Part II

Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Bricanyl® SA 7.5mg Tablets.

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 7.5 mg of terbutaline sulphate.

For excipients, see 6.1.

3 PHARMACEUTICAL FORM

Film-coated prolonged-release tablets.

A white to faintly yellow, circular, biconvex tablet engraved with '$^{A}_{B}$ $^{A}_{D}$' on one side.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Terbutaline is a selective β_2-adrenergic agonist recommended for 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 adminstration

Adults: 1 tablet morning and evening.

The inactive components in Bricanyl SA form a matrix which is insoluble in the digestive juices. The empty matrix may sometimes pass through the digestive system unchanged and be excreted.

The tablet may not be divided or chewed, but must be swallowed whole together with liquid.

Elderly:
Dosage as for adults.

4.3 Contraindications

Bricanyl oral preparations are contra-indicated in patients with a history of hypersensitivity to any of their constituents.

4.4 Special warnings and special precautions for use

Care should be taken with patients suffering from myocardial insufficiency or thyrotoxicosis.

Due to the hyperglycaemic effects of β_2-stimulants, additional blood glucose measurements are initially recommended when Bricanyl therapy is commenced in diabetic patients.

If a previously effective dosage regime 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.

Potentially serious hypokalaemia may result from β_2-agonist therapy, mainly with parental 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. It is recommended that serum potassium levels are monitored in such situations

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

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 β-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.

Hypokalaemia may result from β_2-agonist therapy and may be potentiated by concomitant treatment with xanthine derivatives, corticosteroids and diuretics (*see section 4.4 Special warnings and precautions for use).*

4.6 Pregnancy and lactation

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

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 β_2-agonist treatment.

4.7 Effects on ability to drive and use machines

Bricanyl does not affect the ability to drive or use machines.

4.8 Undesirable effects

The frequency of side-effects is low at the recommended doses. Side-effects which have been recorded such as tremor, headache, nausea, tonic cramp, mouth and throat irritation, tachycardia and palpitations are all characteristic of sympathomimetic amines. A few patients feel tense; this is also due to the effects on skeletal muscle and not to direct CNS stimulation. Whenever these side-effects have occurred, the majority have usually been spontaneously reversible within the first week of treatment. As with other β_2-agonists, tremor is dose related.

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

Tachycardia, with or without peripheral vasodilation, has been rarely reported during β_2-agonist therapy. Cardiac arrhythmias, including atrial fibrillation, supraventricular tachycardia and extrasystoles, have been reported in association with β_2-agonist, usually in susceptible patients.

Potentially serious hypokalaemia may result from β_2-agonist therapy.
(See also *Section 4.4 Special Warnings and precautions for use.*)

Hypersensitivity reactions, including angioedema, urticaria, exanthema, bronchospasm, hypotension and collapse, have

been reported with β_2-agonist therapy.

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.

4.9 Overdose

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

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

b) Severe cases:
Gastric lavage, activated charcoal. 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 β-blocker (e.g. metoprolol) is recommended for the treatment of arrhythmias causing haemodynamic deterioration. The β-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 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

Terbutaline is a selective beta$_2$-adrenoceptor agonist.

5.2 Pharmacokinetic properties

In man, terbutaline and its metabolites are excreted predominantly in the urine.

In fasting subjects, 30-70% of an oral dose of terbutaline is absorbed. Bioavailability of terbutaline after oral administration is much lower than the amount absorbed, due to the first pass effect. Bioavailability of sustained release tablets is increased after fasting. Studies in healthy volunteers given repeat dose Bricanyl SA of, 7.5mg to attain steady state show:

a) Peak plasma concentration reached in 4-8 hours
b) Mean plasma concentration at steady state is 2.7mg/ml
c) Single dose renal clearance – 63% (N.B. Does not change at steady state).

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. Terbutaline has been extensively over many years for the relief of bronchospasm without identifying any areas of concern.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Polyvinyl chloride
Silica, Colloidal Anhydrous
Tartaric Acid
Ethylcellulose
Stearyl alcohol

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

Brown glass bottles with a polyethylene cap containing 60 tablets.

6.6 Instructions for use and handling

No special requirements.

7 MARKETING AUTHORISATION HOLDER

AstraZeneca UK Ltd
600 Capability Green
Luton LU1 3LU
UK

8 MARKETING AUTHORISATION NUMBER

PA 970/37/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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Date of last renewal: 23rd February 2002

10 DATE OF REVISION OF THE TEXT

September 2003