

B₆-Vicotrat[®] 300 mg



1. NAME OF THE MEDICINAL PRODUCT

B₆-Vicotrat[®] 300 mg

Coated tablet

Active pharmaceutical ingredient: pyridoxine hydrochloride

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 coated tablet contains 300 mg pyridoxine hydrochloride (vitamin B₆ hydrochloride)

Other ingredients with known effect: Lactose monohydrate, sucrose

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Coated tablet

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

B₆-Vicotrat[®] 300 mg is administered in adults for:

- Therapy for peripheral neuropathy due to drug induced vitamin B₆ deficiency (pyridoxine antagonists such as isoniazid, D-penicillamine, cycloserine e.g.).
- Therapy for pyridoxine dependent disorders (primary hyperoxaluria type I, homocystinuria, cystathioninuria, xanthurenic acid uria, sideroblastic anaemia, vitamin B₆ deficiency induced hypochromic microcytic anaemia).

4.2 Posology and method of administration

Dosage

Adults

Therapy for peripheral neuropathy due to drug induced vitamin B₆ deficiency.

Dosage must be defined by the treating doctor individually. Normally 50 to 300 mg pyridoxine hydrochloride daily are recommended.

Therapy for pyridoxine dependent disorders (primary hyperoxaluria type I, homocystinuria, cystathioninuria, xanthurenic acid uria, vitamin B₆ deficiency contingent hypochromic microcytic anaemia).

Dosage must be defined by the treating doctor individually. Normally 10 to 250 mg pyridoxine hydrochloride daily are recommended, in single cases even up to 600 mg pyridoxine hydrochloride per day (1 tablet B₆-Vicotrat 300 mg contains 300 mg pyridoxine hydrochloride).

Therapy for pyridoxine dependent disorders (sideroblastic anaemia).

Dosage must be defined by the treating doctor individually. Normally dosages as of 200 mg pyridoxine hydrochloride are recommended.

Children and adolescents

The pharmaceutical form and the dosage of 300 mg are not suitable for treatment of pyridoxine dependent cramp conditions in children and adolescents. Pharmaceuticals with lower amount of pyridoxine hydrochloride are available.

Note

For the treatment of simple vitamin B₆ deficiency 25 mg pyridoxine hydrochloride (vitamin B₆) are sufficient.

Method and duration of administration

Tablets should be taken unbrokenly with sufficient liquid.

Duration of treatment is adjusted to form and severity of the underlying illness and must be defined by the treating doctor individually.

4.3 Contraindications

Hypersensitivity to pyridoxine hydrochloride (vitamin B₆) or to any of the excipients listed in section 6.1.

Because of the amount of pyridoxine hydrochloride B₆-Vicotrat 300 mg is not appropriate for children and adolescents.

4.4 Special warnings and precautions for use

At long-term intake of daily doses of more than 50 mg pyridoxine hydrochloride or at short-term intake of doses in gram range peripheral sensory neuropathies were observed. If signs of a peripheral sensory neuropathy (paresthesia) occur the dosage has to be checked and adjusted if necessary.

Patients suffering from the rare hereditary fructose or glucose intolerance, glucose-galactose-malabsorption or from saccharase-isomaltase- or lactase-deficiency should not take B₆-Vicotrat 300 mg.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant administration of pyridoxine antagonists (e.g. hydralazine, isoniazid (INH), cycloserine, D-penicillamine) may increase the demand of vitamin B₆.

Vitamin B₆ in daily doses of more than 5 mg can reduce the effect of L-dopa.

4.6 Fertility, pregnancy and lactation

During pregnancy and lactation recommended daily supply for vitamin B₆ is 2.4 - 2.6 mg. There are no risks known so far for treatment with vitamin B₆, using the recommended doses for B₆-Vicotrat 300 mg. Methodic studies for treatment with vitamin B₆ in dosages more than the stated daily requirement do not exist. Therefore administration of this drug should be decided by the treating doctor only according to an accurate benefit/risk analysis. In pregnant women the daily dose for prophylaxis should not exceed 10 mg vitamin B₆, respectively 100 - 200 mg vitamin B₆ in case of "morning sickness".

