SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Terbutaline Sulfate 2.5mg/ml Nebuliser Solution

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each ampoule contains 5mg terbutaline sulfate in 2ml.

For the full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Nebuliser solution.

A clear, colourless to yellow solution contained within clear plastic single dose ampoules.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
Terbutaline Sulfate Nebuliser Solution is indicated for the relief of severe bronchospasm in bronchial asthma and in chronic bronchitis, emphysema and other bronchopulmonary disorders in which bronchospasm is a complicating factor.

4.2 Posology and method of administration

Posology

Dosage:
Adults (including the elderly): One or two ampoules (5 or 10mg), two to four times daily.
Children (>25kg): One ampoule (5mg), two to four times daily
Children (<25kg): Not recommended

In acute severe asthma, additional doses may be necessary.

In domiciliary practice, the benefits of increasing the dose of nebulised terbutaline should be considered against a potential masking of a deterioration in the patients underlying conditions. In such circumstances, a medical assessment should be considered, as alternative therapy may be indicated.

Method of administration

Terbutaline Sulfate Nebuliser Solution should be administered by a power operated nebuliser via a face mask or mouth piece. Terbutaline Sulfate has a duration of action of up to 6 hours.

4.3 Contraindications

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

Terbutaline Sulfate Nebuliser Solution should not be used in patients with hypertrophic cardiomyopathy because of the positive inotropic effects of beta2-agonists.

4.4 Special warnings and precautions for use

Terbutaline Sulfate Nebuliser Solution is for use with a nebuliser under the direction of a physician. The solution must not be injected or administered orally.

In patients with severe or unstable asthma, bronchodilators should not be the only or main treatment. Regular medical assessment is required including lung function testing as they are at risk of severe attacks and even death. Oral corticosteroid therapy and / or inhaled corticosteroids should be considered. Increasing use of bronchodilators to relieve symptoms indicates the deterioration of asthma.

Patients receiving treatment with Terbutaline Sulfate Nebuliser Solution at home should be warned that if their usual dose is less effective or its duration of action is reduced, they should not increase either the dose or frequency of treatment, but should consult their doctor. In this situation, patients should be reassessed and consideration given to the need for increased anti-inflammatory therapy.

Terbutaline Sulfate Nebuliser Solution should be used with caution in patients suffering from myocardial insufficiency or thyrotoxicosis.

As beta2-stimulants have hyperglycaemic effects, additional blood glucose measurements are initially recommended when treatment with Terbutaline
Sulfate Nebuliser Solution is started in diabetic patients. The patients general condition should be reappraised if the treatment becomes shorter acting or less effective.

Beta2-agonist therapy may result in potentially serious hypokalaemia. In patients with severe asthma particular caution is required as concomitant treatment with xanthine derivatives, steroids, diuretics or hypoxia can potentiate this effect. The monitoring of serum potassium levels is recommended in such situations.

4.5 Interaction with other medicinal products and other forms of interaction

The effect of beta-stimulants may be partially or totally inhibited by beta-blocking agents, especially non-selective ones such as propranolol. Terbutaline Sulfate Nebuliser Solution and non-selective beta-blocking drugs should, therefore, not usually be prescribed together. Caution is advised when using Terbutaline Sulfate Nebuliser Solution in patients receiving other sympathomimetics.

There is theoretical synergism between terbutaline and theophylline as bronchodilators. However, this is not seen in practice, their effects being additive at best.

4.6 Fertility, pregnancy and lactation

Pregnancy
Although no teratogenic effects have been observed in patients, nor has any evidence of teratogenicity been found in animal studies, terbutaline should only be administered with caution during the first trimester of pregnancy.

Breast-feeding
Although terbutaline is excreted in breast milk, it is unlikely to have an effect on the infant at therapeutic doses.

Nevertheless, use should be restricted to situations where it is felt that the expected benefit to the mother is greater than any possible risk to the neonate.

4.7 Effects on ability to drive and use machines

Patients should be advised not to drive after taking high doses of Terbutaline Sulfate Nebuliser Solution.
4.8 Undesirable effects

The frequency of side-effects is low.

Side effects which have been recorded, such as tremor, headache, nausea, tonic cramp, mouth and throat irritation and palpitations, are all characteristic of sympathomimetic amines. A few patients feel tense; this is also due to 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 β₂-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 β₂-agonist therapy. Cardiac arrhythmias, including atrial fibrillation, supraventricular tachycardia and extrasystoles, have been reported in association with β₂-agonists, usually in susceptible patients.

