# Terbutaline Sulfate

## Bricanyl®
## 500 mcg /mL
## Solution for Injection (IV/SC)
## Beta-2-Adrenoceptor Agonist

### 1. FORMULATION
1 mL contains terbutaline sulfate 500 mcg.

### 2. PHARMACEUTICAL FORM
Terbutaline sulfate (BRICANYL) solution for injection contains no preservatives.

### 3. CLINICAL PARTICULARS

#### 3.1 Therapeutic Indication
Bronchial asthma. Chronic bronchitis, emphysema and other lung diseases where bronchospasm is a complicating factor. Preterm labour.

#### 3.2 Dosage and method of administration
The dose may be given intravenously or subcutaneously.

Terbutaline sulfate (BRICANYL) solution for injection, 1 mL ampoule, is intended for subcutaneous and intravenous injection.

Terbutaline sulfate (BRICANYL) solution for injection, 5 mL ampoule, is intended for infusion after dilution with infusion solutions.

Dosage should be individual.

**Bronchospasm:**
*Intravenous injection*
***Adults:*** 0.25-0.5 mg (0.5-1 mL) is injected slowly intravenously. The solution for injection is diluted with sterile physiological saline up to 10 mL and is given slowly intravenously during 5 minutes. The dose may have to be repeated with short intervals (a few hours). The dose should not exceed 2 mg in 24 hours.

*Intravenous infusion*
***Adults:*** 1-2 mg (2-4 mL) is given during a 24 hour interval as a continuous infusion. An initial loading dose up to 0.10 mg (0.2 mL) can be given over 10 minutes.

***Children:*** Up to 25 µg/kg b.w. (0.05 mL/kg b.w.) is given during a 24 hour interval as a continuous infusion. An initial loading dose up to 1.5 µg/kg b.w. (0.003 mL/kg b.w.) can be given over 10 minutes.

*Subcutaneous injection*
***Adults:*** 1-2 mg (2-4 mL) is given during a 24 hour interval, split into at least 4 occasions.

***Children:*** Up to 25 µg/kg b.w. (0.05 mL/kg b.w.) is given during a 24 hour interval, split into at least 4 occasions.

**Preterm labour:**
The dose must be individually titrated. Pulse rate and blood pressure should be carefully monitored during treatment. Initially 5 µg/min could be given as an infusion during 20 minutes. The dose can then be increased by 2.5 µg/min at 20 minute intervals until contractions stop. More than 10 µg/min should seldom be given, and 20 µg/min should not be exceeded. Let the infusion continue for 1 h at the chosen infusion rate, and then decrease the rate of infusion in steps of 2.5 µg/min at 20 minute intervals down to the lowest maintenance dose that produces continued suppression of the contractions. Keep the infusion at this rate for 12 h and then continue with oral maintenance therapy (5 mg x 3).

The oral treatment should be continued until the end of the 36th week of pregnancy. As an alternative treatment, subcutaneous injections (0.25 mg four times in a 24 h period) could be given for a few days before oral treatment is started.

**Suggestion for dilution:**
5 mg (2 ampoules of 5 mL) in 1000 mL of dextrose solution or physiological saline. Prepared solution contains 5 µg/mL and should be used within 12 hours. Terbutaline sulfate (BRICANYL) should not be diluted in alkaline solutions. Saline should be avoided during pregnancy since the risk of producing pulmonary edema may increase when this diluent is used in pregnant women. If saline has to be used, the patient should be carefully monitored. Terbutaline sulfate (BRICANYL) can be added to infusion solutions in glass bottles as well as in PVC plastic bags.

**3.3 Contraindications**
Hypersensitivity to any of the ingredients. In obstetrics: Intrauterine infection, severe preeclampsia, ablatio placentae.

**3.4 Special warnings and precautions for use**
As for all $\beta_2$-agonists caution should be observed in patients with thyrotoxicosis and in patients with severe cardiovascular disorder, such as ischemic heart disease, tachyarrhythmias or severe heart failure.

Due to the hyperglycemic effects of $\beta_2$-agonists, additional blood glucose controls are recommended initially in diabetic patients.

Potentially serious hypokalemia 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 hypokalemic effect may be potentiated by concomitant treatments (see section 3.5 Interactions). It is recommended that serum potassium levels are monitored in such situations.

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

Hypokalemia may result from $\beta_2$-agonist therapy and may be potentiated by concomitant treatment with xanthine derivatives, steroids and diuretics (see section 3.4 Special warnings and precautions for use).

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

Terbutaline passes over to breast milk but an influence on the child is unlikely with therapeutic doses.

Transient hypoglycemia has been reported in newborn preterm infants after maternal $\beta_2$-agonist treatment.

**3.7 Effects on ability to drive and use machines**
Terbutaline sulfate (BRICANYL) does not affect the ability to drive or use machines.

