PACKAGE LEAFLET: INFORMATION FOR THE PATIENT

# Phenytoin Hikma 50 mg/ml

## solution for injection

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 Hikma 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 Hikma.

**What is in this leaflet**



## 1. WHAT PHENYTOIN HIKMA IS AND WHAT IT IS USED FOR

Phenytoin Hikma 50 mg/ml solution for injection contains phenytoin sodium. Phenytoin sodium belongs to a group of medicines called antiepileptics. Antiepileptic medicines are used for the prevention and treatment of seizures (fits). The medicine will be given to you by a doctor and will be injected into a vein (intravenously).

Phenytoin Hikma is used to:
- Treat the following types of seizure:
  - status epilepticus (a state of persistent seizure). A persistent seizure is when:
  - you have a seizure that does not stop
  or
  - you have a number of seizures and remain unconscious throughout
- Prevent seizures happening during or after neurosurgery (surgery on the brain).

Phenytoin Hikma is **not** effective in absence status epilepticus (a special form of seizures) or in the prevention or treatment of febrile convulsions.

## 2. WHAT YOU NEED TO KNOW BEFORE YOU ARE GIVEN PHENYTOIN HIKMA

**Do not take Phenytoin Hikma:**
- if you are allergic (hypersensitive) to phenytoin, or any of the other ingredients of this medicine (listed in section 6).
- If you are allergic (hypersensitive) to other medicines with a similar chemical structure to phenytoin (e.g. hydantoins)
- If you have severe damage to the blood cells and bone marrow
- If you have grade II and grade III AV block (disorder of heart beat regulation)
- If you have a type of disorder that causes fainting and sometimes fits called Strokes-Adams syndrome.
- If you suffer from sinus bradycardia (slow heart rate of less than 50 beats per minute), sick sinus syndrome or sino-atrial block (disorders of heart beat regulation)
- If you have a had attack within the last three months
- If the output of your heart is poor (ask your doctor).
- 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 Hikma 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
- Diabetes
- Porphyria (an inherited disease that affects haemoglobin biosynthesis)
- Heart rhythm problems (Phenytoin Hikma can treat some rhythm problems, but can make others worse)
- Alcohol dependence
- If you are of Taiwanese, Japanese, Malaysian or Thai origin and tests have shown that you carry the genetic variant CYP2C9*3.

There is a risk of harm to the unborn child if Phenytoin Hikma is used during pregnancy. Women of childbearing age should use effective contraception during treatment with Phenytoin Hikma (see "Pregnancy and breastfeeding").

**Take special care with Phenytoin Hikma**

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.

Phenytoin Hikma should not be given in:
- heart failure (inability of heart to pump properly)
- impaired breathing function
- severe hypotension (systolic blood pressure less than 90 mm Hg)
- the following heart rhythm disturbances:
- grade I AV block
- atrial fibrillation
- atrial flutter

Phenytoin Hikma should be given with special precaution if you suffer from:
- impaired kidney function
- impaired liver function
  your doctor will take blood and urine samples to monitor your liver and kidney function.

If you are diabetic you are more likely to get hyperglycaemia (high blood sugar).

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

Serious skin side effects can rarely occur during treatment with Phenytoin Hikma. This risk 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 taking Phenytoin Hikma.

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

If you are taking Phenytoin Hikma 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).

**Important information regarding treatment**

***If you suffer from slow hydroxylation***

Slow hydroxylation is an inherited disorder. It affects the way your body uses and reacts to medicine.
If you suffer from slow hydroxylation you should therefore take care. You may develop signs of overdose even at moderate doses (see "What you must do if you are given too much Phenytoin Hikma"). In this case your dose should be reduced. Your doctor will take a blood sample to check that the levels of phenytoin are not too high.

***If you switch to another form of medicine that contains phenytoin***

Other medicines that contain phenytoin may not provide you with the same levels of phenytoin as Phenytoin Hikma. If you change your phenytoin medicine, your doctor will monitor you until your phenytoin levels even out. This may take up to 2 weeks.

***If you suddenly stop taking Phenytoin Hikma***
- you may suffer seizures more often
- you may develop status epilepticus (a state of persistent seizure).

To avoid these problems your doctor may:
- reduce your dose of Phenytoin Hikma slowly
- start the new antiepileptic medication at a low dose and gradually increase it

***If you switch treatment to an oral form of phenytoin (e.g. tablets or syrup):***

Your doctor will monitor your progress and take blood samples regularly.

If you are a child, your doctor will also monitor the function of your thyroid gland.

Your doctor will decide if any of the test results mean that you should change or stop treatment.

If you have low plasma protein levels (hypoproteinaemia) you are more likely to develop undesirable effects on your nervous system.

