

## Neurotop®

anticonvulsant - antineuralgic

**Neurotop 200 mg tablets, Neurotop retard 300 mg tablets.**

**Neurotop 400 mg tablets. Neurotop retard 600 mg tablets**

### Composition

Carbamazepine 200 mg	per tablet
Carbamazepine 300 mg	per sustained-release tablet
Carbamazepine 400 mg	per tablet
Carbamazepine 600 mg	per sustained-release tablet

### Characteristics

Carbamazepine has mainly anticonvulsant effects; in addition it shows certain anticholinergic, sedating and anti-depressant qualities as well as an antidiuretic effect via the central nervous system. The excellent efficacy of carbamazepine in the various forms of seizures is manifested particularly by its favourable influence on the accompanying changes in the psychic mood (mood elevating effect).

Carbamazepine is considered the drug of first choice for trigeminal neuralgia.

Abstinence symptoms due to alcohol withdrawal are rapidly improved with the administration of carbamazepine. Following single-dose administration, carbamazepine has a relatively long plasma half-life (25-65 hours); following repeated application, however, elimination is considerably more rapid due to its autoinduction of metabolism (12-17 hours). When using the sustained-release tablets more uniform plasma levels are achieved with only 2 administrations daily.

Carbamazepine is metabolized in the liver and mainly excreted via the kidneys. The substance is distributed also in the fetus and the mother's milk. Bioavailability is almost 100% and serum protein binding is 75-80%. Testing for mutagenicity of carbamazepine and some of its metabolites showed negative results.

### Therapeutic Indications

Epilepsy

Partial seizures - with complex symptomatology  
-with simple symptomatology

Primary generalized epilepsy or secondarily generalized seizures with a tonic-clonic component. Mixed forms of these

seizures; convulsive disorders causing predominantly changes in psychic mood (mood elevating effect). Neurotop is

suitable both for monotherapy and combination therapy. Neurotop is usually not effective in absence (petit mal) seizures.

Prophylaxis of manic-depressive psychosis. Alcohol withdrawal syndrome.

Trigeminal neuralgia. Painful diabetic neuropathy. Diabetes insipidus centralis.

### Administration

For oral administration during or after a meal with liquid. The sustained-release tablets may be broken into bits without any loss of the sustained-release effect.

### Dosage

**Neurotop 200 mg tablets:**

*Anticonvulsive therapy:*

A low initial dosage with gradual increase and concomitant step-by-step reduction of previously used anticonvulsants is advisable.

*Adults and children over 10 years of age:*

In general, initially 1 tablet 2 times per day, then a slow increase up to the individually optimal dose.

*Children:*

Initially 10 to 20 mg per kg body weight daily; then gradual increase up to 20 or 30 mg/kg body weight daily, divided into several doses. Children up to 1 year: 1/2 a tablet daily. Children from 1 to 5 years: 1-2 tablets daily. Children from 6 to 10 years: 2 tablets up to 3 tablets daily.

*Prophylaxis of manic-depressive psychosis:*

In general daily dose is 2 to 3 tablets.

*Trigeminal neuralgia:*

Slow increase of the initial dose of 1 tablet twice a day until patient stays free from pain (3-4 times 1 tablet per day on the average); the smallest efficient dose should then be determined by means of a step-by-step dose reduction.

*Diabetic neuropathy; diabetes insipidus centralis; acute symptoms of alcohol withdrawal:*

The average dose is 3 times 1 tablet per day.

In elderly or underweight patients it is recommended to fix the initial dose at 2 times 1/2 a tablet per day.

**Neurotop 400 mg tablets:**

*Anticonvulsive therapy:*

A low initial dosage with gradual increase, and concomitant step-by-step reduction of previously used anticonvulsants is advisable.

*Adults and children over 10 years of age:*

In general, initially 1/2 a tablet 2 times a day, then a slow increase up to the individually optimal dose.

*Children:*

Initially 10 to 20 mg per kg body weight daily; then gradual increase up to 20 or 30 mg/kg body weight daily, divided in several doses.

Children from 1 to 5 years: 1/2 a tablet up to 1 tablet daily. Children from 6 to 10 years: 1 tablet up to 1 1/2 tablets daily.

*Prophylaxis of manic-depressive psychosis:*

In general daily dose is 1 to 2 tablets.

*Trigeminal neuralgia, diabetic neuropathy; diabetes insipidus centralis:*

The average daily dose is 1/2 a tablet 3 times daily.

*Acute symptoms of alcohol withdrawal:*

During the first 4 or 5 days of treatment 1 tablet 3 times daily, then subsequently 1/2 a tablet 3 times daily for several days.

**Neurotop retard 300 mg tablets:**

*Anticonvulsive therapy:*

A low initial dosage with gradual increase, and concomitant step-by-step reduction of previously used anticonvulsants is advisable.

