

NEW ZEALAND DATA SHEET

1. PRODUCT NAME

BRICANYL TURBUHALER, Inhalation powder 200 micrograms/ inhalation (delivered dose).

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

There are two versions of Bricanyl Turbuhaler, each delivering (ex-mouthpiece) 200 µg of terbutaline sulphate per inhalation (delivered dose):

- Original M2 Turbuhaler version: labelled as the metered dose 250 µg terbutaline sulphate per inhalation.
- M3 Turbuhaler version: labelled as the delivered dose 200 µg terbutaline sulphate per inhalation (corresponding to 250 µg metered dose)

Each delivered dose contains: Terbutaline sulphate 200 µg (which corresponds to 250 µg metered dose).

Excipient with known effect

- M2 Turbuhaler: None
- M3 Turbuhaler: each delivered dose contains approximately 700 µg of lactose monohydrate.

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Inhalation powder

4. CLINICAL PARTICULARS

4.1 THERAPEUTIC INDICATIONS

Relief of bronchospasm occurring in bronchial asthma, bronchitis and other bronchopulmonary conditions where bronchospasm is a complicating factor.

Acute prophylaxis in situations known to induce bronchospasm, e.g. exercise-induced asthma.

4.2 DOSE AND METHOD OF ADMINISTRATION

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 of treatment.

BRICANYL TURBUHALER is inspiratory flow driven and hence there is no need to coordinate the release of the dose and the inhalation as with a pressurised inhaler.

When inhaling, the substance follows the inspired air into the airways. Treatment with BRICANYL TURBUHALER is effective even during an acute asthmatic attack.

The dosage of inhaled terbutaline via BRICANYL TURBUHALER should be individualised. BRICANYL TURBUHALER should be used as required rather than regularly.

Adults and children over 12 years: One to two inhalations as required. In severe cases the single dose may be increased to 6 inhalations. The total dose should not exceed 24 inhalations in 24 hours.

Children (3-12 years): One to two inhalations as required. In severe cases the single dose may be increased to 4 inhalations. The total dose should not exceed 16 inhalations in 24 hours.

When prescribing BRICANYL TURBUHALER to young children it is necessary to ascertain that they can follow the instructions for use.

Instruction for the correct use of turbuhaler

TURBUHALER is inspiratory flow-driven which means that, when the patient inhales through the mouthpiece, the substance will follow the inspired air into the airways.

Note: It is important to instruct the patient

- to carefully read the instructions for use in the information leaflet which is packed with each inhaler
- to breathe in forcefully and deeply through the mouthpiece to ensure that an optimal dose is delivered to the lungs
- never to breathe out through the mouthpiece.

The patient may not taste or feel any medication when using TURBUHALER due to the small amount of drug dispensed.

4.3 CONTRAINDICATIONS

Hypersensitivity to the active substance (terbutaline) or to lactose (which may contain milk protein residue).

4.4 SPECIAL WARNINGS AND PRECAUTIONS FOR USE

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 the sign of worsening asthma. Repeated inhalations of beta2-agonists must then not delay reassessment of the asthma therapy.

As for all beta2-agonists caution should be observed in patients with thyrotoxicosis and in patients with severe cardiovascular disorders, such as ischaemic heart disease, tachyarrhythmias or severe heart failure.

Due to the hyperglycaemic effects of beta2-agonists, additional blood glucose controls are recommended initially in diabetic patients.

Potentially serious hypokalaemia may result from beta2-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). It is recommended that serum potassium levels are monitored in such situations.

BRICANYL should be used with caution if susceptibility to sympathomimetic amines is likely to be increased, for instance in patients with hyperthyroidism not yet under adequate control.

Bricanyl Turbuhaler (M3 version only) contains lactose. The excipient lactose may contain small amounts of milk protein residues. In patients with hypersensitivity to milk protein, these small amounts may cause allergic reactions.

4.5 INTERACTION WITH OTHER MEDICINES AND OTHER FORMS OF INTERACTION

Beta-receptor blocking agents (including eye-drops), especially those which are non-selective, may partly or totally inhibit the effect of beta-agonists.

Halogenated anaesthetics

Halothane anaesthesia should be avoided during beta2-agonist treatment, since it increases the risk of cardiac arrhythmias. Other halogenated anaesthetics should be used cautiously together with beta2-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 section 4.4). Hypokalaemia also predisposes to digoxin toxicity.

4.6 FERTILITY, PREGNANCY AND LACTATION

No teratogenic effects have been observed in patients or in animals. However, caution is recommended during the first trimester of pregnancy.

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 medicine. In the 4 infant studies this did not result in any signs of beta-adrenoceptor stimulation.

Transient hypoglycaemia has been reported in newborn preterm infants after maternal beta2-agonist treatment.

4.7 EFFECT ON ABILITY TO DRIVE AND USE MACHINES

BRICANYL TURBUHALER does not affect the ability to drive or use machines.

4.8 UNDESIRABLE EFFECTS

The frequency of adverse reactions is low at the recommended dose. Terbutaline given by inhalation is unlikely to produce significant systemic effects when given in

recommended doses because pharmacologically active concentrations of the drug are not achieved in the systemic circulation.

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. The majority of these effects reverse spontaneously within the first 1-2 weeks of treatment.

Less common reactions

Cardiovascular:	Ectopic beats.
Gastrointestinal:	Vomiting, bad taste, diarrhoea.
General:	Sweating.
Musculo-skeletal:	Muscle twitching.
Nervous system:	Drowsiness, dizziness, sleep disturbances and behavioural disturbances such as agitation, hyperactivity and restlessness.
Dermatological:	Urticaria and exanthema may occur.

