Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Bricanyl Turbohaler 500 micrograms per metered dose, inhalation powder

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each delivered dose contains:
Terbutaline sulfate 400 micrograms (which corresponds to 500 micrograms metered dose).

Excipients with known effect
Bricanyl Turbohaler 500 micrograms/dose: each delivered dose contains approximately 400 micrograms 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 beta$_2$-adrenergic agonist recommended for the relief and prevention of bronchospasm in bronchial asthma and in chronic bronchitis and other bronchopulmonary disorders in which bronchospasm is a complicating factor.

4.2 Posology and method of administration

Posology

Adults and Children: One inhalation (500 micrograms) (metered dose) as required.
Not more than 4 inhalations should be necessary in any 24 hour period.

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. For further information see section 4.9.

If a previously effective dosage regimen no longer gives the same symptomatic relief, the patient should urgently seek further medical advice. 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.

As for all beta$_2$-agonists caution should be observed in patients with thyrotoxicosis.

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 positive inotropic effect of beta$_2$-agonists, these drugs should not be used in patients with hypertrophic cardiomyopathy.

Due to the hyperglycaemic effects of beta$_2$-agonists, additional blood glucose measurements are initially recommended when Bricanyl therapy is commenced in diabetic patients.

Potentially serious hypokalaemia may result from beta$_2$-agonist therapy, mainly with parenteral or nebulised administration. Particular caution is advised in acute severe asthma as this effect may be augmented by hypoxia. The hypokalaemic effect may be potentiated by concomitant treatment with xanthine derivatives, corticosteroids and/or diuretics (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 interactions

Beta-blocking agents (including eye drops), especially the non-selective ones such as propranolol, may partially or totally inhibit the effect of beta$_2$-stimulants. Therefore, Bricanyl preparations and non-selective β-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.

There are some data which indicate that there is a risk of interaction between monoamine oxidase inhibitors, tricyclic antidepressants and terbutaline.

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.

Transient hypoglycaemia has been reported in newborn preterm infants after maternal beta$_2$-agonist treatment.

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.

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

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

System Organ Class	Frequency Classification	Adverse Drug Reaction Preferred Term
Metabolism and Nutrition Disorders	Common	Hypokalaemia
Psychiatric Disorders	Not known*	Sleep disorder and Behavioural disturbances, such as agitation and restlessness
Nervous System Disorders	Very Common	Tremor Headache
	Not known*	Psychomotor hyperactivity
Cardiac Disorders	Common	Tachycardia Palpitations
	Not known*	Arrhythmias, e.g. atrial fibrillation, supraventricular tachycardia and extrasystoles Myocardial ischaemia
Respiratory, Thoracic and Mediastinal Disorders	Not known*	Bronchospasm**
Gastrointestinal Disorders	Not known*	Nausea
Skin and Subcutaneous Tissue Disorders	Not known*	Urticaria Rash
Musculoskeletal and Connective Tissue Disorders	Common	Muscle spasms

* Reported spontaneously in post-marketing data and therefore frequency regarded as not known
** Drugs for inhalation may through unspecified mechanisms cause bronchospasm.

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:

HPRA Pharmacovigilance
Website: www.hpra.ie

4.9 Overdose

There is a potential for progressive accumulation of dry powder in the mouthpiece of the Bricanyl Turbohaler 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 an adrenergic agonist which predominantly stimulates $beta_2$-receptors, thus producing relaxation of bronchial smooth muscle, inhibition of the release of endogenous spasmogens, inhibitions of oedema caused by endogenous mediators and increased mucociliary clearance.

Inhaled terbutaline acts within a few minutes and has a duration for up to 6 hours. Treatment with Bricanyl Turbohaler is effective even during an acute asthma attack.

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.

5.3 Preclinical safety data

The major toxic effect of terbutaline, observed in toxicological studies, is focal myocardial necrosis. This type of cardiotoxicity is a well-known class-effect, and the effect of terbutaline is similar to or less pronounced than that of other beta-receptor 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

3 years

6.4 Special precautions for storage

Do not store above 30°C.
Replace the cover properly after use.

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 AB
SE-151 85 Sodertalje
Sweden

8 MARKETING AUTHORISATION NUMBER

PA1019/007/002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 7th February 1989

Date of last renewal: 7th January 2009

10 DATE OF REVISION OF THE TEXT

June 2020