

PRODUCT MONOGRAPH

PrBRICANYL® TURBUHALER®

terbutaline sulfate dry powder for oral inhalation

0.5 mg/metered dose

Bronchodilator

AstraZeneca Canada Inc.
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ACTIONS AND CLINICAL PHARMACOLOGY

BRICANYL TURBUHALER (terbutaline sulfate) produces bronchodilation by stimulation of the β_2 -adrenergic receptors in bronchial smooth muscle, thereby causing relaxation of muscle fibers. This action is manifested by an increase in pulmonary function as demonstrated by FEV₁ measurements. BRICANYL TURBUHALER also produces a decrease in airway and pulmonary resistance.

Following inhalation of BRICANYL TURBUHALER, a significant improvement in pulmonary function measurements is well established after 5 minutes. 20 - 30% of the metered dose is deposited in the lungs with an inspiration flow rate of about 60 L/min.

The maximal response is usually attained between 15 and 60 minutes following administration. Significant bronchodilator activity has been observed to persist for 4 to 7 hours.

INDICATIONS AND CLINICAL USE

BRICANYL TURBUHALER (terbutaline sulfate) is indicated as a bronchodilator for the symptomatic relief of bronchial asthma and for relief of reversible bronchospasm which may occur in association with bronchitis and emphysema.

CONTRAINDICATIONS

BRICANYL TURBUHALER (terbutaline sulfate) is contraindicated:

- in patients who are hypersensitive to sympathomimetic amines;
- like other sympathomimetic amines, in patients who are known to have tachyarrhythmias;
- as a tocolytic in patients at risk of premature labour or threatened abortion.

WARNINGS

Like other β_2 -agonist inhalers, BRICANYL TURBUHALER (terbutaline sulfate) should not be used on a regular daily basis without appropriate concomitant anti-inflammatory therapy (see DOSAGE AND ADMINISTRATION).

BRICANYL TURBUHALER should be used with caution in patients with diabetes, hypertension, hyperthyroidism, and a history of seizures. As with other sympathomimetic bronchodilator agents, BRICANYL TURBUHALER should be administered cautiously to cardiac patients, especially those with associated arrhythmias, and coronary insufficiency, to elderly or to patients who are unusually responsive to sympathomimetic amines. Due to the hyperglycemic effects of β_2 -agonists, additional blood glucose controls are recommended initially in diabetic patients.

Occasionally, patients have been reported to have developed severe paradoxical bronchospasm with repeated use of sympathomimetic inhalant preparations. In such instances, the preparation should be discontinued immediately and alternate therapy instituted. Fatalities, the exact cause of which are unknown, have been reported following excessive use of inhaled preparations containing sympathomimetic amines. Cardiac arrest was noted in several instances.

Beta-receptor blocking agents (including eye-drops), especially those which are non-cardioselective, may partially or totally inhibit the effect of beta-receptor stimulants. Severe resistant bronchospasm may be produced with the use of beta-blockers in asthmatic patients.

Potentially serious hypokalemia may result from β_2 -agonist therapy, mainly from parenteral or nebulized administration. Particular caution is advised in acute severe asthma as this may be potentiated by hypoxia and concomitant treatment with xanthine derivatives, steroids and diuretics; it is recommended that serum potassium levels be monitored in such situations.

Use in Pregnancy

The safe use of BRICANYL TURBUHALER has not been established in human pregnancy. The use of this drug in pregnancy, lactation, or women of child-bearing potential requires that the expected therapeutic benefit of the drug be weighed against its possible hazards to the mother or child. Animal reproductive studies have shown no adverse effects on fetal development.

Transient hypoglycemia has been reported in newborn pre-term infants after maternal β_2 -agonist treatment.

Systemic β_2 -agonists should be used with caution before childbirth in view of their inhibiting effect on uterine contractions.

Nursing Mothers

Terbutaline is excreted in breast milk. Caution should be exercised when BRICANYL TURBUHALER is administered to nursing women.

Use in Pediatrics

BRICANYL TURBUHALER is not presently recommended for children below 6 years of age due to limited clinical data in this pediatric group.

PRECAUTIONS

If therapy does not produce a significant improvement or if the patient's condition gets worse, medical advice must be sought in order to determine a new plan of treatment.

With each inhalation a fraction of the delivered dose will be deposited in the oral cavity. To minimize unnecessary systemic exposure to terbutaline, the patients should be advised to, when possible, rinse their mouth after each use (see SYMPTOMS AND TREATMENT OF OVERDOSAGE).

