European Medicines Agency starts review of Short acting Beta-2-Agonists

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Information on Medicinal Product

Short-acting beta-agonists are widely used in Europe to treat asthma, and are usually taken by inhalation using an inhaler device. They relax the smooth muscles, which are found in many organs including on the inner linings of the airways, causing the airways to widen and making it easier to breathe. However, in several European countries, certain short-acting beta-agonists are also approved as 'tocolytics' (medicines that suppress labour contractions) for use in premature labour, since they relax the smooth muscles in the womb. When used for this purpose, they are usually given by injection or as tablets or suppositories, and at higher doses than those used to treat asthma.

Short-acting beta-agonists work by stimulating a receptor on the surface of cells called the 'beta-2 adrenergic receptor', which brings about smooth muscle relaxation. They are called 'short acting' because they work quickly, usually having an effect in less than five minutes and lasting for several hours. Smooth muscles are found in many organs of the body including on the inner linings of the blood vessels, stomach and gut, and reproductive organs.

Short-acting beta-agonists have been authorised by national procedures in several EU Member States and have been marketed for several years under various trade names. The medicines included in this review are fenoterol, hexoprenaline, isoxsuprine, ritodrine, salbutamol and terbutaline, which are authorised for tocolytic treatment. They are available as solutions for injection or infusion, tablets, oral solutions and suppositories.

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Information from European Medicines Agency about the safety concern

The European Medicines Agency has started a review of short-acting beta-agonists, to assess their safety and effectiveness when used to suppress premature labour.

Due to the higher doses there is a known risk of cardiovascular side effects (problems affecting the heart and blood vessels) with these medicines when they are used to suppress premature labour. As a result, the prescribing information contains safety warnings and the medicines must not be used in patients with a history or a risk of cardiovascular disease. Moreover, there is uncertainty about the effectiveness of prolonged use of these medicines (for more than 48 hours) to prevent premature labour. Therefore, concerns have been raised about the benefit of using these medicines as tocolytics compared with the risk of cardiovascular side effects.

The European Medicines Agency will evaluate the latest available evidence on the benefit-risk balance of short-acting beta-agonists when these medicines are used for stopping premature labour in pregnant women.

The review of short acting beta-agonists has been initiated at the request of the Hungarian medicines agency, under Article 31 of Directive 2001/83/EC. The review is being carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which will make a set of recommendations. As short acting beta-agonists are all authorised nationally, the PRAC recommendation will be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which is a regulatory body that represents national medicines regulatory authorities of the EU Member States. This will result in harmonised measures to be implemented in all Member States.

For more information please see the **press release** and issued by the European Medicines Agency.

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Reporting Adverse Drug Reactions

Healthcare professionals and patients are encouraged to maintain vigilance on short-acting beta-2-agonists. Suspected Adverse Drug Reactions (side effects) may be reported using the Medicines Authority yellow card scheme or online at **http://www.medicinesauthority.gov.mt/pub/adr.doc** 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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