AUSTRALIAN PRODUCT INFORMATION

BRICANYL® INJECTION
(terbutaline sulfate) solution for injection

1 NAME OF THE MEDICINE

Terbutaline sulfate

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

BRICANYL Injection solution for injection contains 0.5 mg/mL of terbutaline sulfate with sodium chloride, hydrochloric acid (for pH adjustment) and water for injections as the inactive ingredients.

3 PHARMACEUTICAL FORM

Clear, colourless solution for injection.

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 injection solution is recommended for acute use only.

4.2 DOSE AND METHOD OF ADMINISTRATION

Adults and children over 12 years

0.5 mL. Repeat as required up to every 6 hours.

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.

Renal impairment

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

BRICANYL Injection is for subcutaneous use only. Solutions should not be used if discoloured.

4.3 CONTRAINDICATIONS

Hypersensitivity to sympathomimetic amines or any other ingredient in the medicine.

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.

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.

Lactic acidosis

Lactic acidosis has been reported in association with high therapeutic doses of parenteral short-acting β-agonist therapy, mainly in patients being treated for an acute asthma exacerbation (see Section 4.8 Adverse effects (Undesirable effects) and Section 4.9 Overdose). In patients not adequately responding to acute therapy with Bricanyl Injection, consideration should be given to the presence of lactic acidosis as a possible contributing factor to ongoing respiratory symptoms.

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

No data available.

Paediatric use

No data available.

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.

Systemic corticosteroids

The combination of intravenous β-agonists and systemic corticosteroids is known to increase blood glucose and can deplete serum potassium.

In addition, the risk of pulmonary oedema is heightened when intravenous β-agonists are used in combination with corticosteroids and intravenous fluids.

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 0.7 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.

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.

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. 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

Rare cases of lactic acidosis have been reported with high therapeutic doses of Bricanyl injection.

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).

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).

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

Terbutaline sulfate - a sympathomimetic bronchodilator with a degree of selective β_2-stimulant activity on the respiratory system.

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.

Clinical trials

No data available.

5.2 PRECLINICAL SAFETY DATA

Genotoxicity

No data available.

Carcinogenicity

No data available.

6 PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

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 25°C. Protect from light. Solutions containing terbutaline are sensitive to excessive heat and light.

6.5 NATURE AND CONTENTS OF CONTAINER

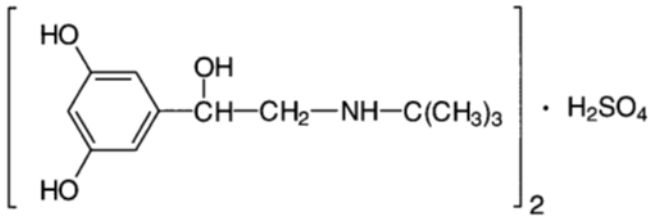
0.5 mg/mL of 5 x 1 mL glass ampoules

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



Chemical name: 2-(tert-butylamino)-1-(3,5-dihydroxyphenyl) ethanol sulfate

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

CAS number

23031-32-5

7 MEDICINE SCHEDULE (POISONS STANDARD)

Prescription only medicine (Schedule 4)

8 SPONSOR

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9 DATE OF FIRST APPROVAL

11 July 1991

10 DATE OF REVISION

28 August 2020

SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
Various	Reformatted PI for new TGA PI form

Doc ID-003669484 v3