BRICANYL® TURBUHALER®

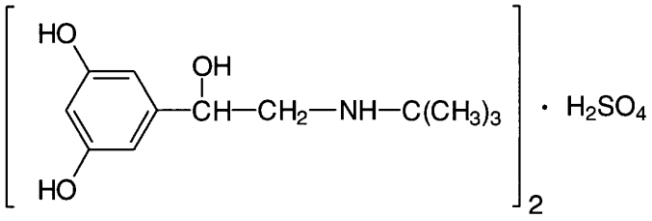
terbutaline sulfate

PRODUCT INFORMATION

NAME OF THE MEDICINE

Terbutaline sulfate, 2-(tert-butylamino)-1-(3,5-dihydroxyphenyl) ethanol sulfate, a sympathomimetic bronchodilator with a degree of selective β_2-stimulant activity on the respiratory system.

The chemical structure of terbutaline sulfate is:



Molecular formula: $(C_{12}H_{19}NO_3)_2.H_2SO_4$

CAS number: 23031-32-5

DESCRIPTION

BRICANYL® TURBUHALER® is a breath activated multiple dose powder inhaler free from propellant, lubricant, preservative, carrier substances or other additives.

PHARMACOLOGY

The tertiary butyl group attached to the terminal nitrogen of the terbutaline molecule is thought to confer selective stimulation of the pulmonary β_2-receptors and only relatively minor stimulation of cardiac β_1 receptors. The presence of the two phenolic hydroxyl groups in the meta positions confers resistance to metabolism by the enzyme catechol-o-methyl transferase. The potent bronchospasmolytic effect is rapid in onset and reaches a maximum about 30 minutes after subcutaneous injection, 1 hour after aerosol and 2 - 3 hours after oral administration. The duration of action is between 4 and 5 hours. In addition to its bronchospasmolytic effect, terbutaline has also been shown to improve mucociliary clearance. Metabolism of terbutaline sulfate which is ingested orally or swallowed following inhalation is principally by conjugation in the gastrointestinal mucosa. The drug is absorbed unchanged from the respiratory tract and is excreted mainly as such in the urine. Practically all of an administered dose of terbutaline is eliminated after 72 hours.

INDICATIONS

For relief of bronchospasm in patients with asthma or chronic obstructive pulmonary disease, and for acute prophylaxis against exercise-induced asthma or in other situations known to induce bronchospasm.

Bricanyl Turbuhaler is intended for short-term management of bronchospasm.

CONTRAINDICATIONS

Hypersensitivity to sympathomimetic amines or any other ingredient.

PRECAUTIONS

Treatment of asthma or COPD should be in accordance with current national treatment guidelines.

Patients with asthma should have a personal asthma action plan designed in association with their general practitioner. This plan should incorporate a stepwise treatment regimen which can be instituted if the patient's asthma improves or deteriorates.

Increasing use of short acting β_2-agonists to control symptoms indicates deterioration of asthma control. Sudden and progressive deterioration in control of asthma or COPD is potentially life threatening and consideration should be given to the need for starting or increasing therapy with corticosteroids.

Cardiovascular diseases and hyperthyroidism

Caution is advised when terbutaline is administered to patients with thyrotoxicosis and to patients with hypertension, coronary artery disease, arrhythmias and tachyarrhythmia.

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 (eg 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.

Arrhythmogenic potential

β_2-stimulants have an arrhythmogenic potential which must be considered for each patient when receiving treatment for bronchospasm.

Diabetes

Due to the blood-glucose increasing effects of β_2-stimulants, extra blood glucose controls are initially recommended when diabetic patients are commenced on terbutaline.

Sensitivity to sympathomimetic amines

Some patients may be unusually sensitive to β-adrenergic stimulants. Terbutaline should be used with caution when an increased susceptibility to sympathomimetic amines can be expected for instance in other patients with hyperthyroidism not yet adequately controlled.

Lack of response

If the usual dose does not provide the usual relief, a non-responsive state may be developing. If a previously effective dose lasts less than usual, patients should be instructed to consult a doctor.

Hypokalaemia

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 *Interactions with other medicines*). It is recommended that serum potassium levels are monitored in such situations.

Acute asthma

If patients with an acute attack of asthma fail to respond to a dry powder inhaler of β_2-agonist they should be advised to follow their personal asthma action plan. Failure to respond to β_2-agonists in general can be due to various reasons related to drug administration or the disease itself. Particularly in children 5 years or younger, and exceptionally in other cases, inspiratory flow through a dry powder inhaler may not be sufficient for optimal drug delivery. If a non-response occurs, medical help should be sought while a β_2-agonist treatment is continued. In such a situation, and if available, a nebuliser or pressurised metered dose inhaler with spacer should be used. (see also *Precautions - Lack of response*).

Cardionecrosis

Animal studies suggest that cardionecrotic lesions may occur with high doses of some sympathomimetic amines. On this evidence, it is not possible to exclude myocardial lesions as a possible hazard resulting from long-term treatment.

Use in pregnancy - Category A

Although no adverse effects in pregnant women or their foetuses have been reported, care with Bricanyl, as with all other drugs, is recommended during the first 3 months of pregnancy.

