

# BRICANYL<sup>®</sup> INJECTION

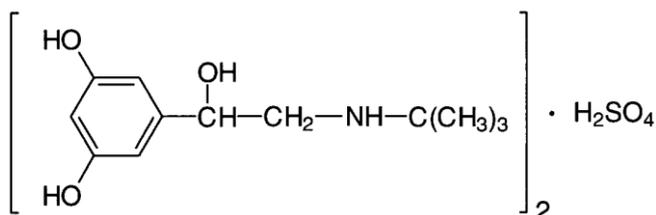
terbutaline sulfate

## 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  $\beta_2$ -stimulant activity on the respiratory system.

The chemical structure of terbutaline sulfate is:



Molecular formula:  $(\text{C}_{12}\text{H}_{19}\text{NO}_3)_2 \cdot \text{H}_2\text{SO}_4$

CAS number: 23031-32-5

### DESCRIPTION

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.

### PHARMACOLOGY

The tertiary butyl group attached to the terminal nitrogen of the terbutaline molecule is thought to confer selective stimulation of the pulmonary  $\beta_2$ -receptors and only relatively minor stimulation of cardiac  $\beta_1$  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 injection solution is recommended for acute use only.

## **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.

### **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**

$\beta_2$ -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  $\beta_2$ -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  $\beta$ -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  $\beta_2$ -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.

### **Lactic acidosis**

Lactic acidosis has been reported in association with high therapeutic doses of parenteral short-acting  $\beta$ -agonist therapy, mainly in patients being treated for an acute asthma exacerbation (see *Adverse effects* and *Overdosage* sections). 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 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  $\mu\text{g}$  /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  $\beta$ -adrenoceptor stimulation.

Transient hypoglycaemia has been reported in newborn preterm infants after maternal  $\beta_2$ -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.

### **$\beta$ -adrenergic blocking drugs**

$\beta$ -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  $\beta_2$ -agonists treatment, since it increases the risk of cardiac arrhythmias. Other halogenated anaesthetics should be used cautiously together with  $\beta_2$ -agonists.

### **Potassium depleting agents and hypokalaemia**

Owing to the hypokalaemic effect of  $\beta$ -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.

### **Systemic corticosteroids**

The combination of intravenous  $\beta$ -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  $\beta$ -agonists are used in combination with corticosteroids and intravenous fluids.

## **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. 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

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

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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 *Overdosage*).

## DOSAGE AND ADMINISTRATION

### Adults and children over 12 years

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

### 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).

## 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.  $\beta_2$ -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  $\beta$ -adrenergic blocking drug such as metoprolol (5-10 mg by slow intravenous injection, repeated if necessary after 5 minutes).  $\beta$ -blockers should be used with care because of the possibility of inducing bronchospasm in sensitive individuals.

### **PRESENTATION AND STORAGE CONDITIONS**

0.5 mg/mL of 5 x 1 mL ampoules.

#### **Storage conditions**

Store below 25°C. Protect from light. Solutions containing terbutaline are sensitive to excessive heat and light. Solutions should not be used if discoloured.

### **NAME AND ADDRESS OF THE SPONSOR**

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### **POISON SCHEDULE OF THE MEDICINE**

S4 - Prescription Medicine

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

11<sup>th</sup> July 1991

### **DATE OF MOST RECENT AMENDMENT**

6 September 2017

Bricanyl is a registered trade mark of the AstraZeneca group of companies.