Epilan® D-Gerot

tablets

Composition:
One tablet contains: Phenytoin 100 mg

Characteristics:
Phenytoin reduces the excitability of structures subject to excitation (such as nerves and muscles) by means of membrane stabilization (hyperpolarization) and by promoting the generation of inhibiting pulses via the neurotransmitter system (GABA). At the same time, phenytoin functions as a competitive and antagonistic agent on the digitalis receptor of the myocardium. The anticonvulsive effect of phenytoin is attributable primarily to an inhibition of the cortical and subcortical (brain-stem) spread of epileptic discharges. In addition, phenytoin has shown itself to be effective as a therapeutic agent in cases of paroxysmal neuralgic pain (such as trigeminal neuralgia).
As a weak acid, phenytoin is practically insoluble in the acid environment of the gastric juice. Absorption takes place primarily in the duodenum and jejunum. Maximum plasma concentration is attained 4–12 hours after ingestion of a single dose. After absorption, phenytoin is bound in a proportion of approximately 90% to plasma proteins, and albumins in particular. Low albumin values, such as occur in cases of nutritional deficiency or liver or kidney disease, increase the free proportion. The plasma half-life of phenytoin is 7–42 hours, and therapeutic steady-state values are reached after 7–10 days.
A balance is achieved between the maternal and fetal blood due to unhindered passage through the placental barrier. Only about 5% of the phenytoin administered is excreted unchanged in the urine and faeces. The remainder is metabolized in the liver to 5-(p-hydroxyphenyl)-5-phenylhydantoin, conjugated with glucuronic acid, and finally eliminated from the organism in the kidneys by glomerular filtration and tubular secretion.
The half-life of phenytoin rises as the plasma concentration increases (e.g. above 25 µg/ml), and approaches a saturation of the metabolizing enzyme system (cytochrom P 450) and a competitive inhibition of the liver hydroxylases by the main metabolite.
As a result of this, dosage increases even in the usual dosage range of 100–300 mg phenytoin per day can lead to intoxication in individual patients. This can be explained by the fact that the serum level may rise exponentially at higher substance doses.

Indications:
Epileptic seizures: Generalized tonic and clonic (grand mal) and focal seizures (Jackson), psychomotor seizures (temporal lobe seizures)

Administration:
Tablets are to be ingested with ample amounts of liquid, without chewing, during or after meals.

Dosage:
Adults:
Patients previously not treated:
In the first week 100 mg phenytoin should be taken daily, increased during the second week to 200 mg daily. The dosage should then be increased until the patient is seizure-free. The dosage may thereafter be reduced to the maintenance dose, which is to be determined individually. In most cases, this amounts to 300 mg in three intakes during the day.
Maximum daily dose: 500 mg
Patients previously treated:
The previous medication should be reduced and replaced by 100 mg phenytoin daily during the first week, by 200 mg daily during the second week, and so on until after about 3–5 weeks the earlier medication has been entirely replaced by Epilan D-Gerot tablets. Sudden therapy change is to be avoided, since this may cause a violent onset of seizures!
Children:
The dosage for children is 4–7 mg daily per kg body weight, divided into 2–3 doses.
Maximum daily dose: 300 mg.
Inadequate success in treatment may be attributable to an excessively low dosage. Accordingly, a slow increase in the dosage by 25–50 mg phenytoin should be carried out, if possible while monitoring the serum level.
Therapeutic serum concentrations are about 5–20 mg/l (20–80 µMol/l).
Dosage for severe renal insufficiency:
Bioavailability increases due to the reduction of the protein binding. It is recommended that the dosage should be adapted in accordance with the phenytoin level in the serum, as well as with the overall clinical picture.

Contraindications:
Hypersensitivity to hydantoin preparations, atrioventricular block 2nd and 3rd degree with ventricular escape rhythm, sinu-atrial block, leucopenia, decompensated liver insufficiency.
Caution is to be taken with patients suffering from severe liver damage and hyperglycemia.

Pregnancy and lactation:
In cases where a tendency to epileptic seizures becomes apparent for the first time during pregnancy, medication with phenytoin should be avoided. In cases in which therapy is already established, the dosage should be reduced to a minimum particularly between the twentieth and fortieth day of pregnancy, since there is the possibility of a fetal hydantoin syndrome arising. Account must be taken of the change in metabolic condition during pregnancy by monitoring the serum level. Combination with other medications is to be avoided as far as possible! During the last two months of pregnancy, treatment with vitamin D, folic acid, and vitamin K has been shown to be beneficial in avoiding osteomalacia and infant haemorrhage.
In view of the fact that phenytoin is transferred into the mother's milk, breast-feeding should be avoided.

