# Short-acting beta agonist tablets and suppositories should no longer be used in obstetric indications

13.09.2013 | Circular Number P20/2013

## Information on Short-acting beta-agonists

Short-acting beta-agonists work by relaxing smooth muscle in the body. Smooth muscle is found in many organs, including on the inner linings of the airways, blood vessels, stomach and gut, and reproductive organs. In the obstetric use (care of pregnant women) short-acting beta agonists are approved to suppress labour contractions in order to prevent the early birth of a child and therefore increase the chances of the newborn's survival.

Short-acting beta-agonists have been authorised and marketed in the European Union for many years under various trade names. The medicines included in the EU review are: fenoterol, hexoprenaline, isoxsuprine, ritodrine, salbutamol and terbutaline. They are available as tablets, oral solutions, solutions for injection or infusion, and suppositories.

In Malta, short acting beta agonists in tablet form are available as in Table 1.

TABLE 1: Short acting beta agonists authorised in Malta in tablet form.

| **Therapeutic Class** | **ATC code** | **Active Ingredient** | **Trade Name** | **License Number** |
|---|---|---|---|---|
| DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES | R03AC02 | Salbutamol 4mg (as sulphate) | Salbutamol Tablets 4mg | AA084/08301 |
| DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES | R03AC02 | Salbutamol 4mg (as sulphate) | Salbutamol Tablets BP 4mg | AA244/24701 |
| DRUGS FOR OBSTRUCTIVE AIRWAY DISEASES | R03AC02 | Salbutamol 4mg (as sulphate) | Salbutamol Tablets BP 4mg | AA702/01401 |
| OTHER GYNECOLOGICALS | G02CA01 | Ritodrine Hydrochloride BP 10mg | Yutopar Tablets | AA244/30201 |

All of the tablets listed above, are licensed for use in obstetric indications. Another two products Salbutamol (as sulphate) 0.5mg/ml solution for injection x 1ml and Salbutamol (as sulphate) 1mg/ml solution for IV infusion x 5ml are used in hospitals in Malta for respiratory conditions. Salbutamol as IV infusion is also indicated to prevent preterm labour.

## Information from European Medicines Agency about the safety concern

The risk of cardiovascular side effects when high doses of short-acting beta-agonists are used is well known. Cardiovascular side-effects vary from common problems such as tachycardia (rapid heartbeat) and other cardiac arrhythmias (irregular heartbeat) to serious events such as pulmonary oedema (fluid accumulation in the lungs). As a result, the medicines used in obstetric indications already carry safety



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warnings in their prescribing information and must not be used in patients with a history or a risk of cardiovascular disease.

Concerns were raised about the cardiovascular risk of the medicines when used to suppress labour contractions compared with their benefit, particularly if used for a prolonged period (more than 48 hours).

The Pharmacovigilance Risk Assessment Committee (PRAC) assessed the available data from clinical studies, post-marketing reports and the published literature, and considered the relevant treatment guidelines. It concluded that there was a risk of serious cardiovascular side effects to both the mother and unborn baby when short-acting beta-agonists are used in obstetric indications, with the data suggesting these mostly occur with prolonged use. Given the cardiovascular risk and the very limited data supporting the benefits of oral (by mouth) forms or suppositories as short- or longer-term tocolytics, the PRAC concluded that their risks were greater than the benefits in obstetric indications and recommended that they should no longer be used in this setting.

The PRAC recommendation is under consideration by the Coordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh).

## In Malta

### For Healthcare Professionals

- The available data showed that injectable forms are effective at suppressing labour contractions in the short term (up to 48 hours). This timeframe can allow for other measures (such as steroid treatment) known to improve the health of the baby around the time of birth to be taken. Therefore the PRAC concluded that the benefits of injectable forms outweighed the cardiovascular risks in specific conditions.
- Injectable forms should be used to suppress premature labour for no more than 48 hours, between the 22$^{nd}$ and 37$^{th}$ weeks of pregnancy, with continuous monitoring of the mother and unborn baby.
- The prescribing information for injectibles will be reinforced with warnings on the cardiovascular risks and healthcare professionals will also be informed in writing of the updated recommendations.

For more information please visit **www.ema.europa.eu**

## Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on short acting beta agonists when used in obstetric indications. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority yellow card scheme or online at **http://www.medicinesauthority.gov.mt/adrportal** or to the marketing authorisation holder or their local representatives.

***Healthcare professionals and patients are encouraged to regularly check the Medicines Authority website for product safety updates as these are issued on an ongoing basis.***



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