AUSTRALIAN PRODUCT INFORMATION

Bricanyl® Turbuhaler®
(terbutaline sulfate)
Powder for inhalation

1 NAME OF THE MEDICINE

Terbutaline sulfate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Bricanyl Turbuhaler delivers (ex-mouthpiece) 400 μg of terbutaline sulfate per inhalation (delivered dose):

- M3 Turbuhaler version: labelled as the delivered dose 400 μg terbutaline sulfate per inhalation (corresponding to 500 μg metered dose). It is free from propellant, lubricant, preservative or carrier substances but contains the excipient, lactose monohydrate.

Excipient(s) with known effect: lactose monohydrate (M3 Turbuhaler). For the full list of excipients, see Section 6.1 List of excipients).

3 PHARMACEUTICAL FORM

Powder for inhalation

4 CLINICAL PARTICULARS

4.1 THERAPEUTIC 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.

4.2 DOSE AND METHOD OF 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 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 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.

Special patient populations

Renal impairment

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

Hepatic impairment

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

Use in paediatric patients

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.

Method of administration

For detailed instructions, see the Turbuhaler instructions leaflet provided in each pack of Bricanyl Turbuhaler. Patients should be instructed on how to administer the product correctly and advised to read the instruction leaflet carefully.

4.3 CONTRAINDICATIONS

Hypersensitivity to sympathomimetic amines or any other ingredient in the product (see Section 6.1 List of excipients).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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.

Patients who are prescribed regular maintenance treatment for asthma should be advised to continue taking their maintenance treatment medication even when symptoms decrease and they do not require Bricanyl Turbuhaler.

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 of the underlying condition and warrants a reassessment of the therapy.

Increasing use of short acting β_2-agonists (SABA) 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.

Over-reliance of SABA reliever in patients with asthma

Irrespective of asthma severity, having uncontrolled asthma is an important risk factor for exacerbations. Dispensing of three or more SABA inhalers in a year is associated with an increased risk of severe exacerbations and mortality. The risk increases with the number of inhalers dispensed.

In mild asthma patients, there is an increased risk of severe exacerbations associated with over-reliance on SABA monotherapy.

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.

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 Section 4.5 Interactions with other medicines and other forms of interactions). 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 *Lack of response* above).

Lactose

Bricanyl Turbuhaler (M3 version) contains lactose monohydrate (approximately 400 µg/inhalation delivered dose) which may contain small amounts of milk protein residues. This amount does not normally cause problems in lactose intolerant people. In patients with hypersensitivity to milk protein, these small amounts may cause allergic reactions.

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 the elderly

See Section 4.2 Dose and method of administration.

Paediatric use

See Section 4.2 Dose and method of administration.

Effects on laboratory tests

No data available.

4.5 INTERACTIONS WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTIONS

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 Section 4.4 Special warnings and precautions for use - *Hypokalaemia*). Hypokalaemia also predisposes to digoxin toxicity.

4.6 FERTILITY, PREGNANCY AND LACTATION

Effects on fertility

No data available.

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 0.7µg/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.

4.7 EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

The effects of this medicine on a person's ability to drive and use machines were not assessed as part of its registration. However, adverse effects of terbutaline sulfate include dizziness and drowsiness which could affect the ability to drive or use machines (see Section 4.8 Adverse effects (Undesirable effects)).

4.8 ADVERSE EFFECTS (UNDESIRABLE 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 Section 4.9 Overdose). In rare cases, through unknown mechanisms, drugs for inhalation may cause bronchospasm.

Reporting suspected adverse effects

Reporting suspected adverse reactions after registration 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 at www.tga.gov.au/reporting-problems.

4.9 OVERDOSE

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 Section 4.4 Special warnings and precautions for use) sometimes occur. β_2-agonists may cause hypokalaemia 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.

5 PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Mechanism of action

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 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.

Clinical trials

No data available

5.2 PHARMACOKINETIC PROPERTIES

Absorption

The drug is absorbed unchanged from the respiratory tract.

Metabolism

The presence of the two phenolic hydroxyl groups in the meta positions confers resistance to metabolism by the enzyme catechol-o-methyl transferase. Metabolism of terbutaline sulfate which is ingested orally or swallowed following inhalation is principally by conjugation in the gastrointestinal mucosa.

Excretion

The drug is excreted mainly unchanged in the urine. Practically all of an administered dose of terbutaline is eliminated after 72 hours.

5.3 PRECLINICAL SAFETY DATA

Genotoxicity

No data available

Carcinogenicity

No data available

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Lactose monohydrate (Bricanyl Turbuhaler M3 version). See Section 2 Qualitative and quantitative composition.

6.2 INCOMPATIBILITIES

Incompatibilities were either not assessed or not identified as part of the registration of this medicine.

6.3 SHELF LIFE

In Australia, information on the shelf life can be found on the public summary of the Australian Register of Therapeutic Goods (ARTG). The expiry date can be found on the packaging.

6.4 SPECIAL PRECAUTIONS FOR STORAGE

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

6.5 NATURE AND CONTENTS OF CONTAINER

Bricanyl Turbuhaler is a breath activated multiple dose dry powder inhaler available as single inhaler packs:

- M3 Turbuhaler (AUST R 315075): 120 inhalations

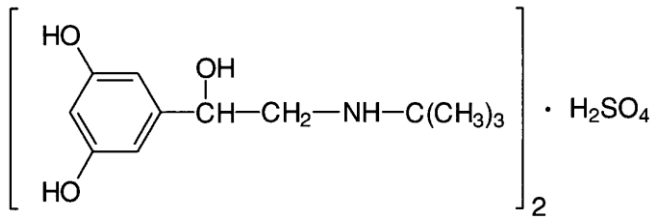
6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

In Australia, any unused medicine or waste material should be disposed of by taking to your local pharmacy.

6.7 PHYSICOCHEMICAL PROPERTIES

Chemical structure

Terbutaline sulfate, 2-(tert-butylamino)-1-(3,5-dihydroxyphenyl) ethanol sulfate, a sympathomimetic bronchodilator with a degree of selective β2-stimulant activity on the respiratory system.



CAS number

23031-32-5

7 MEDICINE SCHEDULE (POISONS STANDARD)

S3 - Pharmacist Only Medicine

8 SPONSOR

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9 DATE OF FIRST APPROVAL

11th July 1991

10 DATE OF REVISION

24 April 2023

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
2, 6.5	Updated to remove information on the M2 Turbuhaler presentation

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