Phenytoin Injection BP

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet:
1. What Phenytoin Injection is and what it is used for
2. Before Phenytoin Injection is used
3. How Phenytoin Injection is used
4. Possible side effects
5. How Phenytoin Injection is stored
6. Further information

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

Phenytoin is one of a group of medicines called hydantoins.

Phenytoin Injection is a medicine which is used to control status epilepticus (serious condition in which seizures (fits) continue for hours or days) or to prevent fits during or after neurosurgery. It can also be used to correct some heart rhythm abnormalities.

2. BEFORE PHENYTOIN INJECTION IS USED

Phenytoin Injection should not be used
- if you have shown signs of hypersensitivity (severe allergy) to phenytoin, any of the ingredients of phenytoin Injection, or medicines of the same class (hydantoins) in the past
- in patients with certain heart conditions

If possible, tell your doctor if any of the above applies to you before this medicine is used.

This medicine must not be injected into an artery. See section 3 for the correct method of administration.

Take special care with Phenytoin Injection
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.

Serious skin side effects can rarely occur during treatment with Phenytoin Injection. This risk may be associated with a variant in genes in a subject of Chinese or Thai
origin. If you are of such origin and have been tested positively carrying this genetic variant (HLA-B*1502), discuss this with your doctor before taking Phenytoin Injection. Some evidence suggests that black patients are also at increased risk of these reactions. In the Caucasian and Japanese population frequency of the genetic variant (HLA-B*1502) is extremely low therefore risk of developing serious skin side effects cannot be concluded.

A combination of phenytoin, radiation therapy to the head and gradual reduction in treatment with corticosteroids may also be associated with the development of serious skin side effects.

Irritation and swelling can occur at and around the site of injection with phenytoin. Build up of fluid beneath the skin, change in colour of the skin and pain may also occur following peripheral intravenous phenytoin injection.

In rare cases, patients taking phenytoin have experienced problems with their internal organs. Outward signs include fever, rash and swollen lymph nodes (isolated small raised lumps under the skin) within 2-12 weeks of beginning treatment. The risk may be increased in black patients, patients who have a family history of or who have experienced these problems in the past and those with decreased ability to fight infections (also known as immunosuppression).

**Special care needs to be taken with Phenytoin Injection**

- if you have a liver or kidney disorder
- if you suffer from diabetes
- if you suffer from low blood pressure
- if you suffer from heart problems
- if you have a condition called prophyria

If possible, tell your doctor if any of the above applies to you before this medicine is used.

**Taking/using other medicines**

Special care is needed if you are taking/using other medicines as some could interact with phenytoin, for example:

- some antibacterials e.g. doxycycline, ciprofloxacin, chloramphenicol, isoniazid, rifampicin, and other sulphonamides
- some antifungals i.e. amphotericin B, ketoconazole, fluconazole, miconazole and itraconazole
- some coumarin anticoagulants, e.g. warfarin and dicoumarol
- medicines used to control diabetes e.g. insulin or oral anti-diabetic agents (eg tolbutamide)
- some pain killers and anti-inflammatory medicines, i.e. phenylbutazone and salicylates such as aspirin
- some medicines used to control anxiety, e.g. chlordiazepoxide, diazepam
- barbiturates, e.g. phenobarbitalone and amylobarbitone
- corticosteroids (used in numerous situations to aid the body’s healing process)
• some medicines used to treat mental problems such as psychoses and depression, e.g. haloperidol, methylphenidate, monoamine oxidase inhibitors, trazodone, thioxanthenes, fluoxetine, fluvozamine, sertraline and tricyclic antidepressants
• oral contraceptives and other medicines which mimic female hormones, e.g. oestrogen and ethinyloestradiol
• antiepileptic medicines, e.g. carbamazepine, ethosuximide, mephenytoin, primidone, sodium valproate, sulphaine, valproic acid, oxcarbazepine and trimethadione
• halothane (an inhaled general anaesthetic)
• some anti-ulcer medicines, e.g. cimetidine and ranitidine
• medicines taken to help the heart, i.e. aspirin, beta-blockers, diazoxide, digoxin, diltiazem, disopyramide, dopamine, frusemide, mexiletine, nifedipine, quinidine, reserpine, amiodarone and verapamil
• medicines often taken while undergoing cancer treatment, i.e. bleomycin, calcium folinate, carboplatin, carmustine, cisplatin, dacarbazine, fluorouracil and vinblastine
• St John’s wort - The herbal remedy 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 preparations
• nelfinavir, used in the treatment of HIV
• others which you may recognise by name: ciclosporin, disulfiram, folic acid, L-dopa, lignocaine, succinimide, viloxazine, theophylline (a xanthine), methotrexate, omeprazole, ticagrelor and vitamin D

If possible, please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

**Phenytoin and alcohol consumption**
The consumption of alcohol, whilst you are being treated with phenytoin can reduce the effectiveness of treatment or increase the side effects.

**Pregnancy and breast-feeding**
This medicine can have negative effects on unborn children and the injectable form will only be used if the baby is at risk from the mother’s convulsions (eg in status epilepticus). Tell your doctor if you are pregnant, trying to become pregnant or breast-feeding. Your doctor will only use this medicine if the expected benefits outweigh any potential risk to your baby.

**Children**
Phenytoin is used for newborns, infants and children.

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

**Driving and using machines**
Do not drive or use machines if you experience any side effect (e.g. dizziness or drowsiness) which may lessen your ability to do so.
Important information about some of the ingredients of Phenytoin Injection
This medicinal product contains 10% vol ethanol (alcohol), i.e. up to 1.6 g per 1 g
dose of phenytoin, equivalent to 57 ml of a 3.5% vol beer or 14 ml of a 14% vol wine.
Harmful to 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.