**3.8 Undesirable effects**

The intensity of the adverse reactions depends on dosage and route of administration. An initial dose titration will often reduce the adverse reactions. Adverse reactions which have been recorded, e.g. tremor, headache, nausea, tonic muscle cramps, tachycardia and palpitations, are all characteristic of sympathomimetic amines. The majority of these effects have reversed spontaneously within the first 1-2 weeks of treatment.

As for all $\beta_2$-agonists, cardiac arrhythmias, e.g. atrial fibrillation, supraventricular tachycardia and extrasystoles have been rarely reported.

Urticaria and exanthema may occur.

Sleep disturbances and behavioural disturbances, such as agitation, hyperactivity and restlessness, have been observed.

During treatment of preterm labour, when high doses of Terbutaline sulfate (BRICANYL) are used, diabetic mothers may develop hyperglycaemia and lactacidosis. In these patients glucose and acid-base balance should be carefully monitored. High doses of $\beta_2$-stimulants may cause hypokalemia as a result of redistribution of potassium. Symptoms of pulmonary edema have also been reported following treatment of preterm labour. An increased tendency to bleeding has been described in connection with caesarean section (give Propranolol, 1-2 mg i.v.) in patients treated with Terbutaline sulfate (BRICANYL) for preterm labour.

**3.9 Overdosage**

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

**Laboratory findings:** Hyperglycemia and lactacidosis sometimes occur. $\beta_2$-agonists may cause hypokalemia as a result of redistribution of potassium.

**Treatment of overdosage:**

Usually no treatment is required. In severe cases of overdosage, the following measures should be considered:

Determine acid-base balance, blood glucose and electrolytes. Monitor heart rate and rhythm and blood pressure. The preferred antidote for overdosage with Terbutaline sulfate (BRICANYL) is a cardioselective beta-receptor blocking agent, but beta-

receptor blocking drugs should be used with caution in patients with a history of bronchospasm. If the $\beta_2$-mediated reduction in peripheral vascular resistance significantly contributes to the fall in blood pressure, a volume expander should be given.

*In preterm labour*
Pulmonary edema: A normal dose of a loop diuretic (e.g. furosemide) should be given intravenously. Increased tendency to bleeding in connection with caesarean section: Give propranolol, 1-2 mg, intravenously.

## 4. PHARMACOLOGICAL PROPERTIES

### 4.1 Pharmacodynamic properties
Pharmaco-therapeutic group: selective $\beta_2$-agonist, terbutaline, ATC code: R03C C03.

Terbutaline is an adrenergic agonist which predominantly stimulates $\beta_2$-receptors, thus producing relaxation of bronchial smooth muscle, inhibition of the release of endogenous spasmogens, inhibition of edema caused by endogenous mediators, increased mucociliary clearance and relaxation of the uterine muscle.
After subcutaneous injection of terbutaline the duration of onset regarding the bronchodilating effect is less than 5 minutes. Maximum effect is reached within 30 minutes.

### 4.2 Pharmacokinetic properties
Terbutaline is metabolized mainly by conjugation with sulphuric acid and excreted as the sulfate conjugate. No active metabolites are formed. The plasma half life is about 16 hours. After intravenous and subcutaneous administration of terbutaline 90% is excreted renally during 48-96 hours. Of this, about 60% consists of unmetabolized terbutaline.

### 4.3 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. Terbutaline has been used extensively over many years for the relief of bronchospasm without identifying any areas of concern.

## 5. PHARMACEUTICAL PARTICULARS

### 5.1 Incompatibilities

Terbutaline sulfate (BRICANYL) solution for injection should not be mixed with alkaline solutions, i.e. solutions with a pH higher than 7.0.

**5.2 Shelf-life**
Please refer to outer carton.

**5.3 Special precautions for storage**
Store at temperatures not exceeding 30ºC. Protect from light.

**5.4 Availability**
Terbutaline sulfate (BRICANYL) 500 mcg/mL –1 mL ampoule (Box of 10's)

Manufactured by Cenexi
52, Rue Marcel et Jacques, Gaucher, 94120 Fontenay Sous-Bois, France
For AstraZeneca AB
SE-151 85 Södertälje, Sweden

Imported by the Marketing Authorization Holder
AstraZeneca Pharmaceuticals (Phils.), Inc.
16th Floor, Inoza Tower, 40th Street, Bonifacio Global City, Taguig, Philippines

**CAUTION**
Foods, Drugs, Devices, and Cosmetics Act prohibits dispensing without prescription.

For suspected adverse drug reaction, please report to the Food and Drug Administration (FDA) at www.fda.gov.ph and to AstraZeneca at patientsafety.ph@astrazeneca.com. The patient should seek medical attention immediately at the first sign of any adverse drug reaction.

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