High doses of vitamin B₆ may impede milk production.
Vitamin B₆ in its pyridoxal form passes into mother's milk.

4.7 Effects on ability to drive and use machines

None particular effects on drivers and the use of machines known so far.

4.8 Undesirable effects

Undesirable effects are due to overdose:

Nervous system disorders

At long-term intake of daily doses more than 50 mg pyridoxine hydrochloride (vitamin B₆) or at short-term intake of doses in gram range peripheral sensory neuropathies were observed (see 4.4 special warnings).

Gastrointestinal disorders

At higher amounts of intake gastrointestinal disorders were described.

Skin and subcutaneous tissue disorders

At very high daily doses photosensitivity was described.

General disorders and administration site conditions

At higher amounts of intake cases of vitamin B₆ addiction were described.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions to Bundesinstitut für Arzneimittel und Medizinprodukte, Abt. Pharmakovigilanz, Kurt-Georg-Kiesinger Allee 3, D-53175 Bonn, Website: www.bfarm.de.

4.9 Overdose

Symptoms of overdose

High doses of vitamin B₆ may impede milk production. Long-term intake (several months to years) of vitamin B₆ in doses more than 50 mg/day as well as short-term intake (2 months) of doses more than 1 g/day can lead to neurotoxic effects.

Basically, an overdose becomes apparent in sensory polyneuropathy, eventually with ataxia. Extreme high doses can manifest in cramps.

Therapy of overdose

If doses more than 150 mg/kg body weight were taken acutely, induced emesis and administration of charcoal are recommended. Emesis is most effective within the first 30 minutes after intake. If necessary, intensive medical measures are required.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: vitamin

ATC code: A11HA02 pyridoxine (vitamin B₆)

Vitamin B₆ in its phosphorylated form (pyridoxal-5'-phosphate, PALP) is the coenzyme of a variety of enzymes, which interfere in the entire unoxidative metabolism of amino acids. They are involved in the synthesis of physiologically active amines (e.g. adrenaline, histamine, serotonin, dopamine, tyramine) by decarboxylation, in anabolic and catabolic metabolisms (e.g. glutamate-oxalacetate-transaminase, alanine transaminase, γ -aminobutyric acid-, α -ketoglutarate-transaminase) by transamination as well as in several cleavages and syntheses of amino acids.

Vitamin B₆ joins in the metabolism of tryptophan at four different positions. Vitamin B₆ catalyses the α -amino- β -ketoacid generation in the context of haemoglobin synthesis. In addition, there are direct biochemical connections with other vitamins of the B-group.

Sources and fulfilment demand

Pyridoxine, pyridoxal and pyridoxamine are widespread in the plant and animal kingdom. Amongst others yeasts, grain (especially seedlings), soybeans, liver, kidneys, brain, muscular meat, milk, dairy products, green vegetables, potatoes, carrots and bananas contain major amounts of vitamin B₆.

Predominantly, pyridoxine is stored in muscular tissue as pyridoxal-5'-phosphate. The demand for vitamin B₆ depends basically on the protein metabolic rate and increases with protein intake. Vitamin B₆ supply of 0.02 mg per gram nutrient protein is recommended. To avoid a deficit, a daily vitamin B₆ supply of 1.8 mg for men and 1.6 mg for women is required. During pregnancy a bonus of 1.0 mg/day, during lactation a bonus of 0.6 mg/day is recommended (DGE 1991). Long-term administration of pharmaceuticals, diseases or metabolism disorders may demand additional supply.

Deficiency syndromes

In humans, pure vitamin B₆ deficiency is rare. Though, fulfilment demand of vitamin B₆ is not always assured in several high-risk groups such as adolescents, pregnant women or seniors. Vitamin B₆ deficiency is often associated with undersupply of further B-complex vitamins. Clinical symptoms can be quite variable. Following disorders can occur in partial consequence of vitamin B₆ deficiency:

- seborrheic, dermatitis like changes, blepharoconjunctivitis,
- hypochromic anaemia,
- peripheral neuritides,
- hyperoxaluria with calculus generation in the efferent urinary tract,
- cerebral cramps.

