

BAMBEC ORAL SOLUTION 1 mg/ml ASTRAZENECA

bambuterol hydrochloride
oral solution

Composition

One ml contains:

Bambuterol hydrochloride 1 mg

Pharmaceutical Form

Oral solution in plastic bottle.

Indications

Bronchial asthma. Chronic bronchitis, emphysema and other lung diseases, where bronchospasm is a complicating factor.

Dosage and method of administration

Bambec should be used as maintenance therapy in asthma and other pulmonary diseases where bronchospasm is a complicating factor.

Bambec is dosed once daily, preferably shortly before bed-time. The dose should be individual.

Adults: The recommended initial dose is 10 mg (10 ml). The dose may be increased to 20 mg (20 ml) after 1-2 weeks, depending on the clinical effect. In patients who previously have tolerated oral beta2-agonists well, the recommended initial dose is 20 mg (20 ml).

In patients with an impaired renal function (GFR \leq 50 ml/min) the recommended initial dose is 5 mg (5 ml).

Elderly: Dosage as for adults.

Children 2-5 years: The recommended normal dose is 10 mg (10 ml).

Children 6-12 years: The recommended initial dose is 10 mg (10 ml). The dose may be increased to 20 mg (20 ml) after 1-2 weeks, depending on the clinical effect.

Because of differences in kinetics, doses above 10 mg (10 ml) are not recommended in Oriental children.

Contra-Indications

Hypersensitivity to any of the ingredients or to terbutaline.

Special warnings and special precautions for use

As terbutaline is excreted mainly via the kidneys, the initial dose of Bambec should be halved in patients with an impaired renal function (GFR \leq 50 ml/min).

In patients with liver cirrhosis, and probably in patients with other causes of severely impaired liver function, the daily dose must be individualized, taking into account the possibility that the individual patient could have an impaired ability to metabolize bambuterol to terbutaline. Therefore, from a practical point of view, the direct use of the active metabolite, terbutaline (Bricanyl), is preferable in these patients.

As for all β 2-agonists, caution should be observed in patients with thyrotoxicosis and in patients with severe cardiovascular disorder, such as ischemic heart disease, tachyarrhythmias or severe heart failure.

Due to the hyperglycemic effects of β 2-agonists, additional blood glucose controls are recommended initially in diabetic patients.

Potentially serious hypokalemia may result from β 2-agonist therapy. Particular caution is recommended in acute severe asthma as the associated risk may be augmented by hypoxia. The hypokalemic effect may be potentiated by concomitant treatments (see Interactions). It is recommended that serum potassium levels are monitored in such situations.

Interactions

Bambuterol prolongs the muscle-relaxing effect of suxamethonium (succinylcholine). This is due to the fact that plasma cholinesterase, which inactivates suxamethonium, is partly inhibited by bambuterol. The inhibition is dose-dependent and fully reversible. This interaction should also be considered with other muscle relaxants which are metabolized by plasma cholinesterase.

Beta-receptor blocking agents (including eye-drops), especially those which are non-selective, may partly or totally inhibit the effect of beta-stimulants.

Hypokalemia may result from β_2 -agonist therapy and may be potentiated by concomitant treatment with xanthine derivatives, steroids and diuretics (see Warnings and Precautions).

Pregnancy and lactation

Although no teratogenic effects have been observed in animals after administration of bambuterol, caution is recommended during the first trimester of pregnancy. It is not known whether bambuterol or intermediary metabolites pass over to breast milk. Terbutaline passes over to breast milk but an influence on the child is unlikely with therapeutic doses. Transient hypoglycemia has been reported in newborn preterm infants after maternal beta2-agonist treatment.

Undesirable effects

Adverse reactions which have been recorded, e.g. tremor, headache, tonic muscle cramps and palpitations, are all characteristic of sympathomimetic amines. The intensity of the adverse reactions is dose-dependent. The majority of these effects have reversed spontaneously within the first 1-2 weeks of treatment.

Urticaria and exanthema may occur.