**Other medicines and Phenytoin Hikma**

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 Hikma works, or Phenytoin Hikma 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, 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
- Anticoagulants e.g. rivaroxaban, dabigatran, apixaban, edoxaban
- Lacosamide
- Ticagrelor
- 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 drugs 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 Hikma may also interfere with certain laboratory tests that you may be given.

**Phenytoin Hikma with drinking alcohol**

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

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## **Phenytoin Hikma 50 mg/ml** solution for injection

Active substance: phenytoin sodium

The following information is intended for medical or healthcare professionals only:

**Method of administration:**

The solution for injection is for intravenous use only as absorption is delayed and unreliable after intramuscular administration. Phenytoin Hikma should be injected slowly directly into a large vein through a large-gauge needle or intravenous catheter. Subcutaneous or perivascular injection should be avoided, as the alkaline phenytoin solution for injection can cause tissue necrosis.

**Handling and Preparation**

The solution for injection must not be mixed with other solutions, as phenytoin can crystallise out.

Before use, the ampoules should be checked for precipitation and discolouration.
The product should not be used if a precipitate or haziness develops in the solution in the ampoule.
Phenytoin Hikma 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.
Only a clear solution should be administered. A slight yellow discolouration has no effect on the efficacy of this solution.

For single use only. Any unused product should be discarded.

Duration of administration is dependent on the underlying disease and the course of the illness. If the medicine is well-tolerated, it can be used indefinitely.

**Dosage**

The therapeutic range for plasma concentration is generally between 10 and 20 micrograms/ml phenytoin; concentrations over 25 micrograms/ml phenytoin may be in the toxic range.

***Status epilepticus and series of seizures***

Continuous monitoring of ECG, blood pressure and neurological status and regular determination of plasma phenytoin concentrations is essential. In addition, resuscitation facilities should be readily available.

Adults and adolescents over 12 years of age
The initial dose is 1 ampoule of Phenytoin Hikma (equivalent to 230 mg phenytoin), administered at a maximum rate of 0.5 ml/min (equivalent to 23 mg phenytoin per minute). If the seizures do not stop after 20 to 30 minutes, the dose can be repeated.

If the seizures stop, a dose of 1 ampoule Phenytoin Hikma (equivalent to 230 mg phenytoin) can be given every 1.5 to 6 hours up to a maximum daily dose of 17 mg/kg bodyweight (or 6 ampoules - equivalent to 1380 mg phenytoin), to achieve rapid saturation.

At a maximum daily dose of 17 mg/kg bodyweight, this is equivalent to

| *Bodyweight* | *Ampoules* | *Phenytoin* |
|---|---|---|
| 41 kg | 3 | 690 mg |
| 54 kg | 4 | 920 mg |
| 68 kg | 5 | 1150 mg |
| 81 kg | 6 | 1380 mg |

Children up to 12 years of age
On day 1 the maximum daily dose is 30 mg/kg bodyweight, on day 2 20 mg/kg bodyweight, on day 3 10 mg/kg bodyweight. The maximum injection rate is 1 mg/kg bodyweight per minute.

Day 1
At a maximum daily dose of 30 mg/kg bodyweight, this is equivalent to

| *Bodyweight* | *Ampoules* | *Phenytoin* |
|---|---|---|
| 8 kg | 1 | 230 mg |
| 15 kg | 2 | 460 mg |
| 23 kg | 3 | 690 mg |
| 31 kg | 4 | 920 mg |
| 38 kg | 5 | 1150 mg |
| 46 kg | 6 | 1380 mg |

Day 2
At a maximum daily dose of 20 mg/kg bodyweight, this is equivalent to

| *Bodyweight* | *Ampoules* | *Phenytoin* |
|---|---|---|
| 12 kg | 1 | 230 mg |
| 23 kg | 2 | 460 mg |
| 35 kg | 3 | 690 mg |
| 46 kg | 4 | 920 mg |

Day 3
At a maximum daily dose of 10 mg/kg bodyweight, this is equivalent to

| *Bodyweight* | *Ampoules* | *Phenytoin* |
|---|---|---|
| 23 kg | 1 | 230 mg |
| 46 kg | 2 | 460 mg |

***Prophylaxis of seizures***

Adults and adolescents over 12 years of age receive 1 to 2 ampoules of Phenytoin Hikma (equivalent to 230 to 460 mg phenytoin) daily at a maximum rate of injection of 0.5 ml/min (equivalent to 23 mg phenytoin per minute).

**Pregnancy and breast-feeding**
If you are pregnant, think you may be pregnant, or are planning to have a baby, ask your doctor for advice before you are given Phenytoin Hikma.

Phenytoin Hikma can cause major birth defects. If you take Phenytoin Hikma during pregnancy your baby has up to 3 times the risk of having a birth defect than women not taking an antiepileptic medication. Major birth defects including growth, skull, facial, nail, finger and heart abnormalities have been reported. Some of these may occur together as part of a fetal hydantoin syndrome.

