



# Acute cough: for the first time, a clear recommendation for ambroxol as symptomatic treatment

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According to the guidelines of the German Respiratory Society, an acute cold cough without clinical indications of pneumonia or other warning signs, is the domain of self-medication. The duration – up to two weeks – is pivotal for the classification „acute“. From their assessment of randomised, controlled studies, the authors concluded that Ambroxol (like several herbal medicines), shortens the duration and/or reduces the intensity of cough in acute bronchitis. Dextromethorphan is recommended by the guideline authors for a dry, troublesome cough associated with an upper respiratory infection.

The authors of the current guidelines of the German Respiratory Society recognise the value of advice given in the pharmacy on the self-medication of acute cough [1]. Drugs for which clear evidence exists are the focus of the recommendation.

The guidelines on respiratory medicine that appeared in April 2019 describe the treatment in adults of acute cough associated with a cold as a domain of self-medication. The most frequent cause of a cough is a cold, i.e. an acute, spontaneously regressing, generally viral illness affecting the upper and/or lower respiratory tract. The cough is said to be acute if the symptoms last up to two weeks. Coughs are always described as subacute if they last between two and eight weeks. This time span (two to eight weeks) does not imply that the cough has become chronic, but rather that the infection subsides only slowly. Provided no alarm signals such as blood in the sputum, dyspnoea at rest, hoarseness or fever  $\geq 38.5$  °C are mentioned in reply to enquiries by the pharmacist, an attempt to treat the symptoms in the context of self-medication can be undertaken. Patients with the above-named warning signs, heavy smokers, patients with acute heart failure, suspected pneumonia or tuberculosis, or those showing visible cyanosis, should be see a doctor immediately.

If the cough has lasted for more than 8 weeks and the discussion with the patient gives no indication of an underlying respiratory infection, a chronic cough may be present. There are many different causes for this and they need to be clarified and diagnosed by a doctor.

Until now, the important question in self-medication was whether an acute cough was productive (i.e. produces sputum) or was a dry, irritating cough. However, it appears that this approach is now outdated. It is difficult for patients to differentiate between the two and treatment is primarily directed at relieving the most troublesome symptoms. The authors of the guidelines emphasize that the cough symptom picture in an acute cold is essentially triggered by a neuronal hypersensitivity of the cough reflex. This hypersensitivity arises through inflammatory processes and a neuromodulation of the affected mucosae.

According to the guidelines, symptomatic treatment in self-medication with evidence-based protussives (expectorants) and/or antitussives is useful to alleviate and shorten the cough's duration. The promotion of expectoration relieves the cough receptors and thereby reduces the urge to cough. The anti-inflammatory effect described for ambroxol appears to have a positive effect on the hypersensitivity of the cough reflex. In order to improve night-time sleep, expectorants given throughout the day can be combined with a nocturnal cough suppressant. If the unproductive, irritating cough predominates, then cough suppressants can also be given during daytime.

However, relevant studies do not exist for all drugs of these therapeutic classes. This is not the case with ambroxol. According to the guidelines, there is a meaningful placebo-controlled study for this drug [2]. The authors of the guidelines refer to this GCP-compliant (Good Clinical Practice) study, because it provides evidence-based data for the use of ambroxol in an acute cold-associated cough

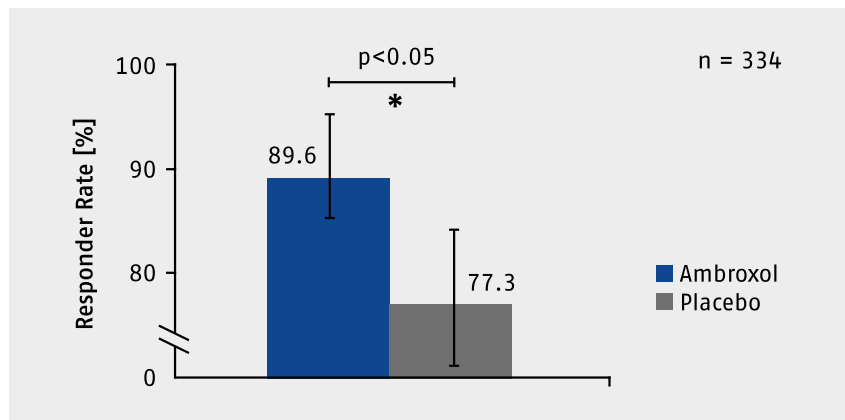


Fig.: Responder rate in the treatment with ambroxol or placebo, recorded by an investigating physician during Visit 2 [2].

and describes the benefits for patients in a manner that is scientifically reliable and relevant for patients.

For a period of two weeks, 676 patients with acute bronchitis were each given a particular defined drug or placebo. Ambroxol was administered in a dose of 30 mg three times daily on the first three days and then in a dose of 30 mg twice daily up to day 14. During the control investigations, doctors examined whether the patients had responded to treatment or not (responder/non-responder rate). The control visits took place at the start of treatment (Visit 1), after one or two weeks (Visits 2+3) and two weeks after the end of treatment (Visit 4).

The results showed that the symptoms rapidly improved in all treatment groups, although the reduction in the patients given placebo was slower and less complete. The responder rate in the patients treated with ambroxol was significantly higher (89.6%) than under placebo (77.3%).

In their recommendation for the use of ambroxol, the authors of the guidelines also refer to real-world evidence [3]. 965 patients who had purchased ambroxol-containing medicines (prolonged release capsules, soft pastilles, paediatric syrup, cough syrup) in a Germany pharmacy were questioned. Many of them reported a favourable subjective effectiveness on the cough during self-medication with ambroxol in acute bronchitis.

**Summary:** The use of ambroxol in self-medication for acute and subacute cough is part of the guidelines of the German Respiratory Society on the diagnosis and treatment of adult patients with cough. In their recommendations, the authors of the guidelines refer to a GCP-compliant (Good Clinical Practice) study as well as to real world data.

#### Literature

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3. Kardos et al. Characterization of differential patient profiles and therapeutic responses of pharmacy customers for four Ambroxol formulations. *BMC Pharmacology and Toxicology* 2018;19:40.

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