Serious or life threatening reactions

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

Overdose of terbutaline may produce significant tachycardia, arrhythmia and hypotension (see section 4.9). In rare cases, through unknown mechanisms, medicines for inhalation may cause bronchospasm.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare professionals are asked to report any suspected adverse reactions <https://nzphvc.otago.ac.nz/reporting/>.

4.9 OVERDOSE

There is a potential for progressive accumulation of dry powder in the mouthpiece of BRICANYL TURBUHALER that could be released if dropped (for example, from a table) towards the end of the inhaler life. To minimize unnecessary systemic exposure to terbutaline, the patient should be advised, when possible, rinse their mouth after each use.

Possible symptoms and signs: headache, anxiety, tremor, nausea, insomnia, tonic muscle cramps, palpitations, tachycardia and cardiac arrhythmias. A fall in blood pressure sometimes occurs.

Laboratory findings: Hyperglycaemia and lactacidosis sometimes occur. Beta2-agonists may cause hypokalaemia as a result of redistribution of potassium.

Treatment of Overdosage

Usually no treatment is required. If it is suspected that significant amounts of terbutaline sulphate have been swallowed, the following measures should be considered:

Gastric lavage, activated charcoal. Determine acid-base balance, blood glucose and electrolytes. Monitor heart rate and rhythm and blood pressure. The preferred antidote for overdosage with BRICANYL is a cardioselective beta-receptor blocking agent, but beta-receptor blocking medicines should be used with caution in patients with a history of bronchospasm. If the beta2-mediated reduction in peripheral vascular resistance significantly contributes to the fall in blood pressure, a volume expander should be given.

For advice on the management of overdose please contact the National Poisons Centre on 0800 POISON (0800 764 766).

5. PHARMACOLOGICAL PROPERTIES

5.1 PHARMACODYNAMIC PROPERTIES

Terbutaline is an adrenergic agonist which predominantly stimulates beta2-receptors, thus producing relaxation of bronchial smooth muscle, inhibition of the release of endogenous spasmogens, inhibition of oedema caused by endogenous mediators and increased mucociliary clearance.

The bronchospasmolytic effect (time to onset, time to maximum effect and duration) and the extent of metabolism are dependent on the route of administration of terbutaline. The time to maximum effect is 30-60 minutes following inhalation.

Inhaled terbutaline acts within a few minutes and has a duration of up to 6 hours.

5.2 PHARMACOKINETICS PROPERTIES

Terbutaline is delivered to the prime site of action in the lungs by TURBUHALER administration.

M2 Turbuhaler Version: About 20-30% of the metered dose is deposited in the lungs at a normal inhalation flow rate.

M3 Turbuhaler Version: The absolute pulmonary bioavailability is about 16% of the delivered dose at a normal inhalation flow rate. Following administration of a single 1.5 mg dose (3 inhalations of 500 µg), maximum plasma concentration (C_{max}) of terbutaline of 12 nmol/L was achieved around 1.3 hours post-dose (t_{max}); the area under the plasma concentration-time curve (AUC) was 89 nmol*h/L and elimination half-life ($t_{1/2}$) was about 12 hours.

Terbutaline is metabolised mainly by conjugation with sulphuric acid and excreted as the sulphate conjugate.

No active metabolites are formed. Inhaled terbutaline is absorbed unchanged from the respiratory tract.

The presence of the two phenolic hydroxyl groups in the meta-positions confers resistance to metabolism by the enzyme catechol-o-methyl transferase. After administration by inhalation between 2-37% of the delivered terbutaline was recovered in faeces and 3-35% in urine.

Excretion of terbutaline sulphate and its metabolites is essentially complete within 72-96 hours after a single parenteral or oral dose.

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

No dosage adjustments are required in the elderly provided hepatic and renal function are normal.

5.3 PRECLINICAL SAFETY DATA

The major toxic effect of terbutaline, observed in toxicological studies, is focal myocardial necrosis. This type of cardiotoxicity is a well-known class-effect, and the effect of terbutaline is similar to or less pronounced than that of other beta-receptor agonists.

6. PHARMACEUTICAL PARTICULARS

6.1 LIST OF EXCIPIENTS

Apart from lactose (BRICANYL TURBUHALER M3 version) BRICANYL TURBUHALER is free from propellants, lubricants, preservatives, carrier substances or other additives.

6.2 INCOMPATIBILITIES

Not applicable

6.3 SHELF-LIFE

M2 Turbuhaler: 24 months.

M3 Turbuhaler: 36 months

6.4 SPECIAL PRECAUTIONS FOR STORAGE

Do not store above 30°C

Should be stored with the cover tightened.

6.5 NATURE AND CONTENTS OF CONTAINER

BRICANYL TURBUHALER is a multidose, inspiratory flow-driven, metered dose powder inhaler delivering (ex mouthpiece) 200 µg of terbutaline sulphate per inhalation (delivered dose). The device is made of plastic parts. There are two versions of the Turbuhaler device:

- Original M2 Turbuhaler: 250 µg per inhalation (metered dose). Each inhaler contains 200 doses.
- New M3 Turbuhaler: 200 µg per inhalation (delivered dose). Each inhaler contains 120 doses.

6.6 SPECIAL PRECAUTIONS FOR DISPOSAL

Return unused and expired medicines to your local pharmacy for disposal.

7. MEDICINE SCHEDULE

Prescription Medicine

8. SPONSOR

AstraZeneca Limited
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9. DATE OF FIRST APPROVAL

27 May 1987

10. DATE OF REVISION OF THE TEXT

8 March 2019

CDS 120816

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SUMMARY TABLE OF CHANGES

Section changed	Summary of new information
Various	Addition of M3 Turbuhaler device
5.3	Section added.