PHENTOLEP®

(Phenytoin Sodium)

ACTION

Phentolep is an anticonvulsant. It works by controlling the excessive activity in the brain that can cause epilepsy or seizures. Phentolep belongs to a group of drugs known as hydantoins.

INDICATION

Phentolep Injection may be used to control status epilepticus of the tonic-clonic (grand mal) type (a condition where seizures rapidly follow each other without regaining consciousness), it may also be used to prevent and to treat seizures that may occur during or after neurosurgery (surgery on the brain or spinal cord) or following a severe head injury.

DOSAGE AND ADMINISTRATION

Phentolep injection must be administered slowly. Intravenous administration should not exceed 50 mg/minute in adults. In neonates the drug should be administered at a rate not exceeding 1 to 3 mg/kg/min.

Dilution of Phentolep injection into intravenous infusion is not recommended due to lack of solubility and resultant precipitation.

The solution 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.

Phentolep injection should be injected slowly and directly into a large vein through a large gauge needle or intravenous catheter. Each injection should be followed by an injection of sodium chloride intravenous infusion 0.9% through the same needle or catheter to avoid local venous irritation due to the alkalinity of the solution. Continuous infusion should be avoided.

Dosage:

The therapeutic range of the plasma concentration is generally between 10 and 20 µg/ml phenytoin concentrations above 25 µg/ml phenytoin may be toxic.

Status Epilepticus, and Serial Seizures: Continuos control of ECG, blood pressure and neurological status, as well as regular measurement of phenytoin plasma concentration must be guaranteed. Moreover, the presence of resuscitation measures should be considered.

• Adults and Adolescents 13 years (or older):

The initial dose is 1 ampoule Phentolep parenteral (corresponding to 230 mg phenytoin). It is administered with maximum injection rate of 0.5 ml/min. (corresponding to 23 mg phenytoin/min.)

If the seizure persists after 20-30 minutes, the dose may be repeated.

When seizures have stopped, dosing may be continued to a maximum dose of 17 mg/kg body weight or 6 Phentolep parenteral ampoules/day (corresponds to 1380 mg phenytoin).

One ampoule Phentolep parenteral (corresponding to 230 mg phenytoin) is administered every 1.5 to 6 hours to attain rapid saturation.

With a maximum daily dose of 17 mg/kg body weight, this corresponds to:

Body weight	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:

Day one: 30 mg/kg body weight
Day two: 20 mg/kg body weight
Day three: 10 mg/kg body weight
Maximum injection rate 1 mg/kg body weight/min.

Maximum daily dose 30 mg/kg body weight, this corresponds to:

Body weight	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

With a maximum daily dose of 20 mg/kg body weight, this corresponds to:

Body weight	Ampoules	Phenytoin
12 kg	1	230 mg
23 kg	2	460 mg
35 kg	3	690 mg
46 kg	4	920 mg

With a maximum daily dose of 10 mg/kg body weight, this corresponds to:

body weight	Ampoules	Phenytoin
23 kg	1	230 mg
46 kg	2	460 mg

Seizure prophylaxis

Adults and adolescents 13 or older are given 1-2 ampoules Phentolep parenteral (corresponding to 230 to 460 mg phenytoin) daily. The maximum injection rate is 0.5 ml/min (corresponding to 23 mg phenytoin/minute).

Children up to 12 years of age are given 5-6 mg/kg body weight. The injection rate is reduced corresponding to the weight and age of the child.

With a daily dose of 5 mg/kg body weight this corresponds to:

Body weight	Volume (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

With a daily dose of 6 mg/kg body weight this corresponds to:

Body weight	Volume (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

CONTRAINDICATIONS

Phentolep is contraindicated in those patients who are hypersensitive to phenytoin or other hydantoins.