In addition, this medicinal product contains propylene glycol, which can cause
alcohol-like symptoms and sodium (1.1 mmol per 5 ml ampoule).

3. HOW PHENYTOIN INJECTION IS USED

This medicine will be given to you by a slow injection via a drip into a vein or, more
rarely, via an injection into a muscle.

**Dose**
Your doctor will calculate the correct does of phenytoin for you.

The dose will depend upon your medical condition, your size, your age and how well
your kidneys, liver and heart are working.  Your doctor will tell how well your liver
and kidneys are working from blood and urine samples.

Where treatment is prolonged, blood samples may be taken to check the level of
phenytoin in the blood.  Subsequent doses may be increased or decreased accordingly.

**If you are given too much or too little Phenytoin Injection**
As this medicine will be given to you whilst you are in hospital it is unlikely that you
will be given too little or too much, however tell your doctor or pharmacist if you
have any concerns.

**Effects when treatment with phenytoin is stopped**
Sudden withdrawal of phenytoin treatment in patients susceptible to fits may cause
status epilepticus. In such cases, phenytoin dosage reduction should be gradual,
perhaps following a switch to a form of phenytoin which can be taken by mouth.

4. POSSIBLE SIDE EFFECTS

Like all medicines, phenytoin can cause side effects, although not everybody gets
them.

**If any of the following happen, tell your doctor immediately:**
- **severe allergic reaction** - you may experience a sudden itchy rash (hives),
  swelling of the hands, feet, ankles, face, lips, mouth or throat (which may
  cause difficulty in swallowing or breathing), and you may feel you are going
to faint
- **rash** (can be severe resulting in painful reddening and blistering of the skin,
  eyes, inside of the mouth and ano-genital region and may lead to skin
  shedding)
- **swollen lymph nodes** (isolated small raised lumps under the skin)
- **chest pains and palpitations**
These are serious side effects. You may need urgent medical attention.

**If any of the following happen, tell your doctor as soon as possible:**

- pain and inflammation at the injection site (in rare instances severe tissue damage has required amputation), some discolouration and pain above the injection site, known as “Purple Glove syndrome” can occur
- tightness of the chest or wheezing
- dizziness/fainting/vertigo
- fever
- persistent pain, tingling or numbness
- contraction of the fingers (bending in to the palm) (Dupuytren’s contracture)
- slurred speech
- muscle twitching and/or rapid uncontrollable eye movements
- fits or seizures
- difficulties associated with muscular movement: loss of muscle co-ordination, clumsiness or unsteadiness, shaking and loss of muscle tone
- bleeding, tender or enlarged gums (may be reduced by maintaining good oral hygiene and massaging the gums)
- joint pain
- yellowing of the eyes and skin
- confusion
- enlargement of facial features including thickening of the lips
- unusual and excessive hair growth on body and face
- increased sweating
- Peyronie’s disease (a condition where male patients experience a deformation of the penis which may cause pain when the penis is erect)
- unusual tiredness, drowsiness or weakness
- a feeling of nervousness
- loss of appetite and weight
- taste changes
- insomnia
- headache
- nausea/vomiting
- constipation
- DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms) that appears initially as flu-like symptoms and a rash on the face and then an extended rash with a high temperature, increased level of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes. The consequences can be life-threatening.

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.

Phenytoin may cause problems with breathing, blood pressure, heart and liver function, blood-sugar levels and blood cell count. Your doctor may do tests to check for these side effects.
Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via:

Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW PHENYTOIN INJECTION IS STORED
Keep out of the reach and sight of children

Expiry
This medicine must not be used after the expiry date which is stated on the ampoule and carton after 'EXP'. Where only a month and year is stated, the expiry date refers to the last day of that month.

Storage
The ampoules should be kept in the outer carton, in order to protect from light, and stored at, or below, 25°C.

Unused portions of opened ampoules must not be stored for later use.

Visible signs of deterioration
Only clear, colourless solutions should be used. Opaque, cloudy or discoloured solutions should not be used.

6. FURTHER INFORMATION
What Phenytoin Injection contains
The active substance is phenytoin sodium. Each millilitre (ml) of solution contains 50 milligrams (mg) of phenytoin sodium.

The other ingredients are ethanol, propylene glycol and Water for Injections. See section 2 ‘Important information about some of the ingredients of Phenytoin Injection’ for further information about ethanol and propylene glycol.

What Phenytoin Injection looks like and contents of the pack
Phenytoin Injection is a clear, colourless solution for injection which comes in glass containers called ampoules.

It is supplied in packs containing 5 x 250 mg/5 ml ampoules.

Marketing authorisation holder and manufacturer
Phenytoin Injection BP

The following information is intended for medical or 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.

Improper administration including subcutaneous or perivascular injection should be avoided.

Intramuscular phenytoin administration may cause pain, necrosis and abscess formation at the injection site.

Incompatibilities
Incompatible with amikacin sulphate, cephapirin sodium, clindamycin phosphate, and many other drugs. It is recommended that phenytoin sodium is not mixed with other drugs or with any infusion solution other than sodium chloride 0.9%.

Instructions for use and handling
For single use. Discard any unused contents.

The product should be visually inspected for particulate matter and discolouration prior to administration.

Phenytoin Injection is suitable for use as long as it remains free of haziness and precipitate. A precipitate might form if the product has been kept in a refrigerator or freezer. This precipitate will dissolve if allowed to stand at room temperature. The product will then be suitable for use.

For infusion administration, Phenytoin Injection 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.