*Adults and children over 10 years of age:*

In general, initially 1/2 a tablet 2 times a day, then a slow increase up to the individually optimal dose. It is preferably the evening dosage which should be increased.

*Children:*

Children from 5 to 10 years: 1/2 a tablet in the morning and in the evening. Children from 6 to 10 years: 1/2 a tablet in the morning and 1/2 a tablet up to 1 tablet in the evening (15 to 20 mg/kg body weight daily).

*Prophylaxis of manic-depressive psychosis:*

In general daily dose is 2 tablets.

*Trigeminal neuralgia:* -

In general initially 1 tablet daily, then slow increase of dosage until release from pain is achieved. Then establish the minimum effective dose by reducing the dosage step-by-step.

*Diabetic neuropathy, diabetes insipidus centralis; acute symptoms of alcohol withdrawal:*

1 tablet in the morning and in the evening.

**Neurotop retard 600 mg tablets:**

*Anticonvulsive therapy:*

A low initial dosage with gradual increase, and concomitant step-by-step reduction of previously used anticonvulsants is advisable.

*Adults and children over 10 years of age:*

In general, 1 tablet daily, preferably in the evening.

*Children:*

children from 6 to 10 years: 1/2 a tablet up to 1 tablet daily (15 to 25 mg/kg body weight daily).

*Prophylaxis of manic-depressive psychosis:*

In general daily dose is 1 tablet.

*Trigeminal neuralgia; diabetic neuropathy, diabetes insipidus centralis:*

The average daily dose is 1 tablet.

*Acute symptoms of alcohol withdrawal:*

The average daily dose is 1 tablet. In severe cases 2 tablets may be taken in the first few days of treatment.

**Dosage in severe renal insufficiency:**

In glomerular filtration rate of less than 10 ml/min and in dialysis 75% of the usual dosage are administered.

**Contraindications**

Hypersensitivity to carbamazepine or related substances (tricyclic antidepressants), atrioventricular block, severe hepatic

insufficiency, bone marrow depression, children under one year of age (Neurotop 400 mg tablets, Neurotop retard 300 mg tablets), children under six years of age (Neurotop retard 600 mg tablets). Caution and Constant monitoring in the case of cardiovascular diseases, disturbed liver and/or kidney function as well as in glaucoma patients.

**Pregnancy and Lactation**

During pregnancy, particularly in the first trimester, the administration of any medication is potentially dangerous. Discontinuation of a necessary anticonvulsive therapy may, however, pose a greater health risk for the mother and the fetus. In animal studies carbamazepine demonstrated a comparatively low teratogenic potential; reduced birth weights and organ weights as well as incomplete ossification and sporadic cleft palate have been observed in rodents after feeding

a daily dosage of 10 to 25 times higher than the human therapeutic dosage calculated with reference to kg of body weight. In order to enhance safety and facilitate determination of the lowest effective dose plasma level determinations (drug monitoring) are recommended (therapeutic range: 3 to 12 mg/l = 13 to 50 µmol/l). In order to achieve a gradual withdrawal of carbamazepine in the newborn, it should be weaned slowly. Because of its sedating effect on the central nervous system carbamazepine in mother's milk may lead to impairment of sucking in the newborn.

### **Cautionary Advice**

Before therapy is initiated, blood assays and liver function tests should be performed. Thereafter,

- blood count: weekly during first month, then monthly;
- liver function: in normal values every 3 to 4 months, in the case of pathological values in shorter intervals.

Carbamazepine therapy is to be discontinued in the case of signs of impaired hematopoiesis, in progressive leukopenia accompanied by clinical symptoms, in occurrence of allergic skin reactions as well as in pronounced deterioration of hepatic function. Regular monitoring and caution in dosage are indicated in cardiovascular diseases, in impaired hepatic and/or renal function as well as in glaucoma patients. With abrupt discontinuation of carbamazepine or change-over to a different anticonvulsive preparation, barbiturate or diazepam protection is recommended:

### **Information for the Patient**

Therapy with Neurotop may not be installed without medical advice and must not be arbitrarily discontinued!

The physician should be consulted immediately after occurrence of first symptoms of side-effects, especially skin eruption, paleness, fatigue, lowered resistance, fever, sore throat, ulcers in the throat and mouth or anywhere else, hemorrhagic diathesis jaundice blood or protein in the urine as well as bradycardia. As the reaction capacity may be reduced by Neurotop, caution is to be exercised when driving or operating machines. During Neurotop therapy, alcohol consumption is to be avoided. The onset or existence of pregnancy must be reported to the treating physician without delay. Before concomitant administration of other medicaments (including drugs you may buy without prescription) during Neurotop therapy the physician should be consulted. The efficacy of hormonal contraceptives (anti baby pill") may be reduced by carbamazepine. Therefore other contraceptive methods should be employed.