WARNINGS

Before administration of phenytoin sodium, following should be considered:

- An allergy to phenytoin, or to any of the other ingredients in the formulation, or to any other hydantoin drug (such as ethatoin or methoin).
- A slow heart beat (less than 60 beat/minute) or any heart problems.
- Low blood pressure.
- A disease of the liver or kidneys.
- Diabetes.
- Porphyria.
- Alcohol intake.

PRECAUTIONS

Laboratory tests:

phenytoin serum level determinations may be necessary to achieve optimal dosage adjustments.

Pregnancy:

A number of reports suggest an association between the use of antiepileptic drugs by women with epilepsy and a higher incidence of birth defects in children born to these women. Data are more extensive with respect to phenytoin and phenobarbital, but these are also the most commonly prescribed antiepileptic drugs; less systematic or anecdotal reports suggest a possible similar association with the use of all known antiepileptic drugs.

If taking during pregnancy (particularly during the first 3 months and the last 3 months), phenytoin may cause birth defects. It may also cause problems with bleeding in neonates.

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.

Drug interactions

There are many drugs which may increase or decrease phenytoin levels or which phenytoin may affect. Serum level determinations for phenytoin are especially helpful when possible drug interactions are suspected. The most commonly occurring drug interactions are listed below.

- Drugs which may increase phenytoin serum levels include: acute alcohol intake, amiodarone, chloramphenicol, chlordiazepoxide, diazepam, dicumarol, disulfiram, estrogens, H 2 -antagonists, halothane, isoniazid, methylphenidate, phenothiazines, phenylbutazone, salicylates, succinimides, sulfonamides, tolbutamide, trazodone.
- Drugs which may decrease phenytoin levels include: carbamazepine, chronic alcohol abuse, reserpine, and sucralfate.
- Drugs which may either increase or decrease phenytoin serum levels include: phenobarbital, sodium valproate, and valproic acid. Similarly, the effect of phenytoin on phenobarbital, valproic acid and sodium valproate serum levels is unpredictable.
- Although not a true drug interaction, tricyclic antidepressants may precipitate seizures in susceptible patients and phenytoin dosage may need to be adjusted.
- Drugs whose efficacy is impaired by phenytoin include: corticosteroids, coumarin anticoagulants, digitoxin, doxycycline, estrogens, furosemide, oral contraceptives, quinidine, rifampin, theophylline, vitamin D.

SIDE EFFECTS

- Palpitations or an irregular heart beat.
- Faintness or dizziness.
- Difficulty in breathing.
- Rapid movements of the eyeball, irregular muscle actions, slurred speech, decreased co-ordination, feeling confused, abnormal sensations (such as prickling, drowsiness, or vertigo).
- Insomnia, nervousness, muscle twitching or other odd uncontrollable movements. Headache, seizures or signs of nerve disease such as pain numbness or muscle weakness.
- Pain, inflammation, or tissue damage at the site of injection.
- Skin rashes or bruising of the skin .
- A persistent sore throat or unexplained fever, any signs of anemia (such as paleness or feeling tired).
- Swollen glands.
- Tummy upset or constipation or yellowing of the skin or the whites of the eyes.
- Coarsening of the facial features, enlargement of the lips or gums, an increase in body hair, contracture of tissue in the penis or contracture of the fingers, pains in the joints, any urinary symptoms (such as blood in the urine, or not passing normal amounts of urine), cough, wheezing or breathlessness.

OVERDOSAGE

The initial symptoms are nystagmus, ataxia, and dysarthria. Other signs are tremor, hyperflexia, lethargy, slurred speech, nausea, vomiting. The patient may become comatose and hypotensive. Death is due to respiratory and circulatory depression. Treatment is nonspecific since there is no known antidote.

PRESENTATIONS

Ampoules:

Phentolep 250 mg: Phenytoin Sodium 250 mg/5 ml

THIS IS A MEDICAMENT

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous.
- Follow the doctor's prescription strictly, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Manufactured by:
HIKMA Pharmaceuticals, Amman-Jordan

Keep medicament out of the reach of children

2INPHN-AE-06/2005