Sleep disturbances and behavioural disturbances, such as agitation, hyperactivity and restlessness, have been observed.

Overdose

No case of Bambec overdose has been reported. However, it is likely that overdosing would result in high levels of terbutaline and therefore the same symptoms and signs as recorded after overdose with Bricanyl: Headache, anxiety, tremor, tonic muscle cramps, palpitations, tachycardia.

A fall in blood pressure sometimes occurs after terbutaline overdose. Laboratory findings: hyperglycemia and lactacidosis sometimes occur. High doses of beta2-agonists may cause hypokalemia as a result of redistribution of potassium.

Overdosage with Bambec is likely to cause a considerable inhibition of plasma cholinesterase, that may last for days (see also under "Interactions").

Treatment of overdose

Usually no treatment is required. In severe cases of overdose, the following measures should be considered:

Gastric lavage, activated charcoal. Determine acid-base balance, blood glucose and electrolytes. Monitor heart rate and rhythm and blood pressure. The preferred antidote for overdose with Bambec is a cardioselective beta-blocking agent, but beta-blocking drugs should be used with caution in patients with a history of bronchospasm. If the beta2-mediated reduction in peripheral vascular resistance significantly contributes to the fall in blood pressure, a volume expander should be given.

Pharmacodynamic properties

Bambec contains bambuterol, a prodrug of the adrenergic beta-receptor agonist terbutaline, which predominantly stimulates beta2-receptors, thus producing relaxation of bronchial smooth muscle, inhibition of the release of endogenous spasmogens, inhibition of edema caused by endogenous mediators and increased mucociliary clearance.

Pharmacokinetic properties

About 20% of an oral dose of bambuterol is absorbed. The absorption is not influenced by concomitant intake of food. After absorption, bambuterol is slowly metabolized via hydrolysis (plasma cholinesterase) and oxidation to active terbutaline. About 1/3 of the absorbed dose of bambuterol is metabolized in the intestinal wall and in the liver, mainly to intermediary metabolites.

Of the administered dose of bambuterol, about 10% is converted to terbutaline in adults. Children have a reduced clearance of terbutaline, but they also generate less terbutaline than adults. Therefore children aged 6-12 years should be given adult doses, whereas smaller children (2-5 years) usually need less.

Maximum plasma concentration of the active metabolite terbutaline is achieved within 2-6 hours. The effect-duration is at least 24 hours. Steady-state is reached after 4-5 days of treatment. The plasma half-life of bambuterol after oral administration is about 13 h. The plasma half-life of the active generated metabolite terbutaline is about 22 h.

Bambuterol and its metabolites, including terbutaline, are mainly excreted via the kidneys.

Preclinical safety data

The acute toxicity of bambuterol has been evaluated in studies in mice and rats and is rated as moderate. Repeated dose toxicity studies (1-12 months) in dogs revealed hyperemia, tachycardia and myocardial lesions, observations consistent with the known effects of β -agonists.

In a 24-month carcinogenicity study in rats, a slightly increased incidence of thyroid follicular adenomas was noted at a dose of bambuterol that was more than 500 times the daily dose in humans. At doses about 150 times the clinical dose no such effect was found. The mechanism of development of thyroid adenomas in rats is considered to be a result of increased secretion of thyroid-stimulating hormone, induced by increased clearance of thyroxine. Such effects have previously been reported for a number of currently marketed drugs.

Pharmaceutical particulars

List of excipients

One ml contains: sorbitol, glycerol, sodium benzoate, citric acid, sodium hydroxide, essence blackcurrant, water purified.

Special precautions for storage

Do not store above 30°C.

Instructions for use/handling

The following instructions apply to opening the Bambec oral solution bottle

Grasp the tear off seal and pull it, until it comes off the bottle.

Push down on the cap and turn it around, until the arrows are lined up.

Lift the cap off. You can now take out the contents of the bottle.

Replace the cap and close it well by turning it around (the cap will then remain child resistant).

Shelf life: Please see outer pack

Pack size: Please see outer pack

Date of revision: November 4, 1997