In the case of acute or rapidly worsening dyspnea, a doctor should be consulted immediately.

Increasing use of β_2 -agonists to control symptoms of bronchial obstruction, especially administration on a regular basis or in high amounts, indicates deterioration of asthma control. Under these conditions, the patient's therapy plan has to be revised. It is inadequate simply to increase the use of bronchodilators under these circumstances, in particular over extended periods of time (see DOSAGE AND ADMINISTRATION). The revised treatment regimen should include concomitant use of other anti-asthma drugs, such as anti-inflammatory agents.

To ensure optimal delivery of BRICANYL (terbutaline sulfate) to the bronchial tree, the patient should be properly instructed in the use of TURBUHALER.

In patients in whom the administration of BRICANYL TURBUHALER induces cardiac irregularities, the administration of the drug should be stopped. If a reduced response to BRICANYL TURBUHALER becomes apparent, the patient should seek medical advice.

In patients requiring concomitant treatment with BRICANYL TURBUHALER and a beta-blocker, it is recommended that a beta-blocker (e.g., metoprolol) with less predominant β_2 -blocking effects be considered. If concomitant treatment is necessary, patients should be monitored carefully for possible deterioration in pulmonary function and the need to adjust the dosage of either drug (see Drug Interactions).

Immediate hypersensitivity reactions and exacerbation of bronchospasm have been reported after terbutaline administration.

Drug Interactions

Sympathomimetic Bronchodilators and Epinephrine

The concomitant use of BRICANYL TURBUHALER with other sympathomimetic bronchodilators or epinephrine is not generally recommended since their combined effect on the cardiovascular system may be deleterious to the patient. If additional adrenergic drugs are to be administered by any route to the patient using BRICANYL TURBUHALER, the

adrenergic drugs must be used with caution. Such concomitant use, however, should be individualized and not given on a routine basis. If regular co-administration is required, alternative therapy should be considered.

MAO Inhibitors and Tricyclic Antidepressants

BRICANYL TURBUHALER should be administered with caution in patients being treated with monoamine oxidase (MAO) inhibitors or tricyclic antidepressants, since the action of BRICANYL on the vascular system may be potentiated.

Beta-Adrenergic Receptor Blockers

Beta-adrenergic receptor blocking agents not only block the pulmonary effect of terbutaline but may produce severe asthmatic attacks in asthmatic patients. Therefore, patients requiring treatment for both bronchospastic disease and hypertension should be treated with medication other than beta-adrenergic blocking agents for their hypertension.

BRICANYL TURBUHALER contains terbutaline sulfate which is sensitive to moisture. Patients should be instructed to avoid exhaling into the device and to replace the cover after using TURBUHALER.

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 hypokalemia

Owing to the hypokalemic effect of beta-agonists, concurrent administration with BRICANYL of serum potassium depleting agents known to exacerbate the risk of hypokalemia, 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 hypokalemia. Hypokalemia also predisposes to digoxin toxicity.

ADVERSE REACTIONS

When treatment with BRICANYL TURBUHALER (terbutaline sulfate) is started, the following adverse reactions can be classified as frequent (i.e., > 1/100): tremor, palpitations, restlessness, headache, muscle cramps, nervousness. Other reported reactions include increased heart rate, tachycardia, ectopic beats, myocardial ischemia, drowsiness, nausea, vomiting, sweating and dizziness. As for all β_2 -agonists, cardiac arrhythmias, e.g., atrial fibrillation, supraventricular tachycardia and extrasystoles have been rarely reported.

These adverse reactions are all characteristic of sympathomimetic amines and initial dose titrations will often reduce these reactions. With the possible exception of muscle cramps, all have been spontaneously reversible within the first two weeks of treatment. Urticaria and exanthema may also occur.

Sleep disturbances and behavioural disturbances, such as agitation, hyperactivity and restlessness, have been observed. As with other inhalation therapy, the potential for paradoxical bronchospasm should be kept in mind with BRICANYL TURBUHALER. If it occurs, the preparation should be discontinued immediately and alternative therapy instituted. Potentially serious hypokalemia may result from β_2 -agonist therapy.

SYMPTOMS AND TREATMENT OF OVERDOSAGE

The symptoms of overdosage are similar to those described above under ADVERSE REACTIONS, and are attributable to excessive β -adrenergic stimulation. To antagonize the effect of excessive stimulation, the judicious use of a β -adrenergic blocking agent such as propranolol may be considered, bearing in mind the danger of inducing an asthmatic attack.

