Bambec Tablets 10mg

Summary of Product Characteristics Updated 15-Jun-2017 | AstraZeneca UK Limited

1. Name of the medicinal product

Bambec Tablets 10 mg

2. Qualitative and quantitative composition

Each tablet contains 10 mg Bambuterol hydrochloride

Excipient(s) with known effect

Each tablet contains 63 mg of lactose (as monohydrate).

For the full list of excipients, see section 6.1.

3. Pharmaceutical form

Tablet

4. Clinical particulars

4.1 Therapeutic indications

Management of asthma, bronchospasm and/or reversible airways obstruction.

4.2 Posology and method of administration

Posology

Bambec is formulated as a tablet and should be taken once daily, shortly before bedtime. The dose should be individualised.

Patients must receive optimal anti-inflammatory therapy (e.g. inhaled corticosteroids, leukotriene receptor antagonists) when using Bambec for management of asthma.

Adults:

The recommended starting doses are 10 mg–20 mg. The 10 mg dose may be increased to 20 mg if necessary after 1–2 weeks, depending on the clinical effect.

In patients who have previously tolerated β_2-agonists well, the recommended starting dose, as well as maintenance dose, is 20 mg.

Elderly:

Dose adjustment is not required in the elderly.

Hepatic Impairment:

Significant hepatic dysfunction: Not recommended because of unpredictable conversion to terbutaline.

Renal impairment:

Moderate to severely impaired renal function (GFR < 50 ml/min): It is recommended that the starting dose of Bambec should be halved in these patients.

Paediatric population:

Until the clinical documentation has been completed, Bambec should not be used in children.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1. Bambec is presently not recommended for children due to limited clinical data in this age group.

4.4 Special warnings and precautions for use

As terbutaline is excreted mainly via the kidneys, the dose of Bambec should be halved in patients with an impaired renal function (GFR ≤ 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 individualised, taking into account the possibility that the individual patient could have an impaired ability to metabolise 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.

Cardiovascular effects may be seen with sympathomimetic drugs, including Bambec. There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischaemia associated with beta agonists. Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving Bambec should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin.

Although Bambec is not indicated for the treatment of premature labour it should be noted that bambuterol is metabolised to terbutaline and that terbutaline should not be used as a tocolytic agent in patients with pre-existing ischaemic heart disease or those patients with significant risk factors for ischaemic heart disease.

Due to the hyperglycaemic effects of β_2-agonists, additional blood glucose controls are recommended initially in diabetic patients.

Due to the positive inotropic effects of β_2-agonists these drugs should not be used in patients with hypertrophic cardiomyopathy.

β_2-agonists may be arrhythmogenic and this must be considered in the treatment of the individual patient.

Unpredictable inter-individual variation in the metabolism of bambuterol to terbutaline has been shown in subjects with liver cirrhosis. The use of an alternative β_2-agonist is recommended in patients with cirrhosis and other forms of severely impaired liver function.

Potentially serious hypokalaemia 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 hypokalaemic effect may be potentiated by concomitant treatments (see section 4.5). It is recommended that serum potassium levels are monitored in such situations.

Asthma patients who require treatment with Bambec must have optimum anti-inflammatory treatment, e.g. inhaled corticosteroids, leukotriene receptor antagonists. The patients must be instructed to continue taking their anti-inflammatory medication after the start of treatment with Bambec, even if the asthma symptoms diminish. If a previously effective dosage regimen no longer gives the same symptomatic relief this suggests that the underlying disease has worsened. The patient should urgently seek further medical advice and a re-evaluation of the asthma treatment must be carried out. Consideration should be given to the requirements for additional therapy (including increased dosages of anti-inflammatory medication). Treatment with Bambec must not be begun or the dose increased during an acute exacerbation of the asthma. Severe exacerbations of asthma should be treated as an emergency in the usual manner.

Precaution should be applied when treating patients predisposed to angle closure glaucoma.

Bambec tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Halogenated anaesthetics

Halothane anaesthesia should be avoided during β_2-agonists treatment, since it increases the risk of cardiac arrhythmias. Other halogenated anaesthetics should be used cautiously together with β_2-agonists.