Potentially serious hypokalaemia may result from β₂-agonist therapy. (See also Section 4.4, Special Warnings and Precautions for use.)

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.

Hypersensitivity reactions, including angioedema, urticaria, exanthema, bronchospasm, hypotension and collapse, have been very rarely reported with β₂-agonist therapy.

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 Yellow Card Scheme; website: www.mhra.gov.uk/yellowcard

4.9 Overdose

Possible symptoms include headache, anxiety, tremor, tonic cramps, palpitations and arrhythmia. A fall in blood pressure sometimes occurs. Laboratory findings can include hypokalaemia, hyperglycaemia and metabolic acidosis.
Treatment of severe overdosage requires determination of acid-base balance, blood sugar and electrolytes, monitoring of heart rate, 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. All beta-blockers should be used with care, especially if the patient is asthmatic, because of the possibility of inducing bronchoconstriction. If the beta2-mediated reduction in peripheral vascular resistance significantly contributed to the fall in blood pressure, a volume expander should be given.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: selective beta2-adrenoceptor agonists, ATC code: R03A C03.

Terbutaline is a selective beta2-adrenoceptor agonist which affects the smooth skeletal muscle. Smooth muscle relaxation is dose dependent. It has an antiallergic effect on mast cells, inhibiting the release of bronchoconstrictor mediators such as histamine and neutrophil chemotactic factor (NCF) after in-vivo antigen provocation testing. It also enhances mucociliary clearance of the respiratory system.

Terbutaline administration produces bronchodilation in normal subjects as well as those with asthma and chronic obstructive pulmonary disease. Asthmatics usually show the largest response. At therapeutic doses it acts on the beta2-adrenoceptors of bronchial muscle to provide bronchodilation. Terbutaline has a duration of action of up to 6 hours in most patients.

5.2 Pharmacokinetic properties

Absorption

When normal subjects inhaled terbutaline from a pressurised aerosol, pulmonary absorption varied between 4 and 13%. Terbutaline is not subject to first pass pulmonary metabolism. Peak plasma concentrations are about one-fifth of those of an identical oral dose and occur within 0.5 - 1 hour, compared with 2 - 3 hours after oral dosing. This lower plasma concentration results in less severe non-respiratory adverse effects.

Biotransformation

There is a large interindividual variability in absorption after oral dosing, absorption ranging from 25 - 80%. There is considerable presystemic metabolism, with less
interindividual variation, approximately 60% of the absorbed dose being metabolised. Metabolism is by conjugation mainly to the sulfate, and to a lesser extent to glucuronide. Conjugation occurs in the liver and gut wall, but their relative importance is uncertain. The majority of an oral dose circulates as the pharmacologically inactive sulfate conjugate.

There is a small proportion of protein binding. Terbutaline is very hydrophilic, crosses the placenta and is excreted in breast milk in similar concentrations to those in plasma, however levels in suckling infants are undetectable.

Elimination
About 90% of the drug is excreted in the urine partly as the inactive conjugates and partly as unchanged terbutaline, the ratio depending upon the route of administration.

5.3. Preclinical Safety Data

There is no evidence of teratogenicity in rats, mice and rabbits. Terbutaline, as with other β-agonists, has been shown to induce mesovarian leiomyomas in rats, but there is no evidence of carcinogenicity.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Sodium chloride
- Disodium edetate
- Water for injections in bulk
- Sulfuric acid

6.2. Incompatibilities

None known.

6.3. Shelf Life

Three years. Ampoules must be used within six months of opening the foil wrap.
6.4. **Special Precautions for Storage**

No special precautions for storage.

Ampoule should be opened immediately before use and any solution remaining after use should be discarded.

6.5. **Nature and Contents of Container**

Unit dose polyethylene ampoules packed into cartons. Each carton contains 20 ampoules in foil wrapped strips of 5 or 10.

6.6 **Special precautions for disposal**

Terbutaline Sulfate Nebuliser Solution is for inhalation from a suitable nebuliser which should be operated according to the manufacturer’s instructions. The method of opening the ampoules is to hold upright, twist and pull off the plastic seal.

7 **MARKETING AUTHORISATION HOLDER**

Breath Limited  
Whiddon Valley  
Barnstaple  
North Devon  
EX32 8NS  
United Kingdom

8. **MARKETING AUTHORISATION NUMBER**

PL 18023/0004

9. **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

31/05/2006

10. **DATE OF REVISION OF THE TEXT**