There is a potential for progressive accumulation of dry powder in the mouthpiece of BRICANYL TURBUHALER (terbutaline sulfate) that could be released if dropped (e.g., 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 (see PRECAUTIONS).

DOSAGE AND ADMINISTRATION

Dosage should be individualized, and patient response should be monitored by the prescribing physician on an ongoing basis.

BRICANYL TURBUHALER

Adults and Children \geq 6 Years

The generally recommended dose of BRICANYL TURBUHALER (terbutaline sulfate) is one inhalation (0.5 mg) taken as required. This will usually be adequate to relieve bronchospasm in the majority of patients, however, if required, a second dose may be taken, preferably after waiting five minutes for the effect of the first dose to be obtained. If a more severe attack has not been relieved by the second administration, higher doses may be required. In these cases, patients should immediately consult their doctor or the nearest hospital.

More than six doses (six inhalations of BRICANYL TURBUHALER) should not be necessary in any 24 hour period.

If a previously effective dosage regimen fails to provide the usual relief, or the effects of a dose last for less than three hours, medical advice should be sought immediately; this is a sign of seriously worsening asthma that requires reassessment of therapy.

Treatment with β_2 -agonists in bronchial asthma should be on demand, e.g., symptoms oriented. **Patients must not use them on a daily basis for control of bronchospasm without using other concomitant anti-asthma medication(s) according to the present practice for asthma treatment to control airway inflammation.**

The daily dose of BRICANYL TURBUHALER should not be increased without adequate reassessment of the therapy plan.

As with other β_2 -agonists, increasing demand for BRICANYL TURBUHALER (terbutaline sulfate) in bronchial asthma is a sign of poor asthma control and indicates that the treatment plan should be revised.

When prescribing BRICANYL TURBUHALER to children, it is necessary to ascertain that they can follow the instructions for use. BRICANYL TURBUHALER is not recommended for use in children below the age of 6 years.

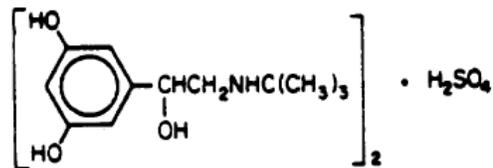
NOTE: The medication from BRICANYL TURBUHALER is delivered to the lungs as the patient inhales and, therefore, it is important to instruct the patient to breathe in forcefully and deeply through the mouthpiece. The patient may not taste or feel any medication when using BRICANYL TURBUHALER due to the small amount of drug dispensed.

PHARMACEUTICAL INFORMATION

Drug Substance

Proper name: terbutaline sulfate

Chemical Structure:



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

Molecular Weight: 548.6

Chemical Name: 1-(3,5-dihydroxyphenyl)2-t-butylamino ethanol sulfate

Description: Terbutaline sulfate is a water soluble, white to off-white crystalline powder.

Dosage Form

Composition:

BRICANYL TURBUHALER

Ingredient *mg/inhalation*

terbutaline sulfate 0.5

Stability and Storage Recommendations

BRICANYL TURBUHALER should be stored with the cover tightened, at room temperature (15 - 30°C).

AVAILABILITY OF DOSAGE FORMS

TURBUHALER

BRICANYL TURBUHALER (terbutaline sulfate) is supplied in 100 doses of micronized terbutaline sulfate. Each inhalation from the multiple dose powder inhaler contains 0.5 mg of terbutaline sulfate; no additives or carrier substances are included in the inhalation.

BRICANYL TURBUHALER cannot be re-filled and should be discarded when empty.

PHARMACOLOGY

Animal

Terbutaline sulfate has been shown by pharmacological studies in animals to exert a preferential effect on β_2 -adrenergic receptors, such as those located in bronchial smooth muscle.

Bronchodilator Effect

In Vitro Studies

The bronchospasmodic effect of terbutaline sulfate, L-epinephrine, orciprenaline and isoproterenol has been studied on spirally cut trachea from guinea pig and rabbit, and on cat bronchi. All four compounds relaxed pilocarpine induced contraction. The order of potency (by weight) was as follows: isoproterenol, L-epinephrine, terbutaline sulfate (dl form), orciprenaline.

Terbutaline sulfate was added to organ baths containing spirally cut guinea pig trachea and right auricle. Epinephrine was studied as a reference drug. At low concentration rates, terbutaline sulfate produced a relaxation of the trachea without increasing the force of auricular contraction while epinephrine produced a similar degree of tracheal relaxation but also increased auricular contraction force. At higher concentrations, terbutaline sulfate also stimulated auricular contraction force.