Indications for vitamin B₆ deficiency are amongst others:

- increased excretion of xanthurenic acid after tryptophan burden.
- reduced excretion of 4-pyridoxine acid.
- decreased serum levels for pyridoxal-5'-phosphate.
- decreased activity of the erythrocytic glutamate-oxalacetate-transaminase.

5.2 Pharmacokinetic properties

Pyridoxine, pyridoxal and pyridoxamine are absorbed quickly mostly in the upper gastrointestinal tract and are excreted at a maximum between 2 and 5 hours. The main excretion product is 4-pyridoxine acid. The phosphorylation of the CH₂OH-group in 5-position (PALP) is the precondition for the function as a coenzyme. In the blood PALP is bound to proteins for almost 80 %.

The stock of vitamins B₆ in the body is 40 - 150 mg, daily renal excretion is 1.7 - 3.6 mg and the daily turnover rate is 2.2 - 2.4 %.

By means of pharmacokinetic model calculations the following half-lives $t_{1/2}$ for vitamin B₆ kinetics in the body are estimated:

- a) Absorption of B₆ from the gastrointestinal tract into blood plasma
 $t_{1/2} = 10-30$ min.
- b) Excretion from blood plasma
 $t_{1/2} = 1-1.5$ hours.
- c) Absorption from blood plasma and extraction from the liver into the blood plasma are carried out with approximately the same time constant
 $t_{1/2} = 8-14$ days.

5.3 Preclinical safety data

a) Acute toxicity

See section 4.9 overdose

b) Chronic toxicity

In dogs oral administration of 150 - 200 mg vitamin B₆ (pyridoxine hydrochloride)/kg BW/day over a period of 100 - 107 days caused ataxias, muscular weakness, imbalances as well as degenerative disorders of the axons and myelin sheaths. Furthermore, convulsions and coordinative disorders occurred in animal experiments at high doses of vitamin B₆.

c) Mutagenic and carcinogenic potential

Under conditions of clinical treatment mutagenic effects of vitamin B₆ will not be expected. Long-term studies in animals to the carcinogenic potential of vitamin B₆ are not available.

d) Reproductive toxicity

The placenta is permeable for vitamin B₆ and the foetal concentrations are higher than the maternal ones. Vitamin B₆ is investigated insufficiently in animal experiments. An embryotoxicity study in rats revealed no indications for a teratogenic potential.

In male rats administration of very high doses of vitamin B₆ lead to damages in spermatogenesis.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Calcium behenate (DAB), calcium carbonate, carnauba wax, microcrystalline cellulose, copovidone, glycerol 85 %, lactose monohydrate, corn starch, methyl cellulose, methacrylic acid-methylmethacrylate copolymer (1:1) (Ph. Eu.), povidone K25, hydrogenated castor oil, shellac, high disperse silicon dioxide, sucrose, talc, titanium dioxide, triacetin, bleached wax.

6.2 Incompatibilities

None known so far.

6.3 Shelf life

The shelf life is five years.

This pharmaceutical should not be used after the expiry date.
The expiry date is printed on the blister and on the carton.

6.4 Special precautions for storage

Do not store above 25 °C.

Keep medicine out of the reach of children.

Store the blisters in the box to protect the substance from light.

6.5 Nature and contents of container

Original pack with 50 coated tablets in blisters
Original pack with 100 coated tablets in blisters

6.6 Special precautions for disposal and other handling

No special requirements for disposal.

7. MARKETING AUTHORISATION HOLDER

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8. MARKETING AUTHORISATION NUMBER

6814004.00.01

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 06.06.2000

Date of latest renewal: 01.02.2011

10. DATE OF REVISION OF THE TEXT

February 2015

11. PRESCRIPTION STATE

By prescription only