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PRAC considers risk of severe allergic reactions with ambroxol- and bromhexine-containing medicines to be small

Update of product information is recommended

The EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has completed a review of medicines containing ambroxol or bromhexine. This follows concerns over the risk of allergic reactions with these medicines, which are widely used as expectorants (to help clear mucus from the airways).

The PRAC considers that the risk of allergic reactions is small, but has recommended that the product information for these medicines should be updated with further information on severe allergic reactions, and that severe skin reactions (SCARs) should be introduced as a side effect. SCARs include conditions such as erythema multiforme and Stevens-Johnson syndrome.

The review of ambroxol and bromhexine was carried out at the request of the Belgian medicines agency (AFMPS) following reports of allergic reactions and SCARs with ambroxol. Several cases of SCARs, possibly linked to ambroxol, were also identified from the medical literature. The review also covered medicines containing bromhexine, since bromhexine is mainly converted into ambroxol in the body. In addition, there were some reports linking the use of bromhexine with allergic reactions.

The PRAC assessed the available data and all reports of severe allergic reactions and SCARs with ambroxol and bromhexine. The PRAC confirmed the already known risk of allergic reactions, which remains small. The Committee also identified a small risk of SCARs associated with these medicines. Based on these conclusions, the PRAC recommended adding the risk of SCARs to the product information, together with advice to discontinue treatment immediately if symptoms of SCARs occur.

The PRAC recommendation will now be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a final position.

More about the medicines

Ambroxol and bromhexine are mainly used by mouth as expectorants to help make the mucus thinner and therefore easier to be cleared away in patients with short- or long-term diseases of the lungs or airways.

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For ambroxol, lozenge formulations are also available to relieve sore throat. Ambroxol formulations for injection are also used in premature and newborn babies to treat respiratory distress syndrome, a condition in which the baby's lungs are too immature for the baby to breathe properly. Some of these injectable formulations are also used to increase lung development before birth. Injectable formulations are also used to prevent and treat lung complications following surgery.

Ambroxol- and bromhexine-containing medicines are marketed as single products or as fixed combination products with various other active ingredients. The majority of these medicines are available over the counter, whereas some are prescription-only medicines, depending on the condition to be treated and how the treatment is given.

These medicines have been authorised via national procedures in the following countries: Austria, Belgium, Bulgaria, Croatia, Cyprus, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, the Netherlands, Norway, Poland, Portugal, Romania, Slovakia, Slovenia, Spain and Sweden.

More about the procedure

The review of ambroxol and bromhexine was initiated on 4 April 2014 at the request of Belgium, under Article 31 of Directive 2001/83/EC.

The review has been carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which has made a set of recommendations. As ambroxol- and bromhexine-containing medicines are all authorised nationally, the PRAC recommendation will now be forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which will adopt a final position. The CMDh is a regulatory body representing EU Member States, and is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.

If the CMDh position is agreed by consensus, the agreement will be directly implemented by the Member States where the medicines are authorised. Should the CMDh position be adopted by majority vote, the CMDh position will be sent to the European Commission, for the adoption of an EU-wide legally binding decision.

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