### **Side-Effects**

At the onset of therapy anorexia, dryness of the mouth, nausea, diarrhea or constipation may occur.

*The following adverse effects have been sporadically observed:*

headache, dizziness, drowsiness, fatigue, ataxia, disturbances of visual accommodation, nystagmus, diplopia, paresthesia, pareses of the legs, speech disorders. In the elderly eventually also confusion, agitation and very infrequently visual hallucinations are possible.

These side-effects usually disappear within 6—14 days without any intervention or following temporary reduction of dosage. *In addition the following has been*

*reported on carbamazepine:*

Allergic skin reactions, fever, individual cases of purpura, exfoliative dermatitis, erythema exudativum multiforme (even as far as Stevens-johnson syndrome), Lyell's syndrome, loss of hair; leukopenia, thrombocytopenia, agranulocytosis, aplastic anemia sporadic leukocytosis thromboembolism acute intermittent porphyria cholestatic or hepatocellular jaundice as well as renal function disturbances (hematuria, proteinuria or even renal failure), swelling of the lymph nodes and hyponatremia (sometimes with vomiting, headache, confusion); decrease of T3 and T4, hypocalcemia, decrease of calcifediol; disturbances of the conductive system (total atrioventricular block), bradycardia; hypersensitivity of the lungs (possibly interstitial pneumonia), aseptic meningitis, peripheral eosinophilia, lupus erythematosus-like syndrome. With high doses tremor (even asterixis), hypertension or hypotension, arrhythmias.

### **Drug Interactions**

By liver enzyme induction the effect of other preparations may be reduced, such as that of oral anticoagulants (coumarin derivatives), quinidine, hormonal contraceptives, or antibiotics (a. g. doxycycline). Inhibition of carbamazepine metabolism (leading to increased plasma concentrations) has been reported in concurrent therapy with erythromycin, triacetyloleandomycin, isoniazid, several calcium channel blockers (a. g. verapamil, diltiazem), dextropropoxyphene and viloxazine. Higher plasma concentrations of carbamazepine may also be found with concurrent administration of other anticonvulsants (phenytoin, primidone or valproic acid) or cimetidine. Combined administration of carbamazepine and lithium may lead to reversible neurotoxic reactions Following therapy with MAO inhibitors carbamazepine is to be administered only after a two-week interval has elapsed. Interactions with laboratory parameters: thyroid function parameters may be changed.

### **Overdosage**

*Signs and Symptoms:*

The presenting signs and symptoms of overdosage usually involve the central nervous, cardiovascular and respiratory systems.

*Central nervous system:*

CNS depression; disorientation, somnolence, agitation, hallucination, coma, blurred vision, slurred speech, dysarthria, nystagmus, ataxia, dyskinesia, initially hyperreflexia, later hyporeflexia; convulsions, psychomotor disturbances, myoclonus, hypothermia.

*Respiratory system:*

Respiratory depression, pulmonary oedema.

*Cardiovascular system:*

Tachycardia, hypotension, at times hypertension, conduction disturbance with widening of QRS complex; syncope in association with cardiac arrest.

*Gastrointestinal system:*

Vomiting, delayed gastric emptying, reduced bowel motility. *Renal function:*

Retention of urine, oliguria or anuria; fluid retention, water intoxication due to an ADH-like effect of carbamazepine. *Laboratory findings:*

Hyponatraemia, possibly metabolic acidosis, possibly hyperglycaemia, increased muscle creatinine phosphokinase.

### **Management**

There is no specific antidote. Management should initially be guided by patient's clinical condition; admission to hospital. Measurement of the plasma level to

confirm carbamazepine poisoning and to ascertain the size of the overdose. Evacuation of the stomach, gastric lavage, and administration of activated charcoal. Supportive medical care in an intensive care unit with cardiac monitoring and careful correction of electrolyte imbalance.

*Special recommendations:*

*Hypotension:*

administer dopamine or dobutamine IV. Disturbances of cardiac rhythm to be handled on individual basis,

*Convulsions:*

administer a benzodiazepine (e.g. diazepam) or another antiepileptic, e.g. phenobarbitone (with caution because of increased respiratory depression) or paraldehyde.

*Hyponatraemia (water intoxication):*

fluid restriction and slow and careful NaCl 0.9% infusion IV., these measures may be useful in preventing brain damage, charcoal haemoperfusion has been recommended, forced diuresis, haemodialysis, and peritoneal dialysis have been reported to be not effective. Relapse and aggravation of symptomatology on the 2nd and 3rd day after overdose, due to delayed absorption, should be anticipated.

**Packs of 100 tablets (10 strips — each Contains 10 tablets)**

*This is a medicament:*

- A medicament is a product which affects your health, and its consumption contrary to the instructions is dangerous for you. Follow strictly the doctor's prescription, 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.