Bricasma® 2.5 mg/mL
	terbutaline sulphate
Solution for nebulization

Qualitative and quantitative composition
1 ml contains terbutaline sulfate 2.5 mg.

Pharmaceutical form
Sterile solution for nebulization in single dose units of 2 ml.
BRICASMA solution for nebulization is isotonic and contains no preservatives.

Therapeutic indication
For the release of bronchospasm in chronic bronchitis, emphysema and other lung diseases where bronchospasm is a complicating factor.

Posology and method of administration
Inhaled bronchodilators should, as initial therapy, be used as required rather than regularly.

BRICASMA solution for nebulization is to be used in nebulizers with or without assisted breathing in acute or subacute disorders where conventional inhalers prove unsatisfactory and in maintenance therapy in severe broncho-obstructive conditions.

Dosage should be individual.
Body weight > 25 kg: 5 mg (1 single dose unit, 2 ml) is inhaled 2 up to 4 times in a 24 h period.

Contraindication
Hypersensitivity to any of the ingredients.

Special warnings and special precautions for use
The patient's inhalation technique should be checked regularly, and the optimal dose of BRICASMA should be adjusted for each nebulizer.

BRICASMA should be used with caution when an increased susceptibility to sympathomimetic amines can be expected for instance in patients with hyperthyroidism not yet under adequate control.

If a previously effective dosage regimen no longer gives the same symptomatic relief, the patient should seek medical care as soon as possible as this could be sign of worsening asthma and repeated inhalations of β₂-agonists must then not delay reassessment of the asthma therapy.

As for all β₂-agonists caution should be observed in patients with thyrotoxicosis. Cardiovascular effects may be seen with sympathomimetic drugs, including BRICASMA. There is some evidence from post-marketing data and published literature of myocardial ischaemia associated with beta agonists.
Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving BRICASMA 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.

Due to the hyperglycemic effects of β2-agonists, additional blood glucose controls are recommended initially in diabetic patients.

Due to the positive inotropic effect of β2-agonists, this drug should not be used with hypertrophic cardiomyopathia.

However these drugs have an arrhythmogenic potential which must be considered in the treatment the individual lung patient.

Terbutaline is not indicated and should not be used for the management of preterm labor. Serious adverse reactions have been reported following administration of terbutaline sulfate to women in labor.

These reports have included transient hypokalemia, pulmonary edema (sometimes after delivery), and hypoglycemia in the mother and / or neonatal child. Maternal death has been reported with terbutaline sulfate and other drugs of this class.

There have been rare reports of seizures occurring in patients receiving terbutaline, which do not recur when the drug is discontinued and have not been explained on any other basis.

Terbutaline sulfate is a sympathomimetic amine and such should be used with caution in patients with cardiovascular disorders (including arrhythmias, coronary insufficiency and hypertension), in patients with hyperthyroidism or diabetes mellitus, history of seizures, or in patients who are unusually responsive to sympathomimetic amines.

Potentially serious hypokalemia may result from β2-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 *Interactions with other medicinal products and other forms of interaction*). It is recommended that serum potassium levels are monitored in such situations. Patients susceptible to hypokalemia should be monitored because transient early alls in serum potassium levels have been reported with β2-agonist.

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

Safety and effectiveness in children below the age of 12 have not been established.

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

**Interactions with other medicinal products and other forms of interaction**

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

Hypokalemia may result from β2-agonist therapy and may be potentiated by concomitant treatment with xanthine derivatives, steroids and diuretics (see Special warnings and special precautions for use).

**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 β2-agonist treatment.

**Effects on ability to drive and use machines**

BRICASMA does not affect the ability to drive or use machine.

**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. Most of the adverse reactions are characteristic of sympathomimetic amines. The majority of these effects have reversed spontaneously within the first 1-2 weeks of treatment.