In Vivo Studies

The bronchospasmodic effect of terbutaline sulfate, orciprenaline and isoproterenol was studied in anesthetized guinea pigs, cats and dogs. It was found that the bronchospasm induced by histamine or acetylcholine could be prevented by appropriate intravenous doses of these agents. The order of potency was as in the *in vitro* studies described above.

Terbutaline sulfate, orciprenaline and isoproterenol administered orally or intraperitoneally to unanesthetized guinea pigs protected the animals against histamine induced bronchoconstriction. As determined graphically, the intraperitoneal doses protecting 50% of the animals were in the following order of potency: Isoproterenol (0.065 mg/kg), terbutaline sulfate (0.15 mg/kg), orciprenaline (0.60 mg/kg). The ED₅₀ following oral administration of each drug showed the following order of potency: terbutaline sulfate (0.4 mg/kg), orciprenaline (1.2 mg/kg), isoproterenol (1.4 mg/kg).

Circulatory Effect

In Vitro Studies

Isolated heart muscle from guinea pigs and rabbits was used to compare the direct effect of terbutaline sulfate, isoproterenol, epinephrine and orciprenaline. The four substances produced increases in both contractile force and heart rate. Relative to the effect of epinephrine, the potencies of the different compounds with respect to the production of 20% inotropic and chronotropic increases were as follows: isoproterenol (15.3 - 42.0), epinephrine (1.0), orciprenaline (0.05 - 0.33), terbutaline sulfate (0.005 - 0.05).

Similar results were obtained using left auricle and papillary muscle preparations from the cat.

In Vivo Studies

In the anesthetized cat, terbutaline sulfate decreased mean arterial pressure, increased pulse pressure and increased heart rate. Decreases in mean arterial pressure were noted at intravenous doses greater than 0.07 µg/kg. Following intravenous isoproterenol administration, increased heart rate and decreased arterial blood pressure were seen at 0.008 µg/kg, which was the lowest dose studied.

In the anesthetized dog, increased heart rate and decreased mean arterial blood pressure were seen at doses of 0.005 µg/kg of isoproterenol, 0.5 µg/kg of orciprenaline and 1.0 µg/kg of terbutaline sulfate.

Other Pharmacological Activities

Terbutaline sulfate was shown to have an inhibiting effect on spontaneous contractions of the rabbit duodenum. In cats, terbutaline sulfate has been shown *in vitro* and *in vivo* to have a relaxing effect on the sphincter of Oddi. Terbutaline sulfate has demonstrated a relaxing effect on rabbit urinary bladder and rat uterine muscle.

Human

Absorption, Distribution, Metabolism and Excretion

Following oral administration of tritiated drug to man, plasma radioactivity peaked at 60 - 90 minutes, and declined with a half-life of 4 - 6 hours. Approximately 24% of the dose was absorbed, as indicated by recovery of radioactivity in urine; 5 - 6% of the dose was excreted in urine as unchanged drug and the remainder was identified as a sulfate conjugate.

Fecal radioactivity accounted for 35 - 56% of the original dose and was identified as unchanged drug.

The disposition of tritiated terbutaline sulfate following inhalation has been studied in man. Serum concentrations of total radioactivity were low. Peak concentrations were seen 3 - 6 hours following administration. Between 2 - 37% of the delivered drug was recovered in feces and 3 - 35% in urine. As with other routes of administration, inhaled drug was shown to be biotransformed by conjugation.

Following intravenous administration to man, 78 - 85% of the administered radioactivity was excreted in urine; 52 - 60% of the dose was excreted as unchanged drug, and 4 - 19% as sulfate conjugate. Less than 3% of the administered dose appeared in feces. Biliary excretion following intravenous dosing has been studied in two subjects with biliary drainage; less than 1% of the administered dose was excreted by this route.

Following subcutaneous administration to man, plasma levels plateaued from 10 - 40 minutes after dosing. Ultimately, 92 - 95% of the administered dose was recovered in the urine; approximately 60% of the administered radioactivity was excreted as unchanged drug. Less than 3% of the dose was excreted in feces.

In vitro experiments indicated that terbutaline sulfate is not metabolized by rat and human liver O-methyltransferases and monoamine oxidases, nor did it inhibit these enzymes significantly.