Problems with neurodevelopment (development of the brain) have been reported in babies born to mothers who used phenytoin during pregnancy. Some studies have shown that phenytoin negatively affects neurodevelopment of children exposed to phenytoin in the womb, while other studies have not found such an effect. The possibility of an effect on neurodevelopment cannot be ruled out.

Phenytoin Hikma should not be given to you during pregnancy, because it might increase the risk of birth defects. You should note that the contraceptive pill may not work when you receive Phenytoin Hikma.

If treatment with Phenytoin Hikma is essential, your doctor will give you the lowest effective daily dose to control your seizures. Pregnancy may also alter the effectiveness of Phenytoin Hikma, so you may need to have blood tests and your dose of Phenytoin Hikma may have to be adjusted.

If you are given Phenytoin Hikma to treat your seizures, the therapy during pregnancy should not be suddenly interrupted, as any abrupt discontinuation of treatment or uncontrolled dose reduction can cause recurrence of seizures, which may harm you and/or your unborn child.

In order to prevent bleeding disorders of your baby, you should be given vitamin K1 in the last week of your pregnancy and your newborn child should receive vitamin K1 after birth.

You should not breast-feed if you are being given Phenytoin Hikma.

**Driving and using machines**
Phenytoin Hikma may cause dizziness or drowsiness. If you experience these symptoms, do not drive or use any tools or machinery and contact your doctor.

**Phenytoin Hikma contains ethanol and sodium**
This medicinal product contains 10 vol % ethanol (alcohol), i.e. up to 394 mg per dose, equivalent to 10 ml beer, 4.17 ml wine per dose. It may be harmful for those suffering from alcoholism. It should be taken into account in pregnant or breast-feeding women, children and high risk groups such as patients with liver disease.

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

**Phenytoin Hikma contains propylene glycol**
May cause alcohol-like symptoms.

## 3. HOW PHENYTOIN HIKMA IS GIVEN

**More detailed information on dosage, handling and preparation of Phenytoin Hikma is given at the end of this package leaflet under the subheading 'The following information is intended for medical or healthcare professionals only'.**

Phenytoin Hikma will be given to you by your doctor by slow injection into a vein. Your doctor will decide on how much you need and when it is to be given. This will depend on your age and weight and the condition for which you need to take Phenytoin Hikma.

When you are given Phenytoin Hikma your doctor will:
- continuously monitor your heart, blood pressure and nervous system
- regularly measure your phenytoin levels

*Duration of therapy*
Phenytoin Hikma can be used long-term.

Duration of therapy depends on:
- which illness you are being treated for
- how well you respond to treatment
- how well you tolerate the side-effects (see Section 4 "Possible side effects").

During long-term treatment with Phenytoin Hikma your plasma levels will be monitored so that you can be given the lowest effective dose. This will help to minimise side-effects.

Please speak to your doctor or pharmacist if you feel that the effect of Phenytoin Hikma is too strong or too weak.

**If you are given more Phenytoin Hikma than you should**
Phenytoin Hikma is dangerous in overdose. If you think you have been given too much Phenytoin Hikma, contact your doctor immediately.

If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse. If you are given too much Phenytoin Hikma you may experience the following symptoms:

*Early symptoms*
- involuntary rapid eye movement (nystagmus)
- cerebellar ataxia (a disorder of movement coordination)
- dysarthria (impaired speech)

*Other symptoms*
- tremor (shaking)
- hyperreflexia (increased reflexes)
- somnolence (drowsiness)
- exhaustion
- lethargy (sluggishness)
- slurred speech
- diplopia (double vision)
- dizziness
- nausea (feeling sick)
- vomiting
- coma (loss of consciousness)
- your pupillary reflex (when the pupil of your eye gets smaller in response to light) may disappear
- fall in blood pressure
- effects on breathing. These can be fatal.
- heart failure. This can be fatal.
- irreversible brain damage

If you experience any of these symptoms, you should tell your doctor immediately. Your doctor will take steps to remove the excess phenytoin from your system. Your heart and breathing will be monitored and your symptoms will be treated.

## 4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine 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. 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:**
- **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, a decrease in the number of a type of red blood cell (pure red cell aplasia).
- **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 immunoglobin 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 Hikma 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.

**Reporting of side effects**
If you get any side effects, talk to your doctor, pharmacist 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 Website: 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 provide more information on the safety of this medicine.

## 5. HOW TO STORE PHENYTOIN HIKMA

The storage of Phenytoin Hikma will not be your responsibility.
This medicinal product does not require any special storage conditions.

The pharmacist will ensure that your medicine is not used after the expiry date which is stated on the carton after EXP. The expiry date refers to the last day of that month. The pharmacist will also ensure that Phenytoin Hikma is kept in the original package.

Keep out of the sight and reach of children.

