

# Treatment of sore throat with ambroxol lozenges

## Results of a community pharmacy-based observational study (PHOBS)

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This survey aimed to collect data on how patients self-assess safety and effectiveness of an OTC ambroxol lozenge as well as on its usage pattern in the self-treatment of sore throat. A total of 146 pharmacies took part and 1,488 completed questionnaires were returned to the pharmacies, corresponding to 68 %. The test product was rated by 84.8 % of the patients as having a very good or good therapeutic result and 94.5 % reported that it was well or very well tolerated. These results match with the satisfaction of the therapeutic result reported by 93 %.

This study reflects how the patient uses the product in self-medication. It also confirms earlier experience which shows that community pharmacy-supported cohort studies are feasible and provide valid data on effectiveness and tolerability [16]. The results of the study agree with the data available from clinical trials and spontaneous reports on the safety in use of the active ingredient ambroxol. They show that, with the advice of the pharmacists, patients handle self-medication of sore-throat responsibly and correctly.

Ambroxol, the active ingredient also of Mucosolvan® came on to the market in Germany in 1978. It is used particularly as a cough medicine in acute and chronic airways diseases associated with abnormal mucus secretion and impaired mucus transport. In addition to the secretolytic properties, ambroxol is also known to have local anaesthetic properties [1, 2]. In clinical trials lozenges containing 20 mg ambroxol (Mucoangin®) proved to be effective and safe [3, 4]. The OTC-product was licensed in various European countries via the mutual recognition procedure (MRP) in 2000.

The results of three clinical studies on efficacy carried out in about 1,000 patients provided the basis for the licensing. A fast-acting pain-relieving effect could be shown that was already superior to that of the placebo at the earliest measurement after 30 minutes. This superiority lasted for the whole test period of three hours [3, 4].

There are several possibilities available for the treatment of sore throat: Before the ambroxol lozenges were introduced, substances with local anaesthetic effect were used almost exclusively in combination preparations with antiseptics and/or local antibiotics. The use of ambroxol in a lozenge, on the other hand, is a symptomatic *monotherapy*.

In general, the symptom acute sore throat is unperilous but considerably impairs the patient's wellbeing. Untreated *viral pharyngitis* clears up without complications after about three

days. Sore throats caused by streptococci also clear up spontaneously within seven days [5].

Pharyngitis is mostly treated independently by self-medication with the aid of the pharmacist's advice. Figures on the proportion of patients who first visit the doctor range between 8 and 19 % [6]. In the period between 1989 and 1999 over 70 % of the patients who consulted the doctor straightaway were given systemic antibiotics. According to current guidelines this treatment with antibiotics should only be used in severe cases [7].

A pragmatic approach is to leave the treatment of sore throat almost exclusively to self-medication in the first three days, and to recommend a visit to the doctor if the results are unsatisfactory [8].

It is to be expected that due to the pharmapolitical development the dominance of the pharmacist in the treatment of patients with sore throat will grow. New systematic studies on the use of OTC sore throat products should take more ac-

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count of the pharmacies. One possibility here is the *community pharmacy-supported cohort study*. This method, which is based on doctors' classic post-marketing survey, was also used in the investigation described here.

### Aims of the survey

The aim of the survey was to obtain data on the effectiveness and the safety of the product under real conditions of self-medication. Furthermore, additional information was to be recorded on the symptoms of patients with sore throat and on their usage-pattern. Other central questions were the subjective time of onset of effect and the duration of the condition. The data on the use of OTC products are a useful supplement to the results of clinical trials. Controlled clinical trials are carried out under supervision of a physician, which could affect the way the patients take the medicines. In the case of pharmacy-based patient polls, this influencing factor is absent and the real situation with regard to self-medication can be seen [9–14].

The survey was carried out in accordance with the recommendations of the Federal Institute for Drugs and Medical Devices (BfArM) on planning and conducting post-marketing surveillance studies. In its recommendations the BfArM explicitly mentions the possibility of cooperation with health-care professionals other than the physician [15]. Thus, such a study is also possible in the pharmacy sector. Germany is particularly suitable for carrying out this type of study because the pharmacists are highly qualified.

