SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Bricanyl Turbohaler, 0.5 mg/dose, inhalation powder

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each delivered dose contains:
Terbutaline sulfate 0.4 mg (which corresponds to 0.5mg metered dose).

Excipients with known effect
Bricanyl Turbohaler 0.5mg/dose: each delivered dose contains approximately 0.4 mg of lactose monohydrate.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Inhalation powder.
A white inhaler comprising a blue turning grip, an integral dose indicator and a white cover.

4. CLINICAL PARTICULARS

4.1. Therapeutic Indications

Terbutaline is a selective β_2-adrenergic agonist recommended for the relief and prevention of bronchospasm in bronchial asthma and other bronchopulmonary disorders in which bronchospasm or reversible airways obstruction is a complicating factor.

4.2 Posology and method of administration

Posology

Adults and Children: One inhalation (0.5mg) as required. Not more than 4 inhalations should be required in any 24-hour period.

The duration of action of a single dose is up to 6 hours.

Elderly: Dosage as for adults.

Method of administration

Instructions for use and cleaning are provided in the Patient Information Leaflet, which can be found in each pack.

4.3 Contraindications

Hypersensitivity to the active substance (terbutaline) or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

Patients should be instructed in proper use and their inhalation technique checked regularly.

With each inhalation a fraction of the delivered dose will be deposited in the oral cavity. To minimize unnecessary systemic exposure to terbutaline, the patients should be advised to, when possible, rinse their mouth after each use.

Patients who are prescribed regular anti-inflammatory therapy should be advised to continue taking their anti-inflammatory medication even when symptoms decrease and they do not require Bricanyl Turbohaler.

If a previously effective dosage regimen no longer gives the same symptomatic relief, the patient should seek medical advice as soon as possible as this could be a sign of worsening asthma and warrants a reassessment of the asthma therapy. Consideration should be given to the requirements for additional therapy (including increased dosages of anti-inflammatory medication). Severe exacerbations of asthma should be treated as an emergency in the usual manner.

Overuse of short-acting beta-agonists may mask the progression of the underlying disease and contribute to deteriorating asthma control, leading to an increased risk of severe asthma exacerbations and mortality.

Patients who take more than twice a week additional “as needed” terbutaline should be re-evaluated for proper treatment adjustment as these patients are at risk for overuse of terbutaline.

As for all $beta_2$-agonists caution should be observed in patients with thyrotoxicosis.

Due to the positive inotropic effect of $beta_2$-agonists, these drugs should not be used in patients with hypertrophic cardiomyopathy.

Cardiovascular effects may be seen with sympathomimetic drugs, including Bricanyl. 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 Bricanyl 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.

Due to the hyperglycaemic effects of $beta_2$-agonists, additional blood glucose controls are recommended initially in diabetic patients.

Potentially serious hypokalaemia may result from $beta_2$-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.

Bricanyl Turbohaler contains lactose monohydrate (<1 mg/inhalation). This amount does not normally cause problems in lactose intolerant people. The lactose may contain small amounts of milk protein residues. In patients with hypersensitivity to milk proteins, these small amounts may cause allergic reactions.
Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take this medicine.

4.5 Interaction with other medicinal products and other forms of interaction

Beta-blocking agents (including eye drops), especially the non-selective ones such as propranolol, may partially or totally inhibit the effect of beta-stimulants. Therefore, Bricanyl preparations and non-selective beta-blockers should not normally be administered concurrently. Bricanyl should be used with caution in patients receiving other sympathomimetics.

Halogenated anaesthetics
Halothane anaesthesia should be avoided during $beta_2$-agonists treatment, since it increases the risk of cardiac arrhythmias. Other halogenated anaesthetics should be used cautiously together with $beta_2$-agonists.

Potassium depleting agents and hypokalaemia
Owing to the hypokalaemic effect of beta-agonists, concurrent administration with Bricanyl 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.

Paediatric population
Interaction studies have only been performed in adults.

4.6 Fertility, pregnancy and lactation

Pregnancy

Although no teratogenic effects have been observed in animals or in patients, Bricanyl should only be administered with caution during the first trimester of pregnancy.

Breast-feeding

Terbutaline is secreted via breast milk but any effect on the infant is unlikely at therapeutic doses.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Summary of the safety profile

The frequency of adverse reactions is low at the recommended dose. Terbutaline given by inhalation is unlikely to produce significant systemic effects when given in recommended doses. Most of the adverse reactions are characteristic of sympathomimetic amines. The majority of these effects have reversed spontaneously within the first 1-2 weeks of treatment.

The frequency of side effects is low at the recommended doses.

Bricanyl Turbohaler inhalation powder contains lactose. The excipient lactose may contain small amounts of milk protein residues. In patients with hypersensitivity to milk protein**s**, these small amounts may cause allergic reactions.

Tabulated list of adverse reactions

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥1/10), common (≥1/100 and <1/10), uncommon (≥1/1,000 and <1/100), rare (≥1/10,000 and <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data).

