

A dose of 3.5 to 5 mg per kg of body weight is given intravenously, at a rate not exceeding 50 mg per minute. This may be repeated a second time.

### **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**

Due to decreased clearance of Epanutin, lower or less frequent dosing may be needed. The dose of Epanutin for elderly patients who may be taking other medicines may also need careful consideration and adjustment by their doctor.

### **Kidney or liver problems**

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

### **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 doses.

### **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 is more reliably absorbed than oral phenytoin in very young babies.

### **If you are given more Phenytoin injection than you should**

Phenytoin is dangerous in overdose. If you think you have been given too much phenytoin, contact your doctor immediately.

If you have any further questions on how to take this product, ask your doctor, pharmacist or nurse.

## **4. Possible side-effects**

Like all medicines, Phenytoin injection can cause side-effects although not everybody gets them.

Tell your doctor **immediately** if you experience any of the following symptoms after being given this medicine.

- 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 decreases 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. medicine 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:**

- **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).
- **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:** Increased levels of blood sugar, or decreased levels of blood calcium, phosphates, folic acid and vitamin D.
- **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 defence against infection, inflammation of the wall of the arteries and immunoglobulin abnormalities.
- **Effect on your heart and circulation:** low blood pressure, enlargement of blood vessels. Your blood pressure may also be lowered and experience heart 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 or pharmacist 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, dying or sloughing of skin cells, and formation of an infection at the injection site.
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- **Endocrine disorders:** There have been reports of secondary hyperparathyroidism associated with phenytoin use.

**Reporting of side effects**

If you get any side effects, talk to your doctor or pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via

HPRA Pharmacovigilance  
Earlsfort Terrace  
IRL - Dublin 2  
Tel: +353 1 6764971  
Fax: +353 1 6762517  
Website: www.hpra.ie  
e-mail: medsafety@hpra.ie.

By reporting side effects you can help 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.

The pharmacist will ensure that your medicine is not stored above 25°C, or used after the expiry date which is stamped on the pack. The expiry date refers to the last day of that month. The pharmacist will also ensure that Phenytoin injection is kept in the original package.

The medicine should be used immediately, once opened and discard any unused contents.

## **6. Contents of the pack and other information**

### **What Phenytoin injection 250 mg/5 ml Solution for injection or infusion contains**

Each 5 ml ampoule contains 250 mg of the active substance phenytoin sodium i.e. 50 mg/ml.

The other ingredients are propylene glycol, ethanol (alcohol), sodium hydroxide (for pH-adjustment) and water for injection.

### **What Phenytoin injection looks like and contents of the pack**

Phenytoin injection 250 mg/5 ml solution is available in glass ampoule, is packed in a polystyrene tray or pvc/paper blister within a carton, together with a patient information leaflet.

Pack sizes

1 x 5 ml

5 x 5 ml

10 x 5 ml

Not all pack sizes may be marketed.

## **Marketing Authorisation Holder and Manufacturer**

### **Marketing Authorisation Holder**

Accord Healthcare Ireland Ltd,  
Euro House,  
Euro Business Park,  
Little Island,  
Cork T45 K857,  
Ireland

### **Manufacturer**

Accord Healthcare Limited

Sage House, 319 Pinner Road,  
North Harrow, Middlesex, HA1 4HF,  
United Kingdom

Or

**Wessling Hungary Kft**  
Fõti út 56., Budapest 1047,  
Hungary

**This medicinal product is authorised in the Member States of the EEA under the following names:**

<b>Name of the Member State</b>	<b>Name of the medicinal product</b>
Italy	Fenitoina Accord
Ireland	Phenytoin 250 mg/5 ml solution for injection/infusion
Romania	Fenitoină sodică Accord 50 mg/ml soluție injectabilă/perfuzabilă
United Kingdom	Phenytoin Accord 50 mg/ml solution for injection/infusion

**This leaflet was last revised in 03/2019.**

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The following information is intended for healthcare professionals only:

Practical information on the preparation/handling of the medicinal product is provided here.

**Intra-arterial administration must be avoided in view of the high pH of the preparation.**

**Incompatibilities**

Phenytoin injection should not be mixed with other medicinal products because of precipitation of phenytoin acid.

**Instructions for use and handling**

For single use only. Once opened, use immediately and discard any unused contents.

Parenteral medicinal products should be inspected visually for particulate matter and discolouration prior to administration, whenever solution and container permit. Parenteral Phenytoin injection is suitable for use as long as it remains free of haziness and precipitate.

For infusion administration the parenteral phenytoin should be diluted in 50-100 ml of normal saline, with the final concentration of phenytoin in the solution not exceeding 10 mg/ml. Administration should commence immediately after the mixture has been prepared and must be completed within one hour (the infusion mixture should not be refrigerated). An in-line filter (0.22-0.50 microns) should be used. The diluted form is suitable for use as long as it remains free of haziness and precipitate.