I-APE/APP-0U

BA7Q

NOVARTIS

Pizotifen
Vitamin B-Complex

	Per Capsule	Per 5 mL Syrup
Pizotifen	500 mcg	250 mcg
Vitamin B_1	3.0 mg	700 mcg
Vitamin B_2	3.2 mg	1.14 mg
Vitamin B_6	2.4 mg	700 mcg
Nicotinamide	19.0 mg	5 mg

*(Inn rec.)

Appetens®

Capsule/Syrup

H_1 Receptors - Blocker with Vitamin B-Complex

Properties

Pizotifen has an appetite-stimulating action suitable for increasing body weight in underweight anorectic patients. The compound is well tolerated, permitting treatment of anorexia both in children and adults.

In elderly people, pizotifen has been shown to improve disturbed mood by alleviating symptoms such as hopelessness, feeling of dejection or oppression, asthenia, anxiety, restlessness, sleep disturbances, and impairment of concentration or memory.

Owing to its inhibitory effect on biogenic amines, pizotifen is also used for the prophylactic treatment of migraine.

Pharmacokinetics

Absorption

Absorption of pizotifen is fast (absorption half-life 0.5 to 0.8 hours) and nearly complete (80%).

Biotransformation

Pizotifen is metabolized with a half-life of about 1hour. The main metabolite (N-glucuronide) is eliminated with a half-life of approximately 23 hours.

Distribution

Protein binding of pizotifen amounts to 91%, and the distribution volume to 485 L.

Elimination

Less than 1% of the administered dose of pizotifen is excreted unchanged in the urine, whereas 55% is excreted as metabolites.

Special patient groups

In patients with kidney insufficiency, dosage adjustmentsmay be necessary.

Indications

- Anorexia of somatic or psychogenic origin in under-weight patients, supplementary to the treatment of the underlying condition, such as infectious or parasitic diseases (including convalescence), chronic diarrhea, anorexia nervosa or depressive states in the elderly.
  Note: Priority should always be given to identifying and treating the underlying cause.
- Depressive mood in the elderly.

Posology and method of administration

Anorexia in underweight patients

Adults

Starting with 0.5 mg per day, the dosage should be progressively increased up to 0.5 mg 3 times daily.

Children

Small initial doses should be gradually increased up to an average maintenance of 0.025 mg per kg body weight daily; this dose may be given in 2 Or 3 divided doses or as directed by the physician.

2 to 6 years: 5 to 10 mL syrup (0.25 to 0.50 mg)

6 to 12 years: 10 to 20 mL syrup (0.50 to 1.0mg)

Mood elevation in elderly patients

The dosage should be adjusted to individual needs and the severity of the symptoms. A starting dose of 0.5 mg daily is recommended, preferably increasing by 0.5 mg per day. For most patients, the daily optimum dose is 2 to 3 mg in divided doses, but up to 12 mg were well tolerated. Following improvement, usually within 6 to 8 weeks, gradual reduction, or withdrawal of treatment can be attempted.

Contraindications

Known hypersensitivity to pizotifen or any of the excipients. Appetens should not be given to children under 2 years of age.

Special warnings and special precautions for use

In view of the slight anticholinergic effect of pizotifen, caution is required in patients with narrow-angle glaucoma (except those successfully treated by surgery) or urinary retention (e.g. in prostatic enlargement). Up to now, no untoward reactions have been reported in such patients, not even in the elderly, when given the recommended dose.

Appetens increase appetite and may lead to an increase in body weight. However, weight gain is dependent on adequate food intake, and anorexia must be differentiated from malnutrition.

Appetens should be kept out of the reach of children .

Interaction with other medicaments and other forms of interactions

Central effect of sedatives, hypnotics, antihistamines including certain common cold preparations, and alcohol may be enhanced.

Pregnancy and Lactation

As clinical data with pizotifen in pregnancy are very limited, Appetens should be administered in pregnancy only under compelling circumstances.

Although the concentration of pizotifen measured in the milk of treated mothers are not likely to affect the infant, the use of Appetens in nursing mothers is not recommended.

Effect on the ability to drive and use machines

Patients should be warned that, owing to its possible sedative effect, Appetens may slow their reactions when driving vehicle, operating machinery, etc.

Side effects

Common side-effect is sedation; more rarely on dizziness, dry mouth, nausea, and constipation. In children CNS stimulation may occur. In a few, poorly documented cases, hallucinations were reported during treatment with pizotifen in children and adults, but a causal relationship was not established.

Preclinical safety data

Chronic / subchronic toxicity

In oral 26-week toxicity studies, rats received doses of 5, 16 and 55 mg/kg per day, and dogs, doses of 3, 10 and 30 mg/kg per day. In rats, a slight and dose-dependent impaired weight gain and reduced feed intake were observed. Based on the findings in rats, the potential target organs were the liver and possibly the thyroid. The no-toxic-effect level was 5 mg/kg per day. In dogs, body weights were slightly impaired at 10 mg/kg per day and higher. Based on the findings in the dogs, the potential target organs were again liver and thyroid. The no-toxic-effect level in the dog was 3 mg/kg per day. In 2-year oral toxicity studies in rats, with doses of 3, 9, and 27 mg/kg per day, the no-toxic-effect level could be set between 9 and 27 mg/kg per day. After the 2-year treatment of dogs with 1,3 and 9 mg/kg per day, the liver was identified as potential target organ. 3 mg/kg per day may be regarded as no-toxic-effect level.

Reproduction studies

In embryotoxicity studies in both rats and rabbits, the animals were orally treated with 3,10 and 30 mg/kg per day during organogenesis. No embryolethal or teratogenic effect was observed in rats or rabbits. In a rat study investigating fertility, general reproductive performance and peri-/post-natal effects, the oral doses were 3,10 and 30 mg/kg per day. Pizotifen has no adverse effects on the fertility of the parent generation, and also did not impair the development of their progeny.

Mutagenicity

There was no evidence of a mutagenic potential of pizotifen after in vitro or in vivo examinations.

Overdosage

Symptoms which may be expected are: drowsiness, nausea, hypotension, dizziness, excitatory states (in children), respiratory depression, convulsion (particularly in children), coma.

Treatment: Administration of activated charcoal is recommended; in case of very recent intake, gastric lavage may be considered. If necessary, symptomatic treatment, including monitoring of the cardiovascular and respiratory systems. For excitatory states or convulsion, benzodiazepines may be used.

Caution

Foods, Drugs, Devices and Cosmetics Act prohibits dispensing without prescription.

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