System Organ Class (SOC)	**Frequency Classification**	**Adverse Drug Reaction Preferred term (PT)**
Immune System Disorders	Not Known ^	Hypersensitivity reactions including angioedema, bronchospasm, hypotension and collapse
Metabolism and Nutrition Disorders	Common (≥1/100 to <1/10)	Hypokalaemia (See section 4.4)
Psychiatric Disorders	Not Known ^	Sleep disorder and Behavioural disturbances, such as agitation and restlessness
Nervous System Disorders	Very Common (≥1/10)	Tremor Headache
Cardiac Disorders	Common (≥1/100 to <1/10)	Tachycardia Palpitations
	Not Known ^	Arrhythmias, e.g. atrial fibrillation, supraventricular tachycardia and extrasystoles Myocardial ischaemia (See section 4.4)
Vascular Disorders	Not Known ^	Peripheral vasodilation
Respiratory, Thoracic and Mediastinal Disorders	Not Known ^	Paradoxical bronchospasm *
Gastrointestinal Disorders	Not Known ^	Nausea Mouth and throat irritation
Skin and Subcutaneous Tissue Disorders	Not Known ^	Urticaria Rash
Musculoskeletal and Connective Tissue Disorders #	Common (≥1/100 to <1/10)	Muscle spasms

A few patients feel tense; this is also due to the effects on skeletal muscle and not to direct CNS stimulation.

^ Reported spontaneously in post-marketing data and therefore frequency regarded as not known

* In rare cases, through unspecified mechanisms, paradoxical bronchospasm may occur, with wheezing immediately after inhalation. This should be immediately treated with a rapid-onset bronchodilator. Bricanyl therapy should be discontinued and after assessment, an alternative therapy initiated.

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 or search for MHRA Yellow Card in the Google Play or Apple App Store.

4.9 Overdose

There is a potential for progressive accumulation of dry powder in the mouthpiece of the Bricanyl Turbuhaler that could be released if dropped (for example, from a table) towards the end of inhaler life. To minimize unnecessary systemic exposure to terbutaline, the patients should be advised to, when possible, rinse their mouth after each use.

i) Possible symptoms and signs:
Headache, anxiety, tremor, nausea, tonic cramp, palpitations, tachycardia and arrhythmia. A fall in blood pressure sometimes occurs. Laboratory findings: Hypokalaemia, hyperglycaemia and metabolic acidosis sometimes occur.

ii) Treatment:
Mild and moderate cases: Reduce the dose.

Severe cases: Gastric lavage, administration of activated charcoal (where suspected that significant amounts have been swallowed). Determination of acid-base balance, blood sugar and electrolytes, particularly serum potassium levels. Monitoring of heart rate and rhythm and blood pressure. Metabolic changes should be corrected. A cardioselective beta-blocker (e.g. metoprolol) is recommended for the treatment of arrhythmias causing haemodynamic deterioration. The beta-blocker should be used with care because of the possibility of inducing bronchoconstriction: use with caution in patients with a history of bronchospasm. If the $beta_2$-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

Pharmaco-therapeutic group: selective beta$_2$-adrenoreceptor agonist, terbutaline, ATC code: R03A C03.

Terbutaline sulfate is a selective beta$_2$-adrenoceptor agonist, thus producing relaxation of bronchial smooth muscle, inhibition of the release of endogenous spasmogens, inhibitions of oedema caused by endogenous mediators, increased mucociliary clearance and relaxation of the uterine muscle.

5.2 Pharmacokinetic properties

After inhalation via Turbohaler, the absolute pulmonary bioavailability is about 16% of the delivered dose at a normal inhalation flow rate. Following administration of a single 1.5 mg dose (3 inhalations of 0.5 mg), maximum plasma concentration (C_{max}) of terbutaline of 12 nmol/L was achieved around 1.3 hours post-dose (t_{max}); the area under the plasma concentration-time curve (AUC_{inf}) was 96.6 nmol*h/L and elimination half-life ($t_{1/2}$) was about 12 hours. Terbutaline is mainly metabolised by conjugation with sulphuric acid and excreted as the sulfate conjugate. No active metabolites are formed. Data suggest that inhaled terbutaline acts topically in the airways.

5.3. Pre-clinical Safety Data

The major toxic effect of terbutaline, observed in toxicological studies in rats and dogs at exposures in excess of maximum human exposure, is focal myocardial necrosis. This type of cardiotoxicity is a well-known pharmacological manifestation seen after the administration of high doses of β_2-agonists.

In rats an increase in the incidence of benign uterine leiomyomas has been observed. This effect is looked upon as a class-effect observed in rodents after long exposure to high doses of β_2-agonists.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose monohydrate (which may contain milk protein residue).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months

6.4. Special Precautions for Storage

Do not store above 30ºC.

6.5 Nature and contents of container

Bricanyl Turbohaler consists of a number of assembled plastic details, the main parts being the dosing mechanism, the drug substance store, the desiccant store and the mouthpiece. The inhaler is protected by an outer tubular cover screwed onto a bottom plate.

Each inhaler contains 120 doses.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

No special requirements for disposal.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

AstraZeneca UK Limited,
1 Francis Crick Avenue,
Cambridge,
CB2 0AA,
UK.

8. MARKETING AUTHORISATION NUMBER(S)

PL 17901/0117

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

16/04/2003

10 DATE OF REVISION OF THE TEXT

04/05/2023