### Methods

The pharmacists taking part in this study received an extensive file which contained 15 copies of the questionnaire, the study protocol, the forms for the informed consent of the patients which was required for the study, plus fax forms for reporting adverse drug reactions.

The pharmacists were to recruit patients of both sexes, 18 years or older who came to the pharmacy and requested lozenges containing ambroxol. Each patient selected had to give his or her written consent to take part in the study. Patients willing to take part were to complete a questionnaire containing 33 questions. This consisted of two parts, the first part being completed immediately in the pharmacy with the aid of the pharmacist. Thus, for the later analysis of the symptoms, it was possible to record the symptoms as they were at the time of purchase. The length of time the patient had had the sore throat when the product was bought was also documented at this time. In the second part of the questionnaire the patient was to answer questions mainly concerned with how and when the product was taken, the dose taken, the effect and tolerability perceived. This was to be done at the end of the therapy, which was to be determined by the patient him/herself, generally after three days. The patient was asked to return the completed form to the pharmacy. The pharmacist then had to examine the questionnaire immediately for indications of adverse drug reactions. If there were any, the pharmacists were asked to report them directly to the medical

study director in anonymous form. The questionnaires were sent to an independent institute for analysis. The aim was that each pharmacy would send 10 completed forms for analysis.

### Endpoints on effectiveness and safety

Primary endpoint of the study was the subjective evaluation of the success of the treatment by the patient. The hypothesis for the primary endpoint was that 70% of the patients rate the therapeutic result with "very good" and "good". The secondary endpoint on safety was that 80% of the patients rate the tolerability of the medication with "very good" and "good". Both hypotheses were laid down with other target parameters in the trial protocol and submitted to the authorities before the start of the trial.

Further secondary parameters were number and type of suspected adverse events reported, the patients' symptom profiles, the onset of effect, the description of the effect by the patient, the interval between the intake of two consecutive lozenges, the number of lozenges taken and the question of the patients' preferred source of information on the disease process.

### Results

The observation period lasted eight months during which 146 pharmacies sent 1,488 questionnaires for analysis. The participation of the pharmacies selected by the sales force was 49.2%. This resulted in an average return of 10.2 questionnaires per pharmacy. More than ten questionnaires were returned by 69.2% of the pharmacies (n = 101), 21.2% sent in between 5 and 9 forms and 9.6% provided fewer than 5 questionnaires for analysis. All 1,488 forms received by the statistics institute could be evaluated.

### Demographic data

Table 1 shows the demographic data of the participants. None of the various age groups had any gender-specific high frequencies. Contrary to the requirements of the study protocol 50 patients (3.4%) less than 18 years old were included in the study.

### Complaints and symptoms

As shown in Table 2 nearly 25% came to the pharmacy as soon as the first symptoms appeared.

The most common symptoms were sore throat and difficulty swallowing (Table 2). All complaints reported are typical symptoms of pharyngitis. Many patients (44.8%) complained of additional symptoms of a cold (Table 2). Twenty-two per-

Table 1. Pharmacy-based patient poll – Demographic data

Pharmacies taking part	n = 146
Number of patients involved	n = 1,488
Age (Minimum to maximum)	39.2 +/- 16.0 years (11–97)
Gender	Women 997 (67.3 %) Men 485 (32.7 %)
Period of the investigation	October 2003 to June 2004

**Table 2. Time until purchase of medicine – symptoms described (more than one answer possible)**

Time until purchase	[n]	[%]
Immediately	354	23.8
After 1 day	551	37.0
After 2 days	375	25.2
After 3 or more days	208	13.6
Symptoms	[n]	[%]
Sore throat	985	66.2
Difficulty swallowing, pain on swallowing	736	49.5
Irritation in the throat	364	24.5
Inflammation of the throat	29	19.9
Additional symptoms	[n]	[%]
Cold	667	44.8
Cough	563	37.8
Headache	399	26.8
Joint pains	231	15.5

cent of the patients described exclusively pharyngitis-related symptoms. Most of the patients blamed the sore throat on a cold or influenza, but environmental factors were also mentioned (weather, unsuitable clothing, draught, poor room air and an inadequate immune system). Seventy patients related the symptoms of sore throat to their smoking habit.