Bambuterol prolongs the muscle-relaxing effect of suxamethonium (succinylcholine). A prolongation of the muscle-relaxing effect of suxamethonium of up to 2-fold has been observed in some patients after taking Bambec 20 mg on the evening prior to surgery. The inhibition is dose-dependent and fully reversible after cessation of treatment with bambuterol. This is due to the fact that plasma cholinesterase, which inactivates suxamethonium, is partly inhibited by bambuterol. Studies on the effects on plasma cholinesterase showed that bambuterol inhibited activity, but that this was reversible. However in extreme situations, the interaction may result in a prolonged apnoea time which may be of clinical importance. This interaction should also be considered with other muscle relaxants, which are metabolised 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. Therefore, Bambec tablets and non-selective β-blockers should not normally be administered concurrently.

Potassium depleting agents and hypokalaemia

Owing to the hypokalaemic effect of beta agonists, concurrent administration of serum potassium depleting agents known to exacerbate the risk of hypokalaemia, such as diuretics, methyl xanthines and corticosteroids, should be administered cautiously after careful evaluation of the benefits and risks with special regard to the increased risk of cardiac arrhythmias arising as a result of hypokalaemia (see Section 4.4). Hypokalaemia also predisposes to digoxin toxicity.

Bambec should be used with caution in patients receiving other sympathomimetics.

Six cases have been reported where concomitant treatment with salbutamol and ipratropium, used in asthma (nebuliser), has caused narrow angle glaucoma. Terbutaline is likely to interact, similar to salbutamol, with ipratropium when administered in a nebuliser. The combination is discouraged in predisposed patients.

4.6 Fertility, pregnancy and lactation

Pregnancy

Although no teratogenic effects have been observed in animals after administration of bambuterol, caution is recommended during the first trimester of pregnancy.

Beta-agonists for asthma and other pulmonary diseases should be used with caution at the end of pregnancy because of the tocolytic effect.

Transient hypoglycaemia has been reported in newborn preterm infants after maternal β_2-agonist treatment.

Breast-feeding

It is unknown whether bambuterol or intermediary metabolites are excreted in human breast milk. Terbutaline, the active metabolite of bambuterol, is excreted in breast milk, but at therapeutic doses of terbutaline no effect on breastfed newborns/infants are anticipated. A decision must be made whether to discontinue breast-feeding or to discontinue Bambec therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

4.7 Effects on ability to drive and use machines

Bambec has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Most of the adverse reactions are characteristic of sympathomimetic amines. The intensity of the adverse reactions is dose-dependent. Tolerance to these effects has usually developed within 1-2 weeks.

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: Very common (≥1/10), Common (≥1/100 to <1/10), Uncommon (≥1/1000 to < 1/100), Rare (≥1/10,000 to < 1/1,000), Very rare (<1/10,000) and Not known (cannot be estimated from available data).

System Organ Class (SOC)	**Frequency Classification**	**Adverse Drug Reaction**
Immune system disorders	Not known	Hypersensitivity reactions including Angioedema, Urticaria, Exanthema, Bronchospasm, Hypotension and Collapse.
Metabolism and nutrition disorders	Not known	Hypokalemia Hyperglycaemia
Psychiatric disorders	Very Common	Behavioural Disturbances, such as Restlessness
	Common	Sleep disturbances
	Uncommon	Behavioural Disturbances, such as Agitation
	Not known	Dizziness Hyperactivity

Nervous system disorders	Very common	Tremor, Headache
Cardiac disorders	Common	Palpitations
	Uncommon	Tachycardia Cardiac arrhythmias, e.g. Atrial Fibrillation, Supraventricular tachycardia and Extrasystoles
	Not known	Myocardial ischemia (see section 4.4)
Respiratory, thoracic and mediastinal disorders	Unknown	Paradoxical bronchospasm
Gastrointestinal disorders	Not known	Nausea
Musculoskeletal, connective tissue and bone disorders	Common	Muscle cramps

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 via the Yellow Card Scheme.

Website: www.mhra.gov.uk/yellowcard.

4.9 Overdose

Symptoms

Overdosing may result in high levels of terbutaline and therefore the same symptoms and signs as recorded after overdosage with Bricanyl: Headache, anxiety, tremor, nausea, tonic muscle cramps, palpitations, tachycardia and cardiac arrhythmias.

A fall in blood pressure sometimes occurs after terbutaline overdosage.

Laboratory findings: Hyperglycaemia and lactic acidosis sometimes occur. High doses of β2-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 section 4.5).

Management

Usually no treatment is required. In particularly severe cases of overdosage, the following measures may be considered on a case-by-case basis: Gastric lavage and activated charcoal.