Plasma-binding of terbutaline sulfate has been studied *in vitro* using plasma prepared from human citrated blood. In the concentration range of 0.7 - 64.5 ng/mL, 25% of the drug was bound to plasma protein.

TOXICOLOGY

Acute Toxicity Studies with orally and parenterally administered terbutaline sulfate are summarized below.

Table 1

Species	Route	LD ₅₀ mg/kg
Mouse	i.v.	≈56
	i.p.	263
	s.c.	295
	oral	3,000
Rat	i.v.	≈74
	i.p.	316
	s.c.	800
	oral	≈1,800
Rabbit	i.v.	≈65
	s.c.	≈ 1,600
	oral	≈9,000
Dog	i.v.	> 125
	s.c.	≈300
	oral	≈ 1,000 - 2,000

Similar studies were performed on monkeys exposed in head chambers to an estimated dose of 80.5 mg/kg over 2 hours. Exudate around the mouth, and circumorbital erythema, were seen. Slight bradycardia was observed. Animals recovered and behaved normally during the post-exposure period. At autopsy, marked pulmonary congestion and edema were seen in half of the animals.

In animals, theophylline, chlorpromazine, meprobamate, chlorodiazepoxide, imipramine and phenylbutazone, in doses corresponding to twice the maximal clinical dose, did not influence the toxicity of terbutaline sulfate. Nialamide, however, caused a slight increase in the toxicity. Pre-treatment of animals with a dose corresponding to one third of the LD₅₀ of the above drugs increased the toxicity of terbutaline sulfate. This increase was slight with all drugs except for nialamide, which at this high dose level strongly increased the toxicity.

Subacute and Chronic Toxicity Studies

The effect of repeated daily administration of terbutaline sulfate, subcutaneously and orally, has been studied in rats and dogs. Other sympathomimetic amines were included as reference compounds in most studies.

Clinical manifestations of toxicity included hyperemia of mucous membrane and skin, vomiting after initial dosing, and abnormal quietness or irritability. Dose-related increased heart rate was seen in both species. Decreased blood glucose concentrations were observed in an 18 month rat study.

Myocardial changes, such as focal necrosis or fibrosis or chronic focal myocarditis, were the most significant pathological findings related to treatment and were also seen with each of four other sympathomimetic amines studied as reference compounds. These findings, in relation to terbutaline sulfate, are summarized in Table 2 which shows the dose levels studied for each species and route of administration. Those levels at which myocardial lesions were seen are underlined.

Table 2

Species	Route	Duration	Dose Levels (mg/kg/day)
Dog	subcutaneous	2 weeks	0.0, 0.025, <u>0.5</u> , <u>5.0</u>
		4 weeks	0.0, 0.005, 0.01, 0.025, <u>0.1</u>
	oral	1 month	0.025, 0.25, <u>4.0</u> , <u>20.0</u>
		3 months	0.0, 0.2, 1.0, <u>10.0</u>
		6 months	0.0, 0.3, <u>2.0</u> , <u>10.0-20.0</u>
12 months	0.0, 0.3, 2.0, 10.0-20.0		
Rat	subcutaneous	3 days	0.0, <u>0.025</u> , 0.1, <u>0.5</u> , 1.0, <u>10.0</u> , <u>50.0</u>
		1 month	0.0, 0.1, <u>1.0</u> , <u>5.0</u> , <u>25.0-50.0</u>
	oral	1 month	<u>0.0</u> , <u>10.0</u> , <u>100.0</u> , <u>500.0</u>
		3 months	<u>0.0</u> , <u>0.2</u> , <u>2.0</u> , <u>50.0</u>
		18 months	<u>0.0</u> , <u>2.0</u> , <u>20.0</u> , <u>200.0</u>

In the dog, myocardial lesions were observed after the intratracheal administration of 0.7 mg/kg/day for two days. Morphologically similar toxicity was seen with reference bronchodilating compounds. In a 4 week rat study, myocardial lesions were seen in 4 of 10 animals exposed for 90 min/day to an aerosol cloud containing 4 - 6 mg/L. These lesions were considered similar to the findings in rats and dogs treated with orally or subcutaneously administered drug.

Three-month studies, in which rats and monkeys were exposed to terbutaline sulfate under circumstances calculated to provide inhaled doses of up to 25 and 27.3 mg/kg/day, respectively, failed to reveal drug-related pathology of the myocardium or other tissues.

Reproduction and Teratology Studies

Reproduction and Teratology studies have been performed in mice, rats and rabbits. None of these studies revealed any adverse effects on the reproductive performance, or development of fetus, attributable to terbutaline sulfate.