Side effects:
- Gastrointestinal tract: Nausea, vomiting, stomach-ache; gingival hyperplasia (mainly in adolescents) gigantochellia; obstipation.
- Liver: Increase in gamma-GT or alkaline phosphatase; hepatitis, jaundice.
- Blood: Bone marrow depression with aplastic anaemia, pancytopenia, leucopenia, agranulocytosis, thrombopenia, granulocytopenia; megaloblastal anaemia (folic acid deficiency anaemia); eosinophilia.
- Lymph system: Swelling of the lymph nodes, pseudolymphoma, lymphoma, Hodgkin's disease; transitory antibody deficiency.
- Skin and connective tissue: Hirsutism (mainly in adolescents) chloasma, Dupuytren's contracture, Peyronie's disease, panarteritis nodosa, vasculitis, lupus erythematosus, morbilliform and scarlatiniform exanthemas; Stevens-Johnson's syndrome, Lyell's syndrome.
- Nervous system: Dizziness, insomnia, headache, nervousness, confusion, restlessness, delirious conditions; tremor, myoclonia, asterixis, fidgeting; peripheral neuropathia, nystagmus, vision disorders, dystonia, ataxia, cerebellar degeneration, hyperkinesia, chorea, temporary hemiparesis, spastic paralysis, increase of myasthenia gravis, slurred speech.
- Others: Fever, hyperglycaemia, myocarditis, dyspnoea, interstitial pneumonia, pulmonary infiltrates, interstitial nephritis, splenomegalia, osteomalacia, disturbance of cardiac conduction, polyarthropathia.

Drug Interactions:
An increase in the phenytoin level can be caused by:
Alcohol (acute), tolbutamide, chlordiazepoxide, cumarin, disulfiram, chloramphenicol, isoniacid, sulfonamides, salicylates, phenylbutazone, phenothiazine, diazepam, oestrogens, ethosuximide, halothane, methylphenydate, cimetidin, omeprazol, imipramin, trazodone, phenyramidol, sultiame, thyroid preparations, viloxazine.
A reduction in the phenytoin level may be caused by:
Alcohol (chronic), reserpine, barbiturates, carbamazepine.
Phenoarbital and valproic acid may raise the phenytoin level as well as lower it.
Phenytoin may reduce the effect of the following pharmaceutical preparations:
Quinidine, vitamin D, digitoxin, rifampin, doxycycline, furosemide, corticosteroids, oral contraceptives, oral anticoagulants, verapamil. Through displacement of methotrexate from its protein-binding, phenytoin may lead to an increase of the unbound ratio and thus to an increased action of methotrexate.
Laboratory tests:
Phenytoin may interfere with the metyrapone and dexamethasone tests as well as with the determinations of calcium and glucose in blood, furthermore phenytoin may reduce protein-bound iodine due to displacement.

Cautionary Advice:
Regular blood counts and liver function tests are required.
Due to the possibility of the thyroid hormone system being affected by anti-epileptic long-term therapy, laboratory examinations are advisable every six months, especially for children.
Abrupt discontinuation of phenytoin treatment in epileptics may initiate a convulsive attack. Accordingly, any reduction in dosage should be carried out step by step, over a period of several weeks. In the event of an allergic reaction making it necessary for therapy to be interrupted immediately, another anti-epileptic agent has to be taken at the same time which does not belong to the hydantoin class.
A megaloblastal anaemia which may occur during therapy with phenytoin should be treated by substitution with folic acid. In the event of osteomalacia, substitution with vitamin D is recommended. In long-term therapy, at least 100 mcg (4000 units) of vitamin D per week should be added.

Overdosage:
Initial symptoms of acute intoxication are nystagmus, ataxia, and dysarthria. The patient then becomes comatose; no pupil reflexes, and hypotension. Death due to central respiratory depression is possible.

Treatment of acute intoxication:
Non-specific, since no antidote is known. Haemodialysis, peritoneal dialysis, total substitution transfusion, or forced diuresis have been only slightly effective in the cases published hitherto, since phenytoin is 90% protein-bound, and only slightly water-soluble. The preferred method to be recommended is therefore an intensive internal therapy, without any special detoxification procedures, but with serum levels being monitored.

Information for the Patient:
The intake of phenytoin is neither to be started nor to be discontinued without medical control. The physician should be consulted immediately after occurrence of first symptoms of side-effects (especially rash, fever, sore throat or ulcers in the throat and mouth or anywhere else, as well as jaundice). At the beginning of phenytoin treatment, with higher dosages and/or in combination with other pharmaceutical preparations affecting the central nervous system, the reaction capacity may be altered so that the ability to operate machines or to drive may be impaired. This applies in particular in combination with alcohol. Thus the consumption of alcoholic beverages should be avoided. The physician is to be informed without delay of any pregnancy. During a treatment with phenytoin the physician is to be consulted prior to the application of any other medication. Due to the fact that phenytoin may reduce the effect of oral contraceptives, other contraceptive methods should be employed. Intensive oral hygiene is to be taken care for, which minimizes the risk of onset and severity of gingival hyperplasia.

Pack Size: 100 tablets

Storage Advice:
Store at room temperature not exceeding 25° C. Protect from light.
Keep out of the reach of children.

Sole Agent in Lebanon and Syria: LIBA PHARM

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Producer:
Gerot Pharmazeutika Vienna, Austria