Determine acid-base balance, blood glucose and electrolytes. Monitor heart rate and rhythm and blood pressure. The preferred antidote for haemodynamically significant cardiac arrhythmias is a cardioselective beta-blocking agent, but beta-blocking drugs should be used with caution in patients with a history of bronchospasm. If the β_2-mediated reduction in peripheral vascular resistance significantly contributes to the fall in blood pressure, a volume expander should be given.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: selective β_2-agonists, bambuterol, ATC code: R03C C12.

Mechanism of action

Bambuterol is an active precursor of the selective β_2-adrenergic agonist terbutaline. Bambuterol is the bis-dimethylcarbamate of terbutaline, and is present in the formulation as a 1:1 racemate.

Pharmacodynamic effects

Pharmacodynamic studies have shown that after oral administration of bambuterol to guinea pigs, a sustained protective

effect was achieved against histamine-induced bronchoconstriction. At equipotent doses, the duration of the relaxing activity was more prolonged than after plain terbutaline. Bambuterol, or the monocarbamate ester, did not exert any smooth muscle relaxing properties. The bronchoprotective effects seen after oral administration of bambuterol are related to the generation of terbutaline, as were the secondary effects (effects on other organs).

Pharmacodynamic studies have been conducted in asthmatics and healthy volunteers. The effects observed were bronchodilation, tremor and increases in heart rate. The metabolic effects included a small increase in blood glucose, while the effect on serum potassium was negligible. In short-term studies on lipoprotein metabolism, an increase in HDL cholesterol has been observed. In conclusion, all pharmacodynamic effects observed can be ascribed to the active metabolite terbutaline.

5.2 Pharmacokinetic properties

Absorption

On average, 17.5% of an oral dose is absorbed. Approximately 70–90% of the absorption occurs in the first 24 hours.

Biotransformation

Bambuterol is metabolised in the liver and terbutaline is formed by both hydrolysis and oxidation. After absorption from the gut, about 2/3 of terbutaline is first-pass metabolised, bambuterol escapes this first-pass metabolism. Of the absorbed amount, about 65% reaches the circulation. Bambuterol therefore has a bioavailability of about 10%.

Distribution

Protein binding of bambuterol is low, 40–50% at therapeutic concentrations.

Elimination

The terminal half-life of bambuterol after an oral dose is 9–17 hours.

Hepatic Impairment

All categories of subjects studied were able to form terbutaline in a predictive way except for liver cirrhotics.

5.3 Preclinical safety data

Bambuterol has not revealed any adverse effects which pose a risk to man at therapeutic dosages in the toxicity studies.

Bambuterol is given as a racemate: (-)-bambuterol is responsible for the pharmacodynamic effects via generation of (-)-terbutaline. (+)-bambuterol generates the pharmacodynamic inactive (+)-terbutaline. Both (+) and (-)-bambuterol are equally active as plasma cholinesterase inhibitors. This inhibition is reversible.

The toxicity studies showed that bambuterol has β_2-stimulatory effects, expressed as cardiotoxicity in dogs, and at high doses, observed in the acute toxicity studies, cholinergic effects.

There is no evidence from the preclinical safety data to indicate that bambuterol cannot be used in man for the intended indications with sufficient safety.

6. Pharmaceutical particulars

6.1 List of excipients

Lactose monohydrate; maize starch; povidone; microcrystalline cellulose; magnesium stearate; water, purified.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30°C.

6.5 Nature and contents of container

Amber glass bottle with LD-polyethene cap: 7, 14, 28, 30, 56 or 100 tablets.

HDPE container with LD-polyethene cap: 7, 14, 28, 30, 56 or 100 tablets.

HDPE container with polypropylene cap: 7, 14, 28, 30, 56 or 100 tablets.

PVC blisters: 7, 14, 28, 30, 56 or 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

No special requirements.

7. Marketing authorisation holder

AstraZeneca UK Ltd.,

600 Capability Green,

Luton, LU1 3LU, UK.

8. Marketing authorisation number(s)

PL 17901/0103

9. Date of first authorisation/renewal of the authorisation

Date of first authorisation: 4th August 1992

Date of latest renewal: 21st May 2002

10. Date of revision of the text

25th January 2017

Company Contact Details

AstraZeneca UK Limited

Address
Horizon Place, 600 Capability Green, Luton, Bedfordshire, LU1 3LU

Fax
+44 (0)1582 838 000

Medical Information e-mail
medical.informationuk@astrazeneca.com

Medical Information Fax
+44 (0)1582 838 003

Telephone
+44 (0)1582 836 000

Medical Information Direct Line
0800 783 0033

Customer Care direct line
+44 (0)1582 837 837

Medical Information Website
https://medicalinformation.astrazeneca.co.uk/