<table>
<thead>
<tr>
<th>Frequency Classification</th>
<th>Adverse Drug Reaction</th>
<th>Preferred term (PT)</th>
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</thead>
<tbody>
<tr>
<td>Very common ≥1/10</td>
<td>Nervous system disorders</td>
<td>Tremor, headache</td>
</tr>
<tr>
<td>Common &lt;1/10 and ≥1/100</td>
<td>Cardiac disorders</td>
<td>Tachycardia, palpitations</td>
</tr>
<tr>
<td></td>
<td>Musculoskeletal and connective tissue disorders</td>
<td>Tonic muscle cramps</td>
</tr>
<tr>
<td></td>
<td>Metabolism and nutrition disorders</td>
<td>Hypokalaemia</td>
</tr>
<tr>
<td>Frequency Classification</td>
<td>Adverse Drug Reaction</td>
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<td>--------------------------</td>
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<td></td>
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<tr>
<td></td>
<td>System Organ Class (SOC)</td>
<td>Preferred term (PT)</td>
</tr>
<tr>
<td>Rare ≤1/1000 and ≥1/10000, Frequency unknown*</td>
<td>Cardiac disorders</td>
<td>Cardiac arrhythmias, e.g. atrial fibrillation, supraventricular tachycardia and extrasystoles myocardial ischemia</td>
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<td></td>
<td>Gastrointestinal disorders</td>
<td>Nausea</td>
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<td></td>
<td>Psychiatric disorders</td>
<td>Sleep disturbances and behavioural disturbances, such as agitation, hyperactivity and restlessness</td>
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<tr>
<td></td>
<td>Metabolism and nutritional disorders</td>
<td>Lactic acidosis</td>
</tr>
<tr>
<td></td>
<td>Skin and subcutaneous tissue disorders</td>
<td>Urticaria and exanthema</td>
</tr>
</tbody>
</table>

* Reported spontaneously in post-marketing data and therefore frequency regarded as unknown

**Overdose**

Too frequent administration, as with other sympathomimetic agents, may cause nausea, headaches, changes in blood pressure, anxiety, tension, insomnia, tremor. The symptoms and sign are those characteristic of excessive sympathetetic stimulation.

Possible symptoms and sign: Headache, anxiety, tremor, nausea, tonic muscle cramps, palpitation, tachycardia and cardiac arrhythmia. A fall in blood pressure sometimes occurs.

Laboratory findings: Hyperglycaemia and lactic acidosis sometimes occur (see Special warnings and special precautions for use). β₂-agonist may cause hypokalemia as a result of redistribution of potassium.

Treatment of overdose: Usually no treatment is required.

If it can be suspected that significant amounts of terbutaline sulphate have been swallowed, the following measures should be considered:

Gastrict lavage, activated charcoal. Determine of acid-base balance, blood sugar and electrolytes. Monitor of heart rate and rhythm and blood pressure. Metabolic changes should be corrected. A cardio-selective β-blocker (e.g. metoprolol) is recommended for the treatment of arrhythmias causing a hemodynamic deterioration. The β-blocker should be used with care because of the possibility of inducing bronchial obstruction.

If the β₂-mediated reduction in peripheral vascular resistance significantly contributes to the fall in blood pressure, a volume expander should be given.
Mild and moderate cases: Reduce the dose. Then increase the dose more slowly until the broncholytic effect is insufficient.

**Pharmacodynamic properties**
Pharmacotherapeutic group: selective β₂-agonist, terbutaline, ATC code: R03A C03.

Terbutaline is an adrenergic agonist which predominantly stimulates β₂—receptors, thus producing relaxation of bronchial smooth muscle inhibition of the release of endogenous spasmogens, inhibition of edema caused by endogenous mediators and increased mucociliary clearance.

Inhaled terbutaline acts within a few minutes and has a duration for up to 6 hours. BRICASMA solution for nebulization is to be used in nebulizers with or without assisted breathing in acute or subacute disorders where conventional inhalers prove unsatisfactory, and in maintenance therapy in severe broncho-obstructive condition.

BRICASMA solution for nebulization is ready for use without dilution. BRICASMA solution for nebulization is isotonic and contains no preservatives.

**Pharmacokinetic properties**
Terbutaline is metabolized mainly by conjugation with sulphuric acid and excreted as the sulphate conjugate. No active metabolites are formed.

**List of excipients**
Sodium chloride, disodium edetate, hydrochloric acid, water.

**Incompatibilities**
BRICASMA solution for nebulization should not be mixed with alkaline solution i.e. solution with a pH higher than 7.0.

**Special precautions for storage**
Store below 30°C. Do not refrigerate. Protect the ampoules from light.

**Shelf-life**
Please see outer pack.

Each single dose unit must be used within 24 hours after it is opened. Once the container has been opened, any remaining product cannot be regarded as sterile. This must be considered if the intention is to use the remaining content at a later occasion.

**HARUS DENGAN RESEP DOKTER**

**Pack size**
Box of 2 packs of aluminium foil @ 5 respules @ 2 ml (Reg. No.: DKI1151302768A1)
Manufactured by:
AstraZeneca AB
SE-151 85 Södertälje
Sweden

Imported by:
PT AstraZeneca Indonesia
Cikarang, Bekasi – Indonesia

Date of revision text
As on approval date
ANGEL Doc. ID:

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