

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Cough is an important physiologic mechanism that defends against respiratory pathogens and help to clear the throat of mucus, foreign particles, and noxious substances.

Cough could be classified as acute (i.e. duration of 3 weeks or less), or chronic (i.e. duration of longer than 8 weeks) and it is a symptom of diverse infectious and non-infectious disorders. Acute cough is most commonly caused by a viral upper respiratory tract infection (e.g. the common cold). The most common causes of chronic cough in nonsmokers are respiratory infections, asthma and stomach reflux disease. Cough can be induced by some medications.

Overall prevalence

In several epidemiological surveys, persistent cough is reported as a symptom that affects a large proportion of the general population, for example in 18% of the US population, in up to 16% of a southeast English population and in 11% of the Swedish population.

Complications

Common complications include exhaustion, insomnia, musculoskeletal pain, hoarseness, excessive perspiration and urinary incontinence.

VI.2.2 Summary of treatment benefits

Ambroxol hydrochloride increases airway secretions and pulmonary fluid production, and stimulates its clearance.

This leads to improved mucus flow and movement (mucociliary clearance), as demonstrated in pharmacological studies. The increase in secretions and mucociliary clearance boosts expectoration and coughing.

A large analysis of several clinical trials of oral mucolytic drugs for exacerbations of chronic obstructive pulmonary disease (COPD) can be taken as an example of treatment benefit. Patient not receiving treatment had an average of 2.7 exacerbations a year, while patients receiving treatment had a significant 29% reduction in the number of exacerbations. This finding suggests that the effect of thickened mucus itself is a significant contributor to sickness, at least for COPD.

VI.2.3 Unknowns relating to treatment benefits

Ambroxol Hydrochloride Unither Pharmaceuticals is a new medicinal product containing ambroxol hydrochloride for oral solution. However, clinical and even more post-marketing safety data for the active substance have been extensively collected. It is believed that ambroxol benefits are well-known. It should be stressed, however, that ambroxol is not well studied in children below 12 years of age.

VI.2.4 Summary of safety concerns

Risk	What is known	Preventability
<p>Important identified risk: Serious skin reactions</p>	<p>Very rare cases of severe skin damage, (Stevens-Johnson syndrome and toxic epidermal necrolysis), have been reported in temporal association with the administration of expectorants such as ambroxol. It unknown how often they occur, but most likely in less than 1 in 10,000 people using ambroxol. Occurrence of such severe reactions is unpredictable. It is believed to be an allergic reaction in predisposed individuals.</p> <p>The patient may experience non-specific prodromes reminiscent of flu-like illness: fever, body pain, rhinitis, cough and sore throat.</p>	<p>The risk may be minimised by an advanced awareness of consumers and health care professionals of early symptoms.</p> <p>Treatment should be interrupted and medical care sought immediately in case of occurrence of such suggestive symptoms.</p>
<p>Important identified risk: Concomitant administration of antitussives</p>	<p>Ambroxol promotes clearance of airway secretions, but cough is necessary to eliminate the secretions. Ambroxol should, therefore, not be combined with cough suppressants as this leads to accumulation of secretions and airway congestion. Cough and cold preparations containing substances such as dextromethorphan and codeine are examples of medications which should be avoided. However, other over-the-counter and prescription products may also suppress cough.</p>	<p>The risk may be minimised by an advanced awareness of consumers and health care professionals.</p>
<p>Missing information: Use in children under age of 12 years.</p>	<p>The product has been used in children, but the information is limited. In the absence of convincing clinical data, the product should therefore not be used in children under age of 12 years.</p>	<p>The risk may be minimised by an advanced awareness of consumers and health care professionals.</p>
<p>Missing information: Use during Pregnancy and breastfeeding.</p>	<p>The product has been used in pregnant women, but the information is limited. In the absence of convincing clinical data, the product should not be used in early pregnancy. The usual precautions regarding the use of medicinal products during pregnancy should be taken. In</p>	<p>The risk may be minimised by an advanced awareness of consumers and health care professionals.</p>

	<p>particular, the use of Ambroxol Hydrochloride Unither Pharmaceuticals 30 mg/ 5 ml, oral solution is not recommended during the first trimester.</p> <p>Ambroxol hydrochloride is excreted in human milk. Although no adverse effects are expected in breastfed infants, the use of Ambroxol Hydrochloride Unither Pharmaceuticals 30 mg/ 5 ml, oral solution is not recommended during breastfeeding.</p>	
--	--	--

VI.2.5 Summary of additional risk minimisation measures by safety concerns

Not applicable.

VI.2.6 Planned post authorisation development plan

Not applicable. There are no studies planned and no studies are a condition of the marketing authorisation.

VI.2.7 Summary of changes to the Risk Management Plan over time

Not applicable (first submission)