Use in lactation

Although terbutaline is secreted into breast milk, and milk concentrations are approximately those in maternal plasma, two individual case studies indicate that the infant is likely to receive 0.2-0.7% of the maternal dose (0.4 and 0.7 µg /kg /day respectively), depending (for example) on the time of feeding in relation to administration of the drug. In the 4 infants studied this did not result in any signs of β-adrenoceptor stimulation.

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

INTERACTIONS WITH OTHER MEDICINES

Other sympathomimetic amines

Care is recommended if it is proposed to administer terbutaline in concomitant therapy with other sympathomimetic amines as excess sympathetic stimulation may occur.

β-adrenergic blocking drugs

β-adrenergic blocking drugs, including eye drops, may inhibit the bronchodilating effect of sympathomimetic bronchodilators and may increase airways resistance in asthmatic patients.

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.

Potassium depleting agents and hypokalaemia

Owing to the hypokalaemic effect of β-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 *Precautions - Hypokalaemia*). Hypokalaemia also predisposes to digoxin toxicity.

ADVERSE EFFECTS

Most of the side effects are characteristic of sympathomimetic amines. The incidence and severity of particular side effects depends on the dose and rate of administration. An initial dose-titration will often reduce side effects. At recommended therapeutic doses, the frequency of side-effects is minimal.

More common reactions

More commonly observed side effects include tremor and headache. Commonly observed side effects include nervousness, tachycardia, palpitations, tonic muscle cramps and hypokalaemia.

Less common reactions

Cardiovascular	Ectopic beats
Gastrointestinal	Nausea, vomiting, bad taste, diarrhoea
General	Sweating
Musculoskeletal	Muscle twitching, cramps
Nervous system	Drowsiness, dizziness, sleep disturbance, behavioural disturbances (such as agitation, hyperactivity, restlessness)
Dermatological	Rash, urticaria, exanthema

Serious or life threatening reactions

Cardiac arrhythmias (eg atrial fibrillation, supraventricular tachycardia and extrasystoles) and myocardial ischaemia have been rarely reported.

Overdose of terbutaline preparations may produce significant tachycardia, arrhythmia and hypotension (see *Overdosage*). In rare cases, through unknown mechanisms, drugs for inhalation may cause bronchospasm.

DOSAGE AND ADMINISTRATION

Inhaled bronchodilators should be used *as required* rather than regularly.

Dosage should be individualised. If long-term use of terbutaline is proposed, particularly if the patient is asked to take terbutaline in conjunction with other medications, objective pulmonary function testing (for example, by peak flow meter or spirometer) may be useful as part of assessment of the efficacy or treatment.

Adults and children over 12 years

1 inhalation (=500 µg terbutaline) as required up to every 4 to 6 hours. In severe cases the single dose may be increased to 3 inhalations. The total daily dose should not exceed 12 inhalations per 24 hours.

Paediatric

1 inhalation (=500 µg terbutaline) as required up to every 4 to 6 hours. In severe cases the single dose may be increased to 2 inhalations. The total daily dose should not exceed 8 inhalations per 24 hours.

Use in children

Bricanyl Turbuhaler is suitable for use by children since it is breath activated and does not require coordination of dose release and inhalation as with use of aerosol inhalers.

Impaired hepatic function

Hepatic failure has not been shown to influence the metabolism of terbutaline. However, caution should be exercised in patients with impaired liver function.

Impaired renal function

As terbutaline sulfate is largely excreted in urine, caution should be exercised in patients with renal impairment.

OVERDOSAGE

For information on the management of overdose, contact the Poison Information Centre on 131126 (Australia).

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.

Possible symptoms and signs

Too frequent administration, as with other sympathomimetic agents, may cause nausea, headaches, changes in blood pressure, anxiety, tension, restlessness, insomnia, tremor, excitement, tonic muscle cramps, palpitations, tachycardia and cardiac arrhythmias. The symptoms and signs are those characteristic of excessive sympathetic stimulation.

Laboratory findings

Hyperglycaemia and lactacidosis (see *Precautions* section) sometimes occur. β_2-agonists may cause hypokalemia as a result of redistribution of potassium.

Treatment

The specific antidote for accidental overdosage with terbutaline sulfate is a cardio-selective β-adrenergic blocking drug such as metoprolol (5-10 mg by slow intravenous injection, repeated if necessary after 5 minutes). β-blockers should be used with care because of the possibility of inducing bronchospasm in sensitive individuals.

PRESENTATION AND STORAGE CONDITIONS

500 µg per inhalation, breath activated; propellant and additive free. 100 inhalations.

Storage conditions

Store below 30°C. Replace cap firmly after use.

NAME AND ADDRESS OF THE SPONSOR

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POISON SCHEDULE OF THE MEDICINE

S3 - Pharmacist Only Medicine

DATE OF FIRST INCLUSION IN THE AUSTRALIAN REGISTER OF THERAPEUTIC GOODS (THE ARTG)

11th July 1991

DATE OF MOST RECENT AMENDMENT

3 August 2017

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