

Risk of severe allergic reactions with ambroxol and bromhexine-containing medicines considered small

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has completed a review of the safety of ambroxol and bromhexine-containing medicines*. Ambroxol and bromhexine are indicated for mucolytic therapy in patients with short or long-term respiratory conditions. Ambroxol lozenges are available for pain relief of sore throats. The majority of these medicines are available over-the-counter (OTC) in Ireland and are marketed as single products.

Ambroxol-containing medicines authorised and marketed in Ireland include:

- Ambrobene 3mg/ml and 6mg/ml Oral Solution
- Lysopadol 20mg Lozenges

Bromhexine-containing medicines authorised and marketed in Ireland include:

- Bisolvon 4mg/5ml Oral Solution

The review of these products was initiated following post-marketing reports of hypersensitivity reactions (including anaphylactic reactions) and accumulating evidence from case reports and literature demonstrating that ambroxol is potentially responsible for severe cutaneous adverse reactions (SCARs).

The review has concluded as follows:

- Severe hypersensitivity reactions have been reported in patients receiving ambroxol. These include:
 - Severe allergic reactions including anaphylactic reactions;
 - SCARs including erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis and acute generalised exanthematous pustulosis.

Advice to Healthcare Professionals

- Ambroxol and bromhexine are associated with a small increased risk of immediate and delayed hypersensitivity reactions, anaphylactic reactions including anaphylactic shock, angioedema, pruritus, rash and urticaria.
- There is a possibility of a risk of SCARs (including erythema multiforme, Stevens-Johnson syndrome/toxic epidermal necrolysis and acute generalised exanthematous pustulosis) associated with ambroxol and bromhexine.
- If symptoms of allergy or SCARs occur, treatment with ambroxol or bromhexine should be immediately discontinued.

Key messages

- The PRAC considered that ambroxol and bromhexine are associated with a small increased risk of hypersensitivity reactions.
- The PRAC considered that there is a reasonable possibility of a risk of SCARs associated with ambroxol and bromhexine.
- The PRAC was of the view that the risk of SCARs should be addressed by its inclusion in the product information accompanied by a warning for patients and caregivers to recognise the prodromes of SCARs and to discontinue treatment immediately in the event of such signs.

**Further details on ambroxol and bromhexine-containing products are available at www.hpra.ie*

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