## 6. CONTENTS OF THE PACK AND OTHER INFORMATION

**What Phenytoin Hikma contains**
The active substance is phenytoin sodium.
Each ml of solution contains 50 mg phenytoin sodium (equivalent to 46 mg phenytoin).
Each 5 ml-ampoule of solution for injection contains 250 mg phenytoin sodium (equivalent to 230 mg phenytoin).

The other ingredients are:
- propylene glycol
- ethanol
- sodium hydroxide
- water for injection

**What Phenytoin Hikma looks like and contents of the pack**
Phenytoin Hikma is supplied in clear glass vials called ampoules.

Phenytoin Hikma is a clear solution.

Pack size: Phenytoin Hikma is available in packs of 5 or 50 ampoules.

1 ampoule contains 5 ml solution for injection.

**Marketing Authorisation Holder and Manufacturer**
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Consilient Health

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Children up to 12 years of age receive 5 to 6 mg/kg bodyweight. Rate of injection is reduced according to the weight/age of the child.

At a daily dose of 5 mg/kg bodyweight, this is equivalent to

| *Bodyweight* | *ml* | *Phenytoin* |
|---|---|---|
| 9 kg | 1 | 46 mg |
| 18 kg | 2 | 92 mg |
| 28 kg | 3 | 138 mg |
| 37 kg | 4 | 184 mg |
| 46 kg | 5 | 230 mg |

At a daily dose of 6 mg/kg bodyweight, this is equivalent to

| *Bodyweight* | *ml* | *Phenytoin* |
|---|---|---|
| 8 kg | 1 | 46 mg |
| 15 kg | 2 | 92 mg |
| 23 kg | 3 | 138 mg |
| 31 kg | 4 | 184 mg |
| 38 kg | 5 | 230 mg |
| 46 kg | 6 | 276 mg |

When Phenytoin Hikma is taken long-term, phenytoin plasma levels must be monitored and blood count and liver enzyme activity should be checked at regular intervals (several weeks). A blood count showing moderate, stable leukopenia or an isolated increase in gamma-GT should not normally necessitate withdrawal of treatment.

Osteomalacia (soft bones) may develop in susceptible patients or patients with a calcium metabolism disorder (increased alkaline phosphatase). This normally responds well to administration of vitamin D. Alkaline phosphatase should therefore be checked regularly. Additionally in children, thyroid function should be monitored.

***Switching preparations***
Due to the relatively narrow therapeutic range and the varying bioavailability of the numerous pharmaceutical preparations, when changing from one preparation to another containing phenytoin, the phenytoin-plasma concentrations must be monitored closely. If the dose is kept the same, steady state can be expected after 5 to 14 days.

Therefore the dose (if possible) should be reduced slowly and the new antiepileptic medicine started at a low dose and gradually increased. Abrupt withdrawal of Phenytoin Hikma may increase seizure frequency or lead to status epilepticus.

***Additional information on special populations***
Patients with renal/hepatic impairment:
There is no reference for dosage adjustment for this special group; however, caution should be taken in patients with renal and hepatic disease (see section 4.4). Impaired renal and hepatic functions require careful monitoring.

Elderly (over 65 years):
As for adults; however, complications may occur more readily in elderly patients.

Neonates:
In neonates it has been shown that absorption of phenytoin is unreliable after oral administration. Phenytoin Hikma should be injected slowly intravenously at a rate of 1-3 mg/kg/min at dose of 15-20 mg/kg. This will usually produce serum concentrations of phenytoin within the generally accepted therapeutic range of 10-20 mg/l.

Infants and children:
As for adults. Children tend to metabolise phenytoin more rapidly than adults. This should be considered when determining dosage regimens; monitoring serum levels is therefore particularly beneficial in such cases.

**Therapy of overdosage**

***Symptoms of an overdose***
Signs of overdose can develop in individuals who have different phenytoin plasma levels. Early symptoms include involuntary, rapid eye movement, cerebellar ataxia and dysarthria. Additional symptoms may include: tremor, hyperreflexia, somnolence, exhaustion, lethargy, slurred speech, diplopia, dizziness, nausea, vomiting. The patient may fall into a coma, the pupillary reflex may disappear, and blood pressure fall. Death can result e.g. from central respiratory depression or circulatory failure. The mean lethal (acute) dose is estimated to be 2-5 g phenytoin in adults. The lethal dose for paediatric patients is unknown. Overdose can lead to irreversible degenerative cerebellar changes.

***Treatment of intoxication***
Initial treatment must include gastric lavage, administration of activated charcoal and monitoring on intensive care. Haemodialysis, forced diuresis and peritoneal dialysis are less effective. Experience on the efficacy of haematogenic charcoal perfusion, total plasma substitution and transfusion is inadequate. For this reason, intensive internal treatment without special detoxification procedures should be performed, but phenytoin plasma levels should be checked.