Carcinogenicity Studies

Carcinogenicity studies were conducted in mice and rats. Terbutaline sulfate was given orally at dose levels from 2 - 200 mg/kg/day for 18 months. Results obtained did not suggest carcinogenicity since the number of tumors in control and treated animals were statistically comparable.

Mutagenicity Studies

Studies of terbutaline sulfate have not been conducted to determine mutagenic potential.

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PART III: CONSUMER INFORMATION

BRICANYL[®] TURBUHALER[®]

terbutaline sulfate dry powder for oral inhalation

Read this carefully before you start taking BRICANYL TURBUHALER and each time you get a refill. This leaflet is a summary and will not tell you everything about BRICANYL TURBUHALER. Talk to your doctor, nurse, or pharmacist about your medical condition and treatment and ask if there is any new information about BRICANYL TURBUHALER.

ABOUT THIS MEDICATION

This medicine is for you. Only a doctor can prescribe it for you. Never give it to someone else. It may harm them even if their symptoms are the same as yours.

What the medication is used for:

BRICANYL TURBUHALER is used to treat asthma, bronchitis and emphysema.

What it does:

BRICANYL TURBUHALER contains the medicine terbutaline. Terbutaline belongs to the class of drugs called bronchodilators. Bronchodilators relax the muscles in your airways. This helps to open your airways, making it easier for you to breathe. BRICANYL TURBUHALER relieves sudden symptoms such as wheezing, cough and shortness of breath.

BRICANYL TURBUHALER effect starts within 5 minutes after you have inhaled it and lasts for up to 7 hours.

When it should not be used:

Do not use BRICANYL TURBUHALER:

- if you are allergic to terbutaline sulfate;
- if you have a heart problem called tachyarrhythmia (fast and/or irregular heartbeat);
- to treat or prevent premature labour or miscarriage.

What the medicinal ingredient is:

Terbutaline sulfate.

What the nonmedicinal ingredients are:

BRICANYL TURBUHALER contains no other ingredients.

What dosage forms it comes in:

Dry powder for oral inhalation: 0.5 mg per dose. Each inhaler contains 100 doses.

WARNINGS AND PRECAUTIONS

BEFORE you use BRICANYL TURBUHALER talk to your doctor or pharmacist:

- about **all** health problems you have now or have had in the past, including:
 - heart problems such as irregular heart beat, chest pain;
 - high blood pressure;
 - diabetes;
 - thyroid problems;
 - a history of seizures;
 - low levels of potassium in the blood;
- if you have ever had an allergic reaction to terbutaline or to any other similar medicines;
- if you are over 65 years old;
- if you are pregnant, plan to become pregnant or are breastfeeding.
 - Pre-mature babies born to mothers who use BRICANYL TURBUHALER at the end of pregnancy may experience low blood sugar (hypoglycaemia). The symptoms may include jitteriness, poor body tone, poor feeding. Note that the symptoms of hypoglycaemia may resemble other conditions or medical problems. Always consult your baby's doctor for an opinion.

INTERACTIONS WITH THIS MEDICATION

As with most medicines, interactions with other drugs are possible. Tell your doctor, nurse, or pharmacist about all the medicines you take, including drugs prescribed by other doctors, non-prescription medications, vitamins, minerals, natural supplements, or alternative medicines.

Drugs that may interact with BRICANYL TURBUHALER are:

- Beta-blockers (some medicines for high blood pressure, heart conditions and some eye-drops);
- Epinephrine (also known as adrenaline or adrenalin) for life threatening allergic reactions;
- Monoamine Oxidase Inhibitors for depression;
- Tricyclic Antidepressants for depression;
- Steroid medicines (such as prednisolone);
- Medicines called 'xanthines' (such as theophylline);
- Water pills (diuretics);
- If you are having surgery, tell the doctor (halothane medicines should be avoided).

PROPER USE OF THIS MEDICATION

The dosage of BRICANYL TURBUHALER is individual.

Follow your doctor's directions carefully. They may differ from the information in this leaflet. Check with your doctor or pharmacist if you are not sure.

Usual dose for Adults and children 6 years of age and older:

- one inhalation as needed.

- If needed, you may take a second dose. Wait five minutes for the first dose to take effect before taking the second dose.
- If your symptoms persist after the second dose, consult your doctor or the nearest hospital right away.
- You should not take more than six inhalations (3.0 mg) in a 24-hour period.

