14 January 2016
EMA/168579/2015

Ambroxol and bromhexine expectorants: safety information updated

Risk of allergy and skin reactions included in the product information

On 18 November 2015, the CMDh[1] endorsed by majority vote recommendations to update the product information for ambroxol- and bromhexine-containing medicines with information about the small risk of severe allergic reactions and severe cutaneous adverse reactions (SCARs). The medicines are widely available in the EU for use as expectorants (to help clear mucus from the airways).

The recommendations were originally made by EMA's Pharmacovigilance Risk Assessment Committee (PRAC), which confirmed the previously known risk of allergic reactions and also identified a small risk of SCARs, a group of skin conditions which include erythema multiforme and Stevens-Johnson syndrome.

As a result, SCARs are now listed as side effects in the product information for these medicines, and patients are to stop treatment immediately if symptoms of SCARs occur. Reports of severe allergic reactions and SCARs in patients taking the medicines are rare, and the frequencies of these side effects are unknown.

In making the recommendations, the PRAC evaluated available data on ambroxol and bromhexine, including reports of severe allergic reactions or SCARs.

As the CMDh position was adopted by majority vote, it was sent to the European Commission, which endorsed it and issued an EU-wide legally binding decision.

Information to patients

- There is a small risk of allergy and skin reactions with ambroxol and bromhexine used as expectorants to clear mucus in the airways.
- If you experience skin reactions such as skin swellings or rash, stop treatment immediately and contact your doctor.
- If you are taking ambroxol or bromhexine and have any questions or concerns speak to your doctor of pharmacist.

[1] The CMDh is a medicines regulatory body representing the European Union (EU) Member States.

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Information to healthcare professionals

- Anaphylactic reactions and severe cutaneous adverse reactions (SCARs), including erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis and acute generalised exanthematous pustulosis, have been reported in patients receiving ambroxol.
- As ambroxol is a metabolite of bromhexine, the risk of anaphylactic and severe cutaneous reactions is considered to apply also to bromhexine.
- The risk of anaphylactic reactions and SCARs with ambroxol or bromhexine is low. Frequencies of these side effects are unknown.
- Advise your patients that they should stop treatment immediately if symptoms of progressive skin rash occur.

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.

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.

As these medicines have been authorised via national procedures, approved uses are not the same in all EU countries.

Ambroxol and bromhexine medicines have been authorised in: 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 was carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which made a set of recommendations. As ambroxol- and bromhexine-containing medicines are all authorised nationally, the PRAC recommendation was forwarded to the Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), for a 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.

The CMDh first adopted a position by majority vote in February 2015, following which the European Commission requested clarifications on the PRAC recommendation and CMDh position. A revised CMDh position was subsequently adopted, by majority vote in November 2015. This position was then sent to the European Commission which issued an EU-wide legally binding decision on 14/01/2016.

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