See a doctor right away if:

- your usual dose does not provide relief;
- your breathing condition gets worse;
- the effects of one dose last less than three hours;
- you are using BRICANYL TURBUHALER every day to relieve symptoms.

These may be signs that your asthma is getting worse. Your doctor may prescribe this medication in association with other anti-asthma medication that controls airway inflammation.

Do NOT exceed the dose prescribed by your doctor.

Missed dose:

BRICANYL TURBUHALER should be used as needed rather than regularly. However, if you have been prescribed regular treatment and you forget to take a dose, take one as soon as you remember. If it is very close to the next dosing time, wait until then.

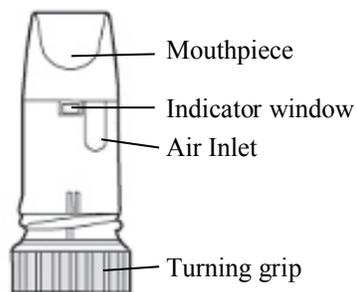
Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

HOW TO USE YOUR BRICANYL TURBUHALER INHALER

Before you start using BRICANYL TURBUHALER for the first time it is important that you read the instructions below and follow them carefully.

TURBUHALER is a multidose inhaler from which very small amounts of powder are administered. When you breathe in through BRICANYL TURBUHALER the powder is delivered to the lungs. It is therefore important that you **inhale as deeply and strongly** as you can through the mouthpiece.



Before you use a **NEW** inhaler for the first time you must prepare the inhaler for use. Follow the steps under “**A. How to prepare a NEW inhaler for use:**”.

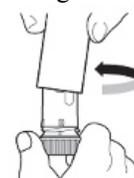
For usual use of your inhaler follow the steps under “**B. How to take a dose:**”.

A. How to prepare a NEW inhaler for use:

You only need to prepare your **NEW** inhaler for use **once**. You do not need to repeat these steps even if your inhaler is not used frequently.

STEP 1 Unscrew and lift off the cover (Figure 1).

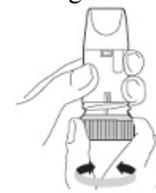
Figure 1



STEP 2 Hold the inhaler upright. Do not hold the inhaler by the mouthpiece.

- Turn the **blue grip** as far as it will go in one direction (clockwise or counter-clockwise, it does not matter which way you turn it first).
- Then turn the blue grip as far as it will go in the opposite direction (Figure 2).
- At some point when you are turning the grip you will hear a “**click**”. This is part of the preparation process.

Figure 2



STEP 3 **Repeat STEP 2** one more time. Then follow the steps under “**B. How to take a dose:**”, **starting at STEP 2.**

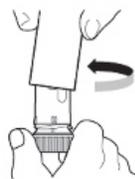
B. How to take a dose:

To properly take a dose, follow these 4 steps:

STEP 1 Unscrew and lift off the

Figure 1

cover (Figure 1).



STEP 2 Hold the inhaler upright. Do not hold the inhaler by the mouthpiece.

- Turn the **blue grip** as far as it will go in one direction (clockwise or counter-clockwise, it does not matter which way you turn it first).
- Then turn the blue grip as far as it will go in the opposite direction (Figure 2).



A dose has now been loaded.

- At some point when you are turning the blue grip, you will hear a “click”. This is part of the loading process.

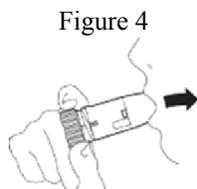
NOTE: If you accidentally **drop, shake** or **breathe out** into BRICANYL TURBUHALER after the dose has been loaded, you will lose your dose. If this happens, repeat STEP 2 to load a new dose.

STEP 3 **Breathe out**, with your mouth away from the mouthpiece (Figure 3). Then, place the mouthpiece gently between your teeth.



STEP 4 Now close your lips over the mouthpiece. Do not bite or chew the mouthpiece.

- **Inhale as deeply and strongly** as you can (Figure 4).
- You may not feel or taste the medication when inhaling. This is common.
- Before you exhale, remember to remove the inhaler from your mouth.



been prescribed. When you have taken the prescribed amount of doses, **replace the cover of the inhaler by screwing it back on.** With each inhalation some medication may stick to the inside of your mouth and throat. To reduce the risk of side effects rinse your mouth with water, and do not swallow.

Note: Do not try to remove the mouthpiece or to twist it unnecessarily. It is fixed to the inhaler and must not be taken off.

I cannot remember how many times I turned the blue grip. What should I do?

The TURBUHALER is designed to load only one dose at a time. If you can't remember how many times you have turned the blue grip, you can start the process again. Follow the steps below. You will not end up loading two doses.

If you are using a **NEW** inhaler for the first time, start at the beginning of STEP 2 under the section “**A. How to prepare a NEW inhaler for use:**”.

For usual use of your inhaler, start at the beginning of STEP 2 under the section “**B. How to take a dose:**”.

How do I know my dose has been loaded?

By turning the blue grip all the way in BOTH directions, you will properly load a dose of your medication. At some point when you are turning the grip you will hear a “click”. This is part of the loading process. If you are not sure you heard the “click”, repeat from the beginning of STEP 2 under the section “**B. How to take a dose:**”. This will not result in two doses being loaded. The TURBUHALER is designed to load only one dose at a time. If you do not hear the “click” sound when the turning grip is rotated, you will not receive any medication. If this problem persists, you need to replace the BRICANYL TURBUHALER.

How do I clean my inhaler?

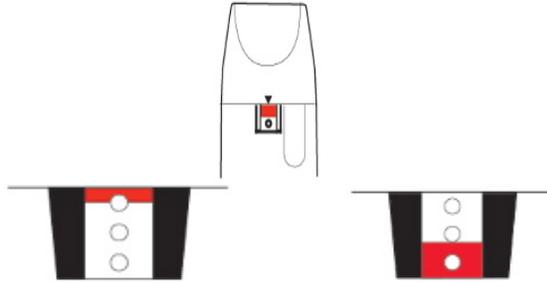
Clean the outside of the mouthpiece once a week with a **dry** tissue. **Never** use water or any other fluid. If fluid enters the inhaler it may not work properly.

How do I know when to start a new inhaler?

BRICANYL TURBUHALER has a dose indicator. When a red mark first appears in the little window underneath the mouthpiece, there are approximately 20 doses left (Figure 5). Now is the time to obtain your next inhaler. When the red mark reaches the bottom of the window, you should discard your inhaler. The sound you hear if you shake the inhaler is produced by a drying agent, not the medication. BRICANYL TURBUHALER cannot be refilled with drug and should be thrown away.

Figure 5

Repeat STEPS 2-4 if more than one dose has



Approximately 20 doses left

EMPTY

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

The most common side effects are nervousness and shakiness. These side effects disappear in most cases over the first few days of treatment.

Side effects may include:

- headache;
- flushing, sweating, hives and rash;
- occasional muscle cramps;
- sleeplessness, drowsiness;
- nervousness, restlessness, agitation, hyperactivity;
- shakiness;
- stomach upset, nausea, vomiting;
- weakness, dizziness;
- nausea and sweating.

BRICANYL TURBUHALER may affect blood sugar levels. If you are diabetic you may need to check your blood glucose more frequently. Your doctor will advise you about this.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and seek emergency medical attention
		Only if severe	In all cases	
Rare	Low potassium levels in the blood: irregular heartbeats, muscle weakness and spasms		X	
Unknown Frequency	Fast or irregular heartbeats for an extended period of time		X	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect	Talk with your doctor or pharmacist		Stop taking drug and seek emergency medical attention
	Only if severe	In all cases	
Paradoxical Bronchospasm: shortness of breath, chest tightness which causes wheezing immediately after inhaling your dose			X
Myocardial Ischemia: chest pain related to heart problems and shortness of breath		X	
Allergic Reaction: swelling of the face, lips, tongue or throat, difficulty swallowing or breathing (or rash and hives in combination with the above)			X

This is not a complete list of side effects. For any unexpected effects while taking BRICANYL TURBUHALER, contact your doctor or pharmacist.

HOW TO STORE IT

Keep BRICANYL TURBUHALER out of the reach and sight of children.

Always replace and tighten the cover after using BRICANYL TURBUHALER. Store the inhaler at room temperature (15-30 °C).

Do not keep or use BRICANYL TURBUHALER after the expiry date indicated on the label.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>) for information on how to report online, by mail or by fax; or
- Call toll-free at 1-866-234-2345

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

NOTE: This CONSUMER INFORMATION leaflet provides you with the most current information at the time of printing.

The Consumer Information Leaflet plus the full Product Monograph, prepared for health professionals can be found at:

www.astrazeneca.ca,

or by contacting the sponsor, AstraZeneca Canada Inc. at: 1-800-668-6000.

This leaflet was prepared by:

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