The patients reported that they were clearly impaired in everyday activities: about half of the patients questioned (45.3%) felt severely impaired, 12% even described this effect as very severe. About one third of the patients (37%) felt that the symptoms did not restrict their everyday activities. 78 patients (5.2%) stated that they were not impaired by the symptoms.

The symptoms lasted for up to three days after the start of the treatment in 79.1% of the patients.

#### Dosage and usage of the medicine

The patients were asked to record exactly when they took the medicine on the first three days of treatment. Most patients (78.7%) used between three and six lozenges on the first day, 6.5% took fewer than three lozenges. The recommended daily dose of six lozenges was exceeded by 5.1% of the patients on the first day. The results on the second day were very similar: 72% of the patients used between two and five lozenges. The median intervals between two consecutive doses on day two were between 2.5 and 4.0 hours.

For 55% of the patients the duration of therapy was not more than three days. Thirty point two percent continued the treatment for another day, 25.8% for another two days and 8.3% for another three days. Only a small number of patients carried on the treatment for more than a total of 7 days ( $n=23$ , 1.5%). The maximum length of treatment was 15 days ( $n=1$ ).

Seventeen point seven percent of the patients reported that they had taken additional products for their sore throat. A total of 177 drugs were taken and could be coded according

to the WHO's anatomical-therapeutic-chemical code (ATC system). Products for colds were mentioned most frequently. Forty-nine patients used additional medicines for the throat, in 26 cases medicines for the stomach were taken. Eighteen patients (1.2%) reported also taking prescription antibiotics.

#### Onset of effect and most important effects

Figure 1 shows that the effect occurs latest within 10 minutes in most patients.

The following effects were mentioned:

- Reduction of the pain in the throat (68.5%)
- Less difficulty swallowing (52.6%)
- Anaesthetic effect (34.8%)
- Reduction of the irritation in the throat (33.4%)

In answer to the question as to where the numbing effect of the local anaesthetic was noticed first, 45.2% of the patients chose the answer "in the mouth", 34.8% "in the throat" and 4.9% ticked both answers. Seven point seven percent of the patients answered "no anaesthetic effect felt". A significant connection with the way the tablet was used could be found: the recommendation that the lozenge be held in the cheek pouch leads to fewer perceptions of a feeling of numbness in the mouth.

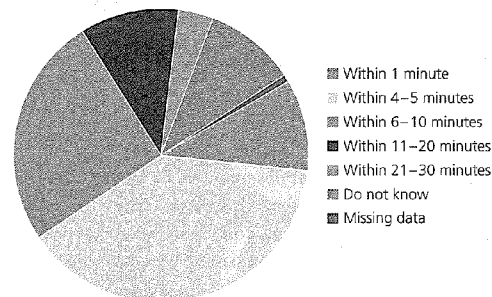


Fig. 1. Onset of effect after sucking the first lozenge

#### Global assessment of the therapeutic result

The limit of 70% for a "good" or "very good" assessment of the therapeutic result was clearly exceeded: 84.8% of the patients rated the therapeutic result as "very good" or "good" (95% confidence interval: 83.8–86.6%) (Table 3).

#### Safety and tolerability

Here, too, the hypothesis that at least 80% of the patients rated the safety and tolerability of the medicine with good or very good was confirmed: 94.5% of those questioned reported a very good or good tolerability (95% confidence interval: 93.2–95.6%) (Table 3). Of the 1,488 patients 97.4% stated that they had no suspected side effects; 24 patients (1.6%) reported 33 suspected side effects. There were not more than three suspected side effects per patient. The remaining patients did not give any information on this. The most common suspected adverse drug reactions ( $n=16$ ) were limited to the oral cavity (Table 4).

Table 3. Assessment of the therapeutic result and the tolerability

Therapeutic result	[n]	[%]
Very good	305	20.5
Good	957	64.3
Adequate	175	11.8
Poor	33	2.2
No data	18	1.2
Tolerability	[n]	[%]
Very good	552	37.1
Good	854	57.4
Adequate	48	3.2
Poor	18	1.2
No data	16	1.1

Table 4. Adverse effects

Adverse effect	[n]
Alteration in taste	6
Dry mouth	2
Feeling of numbness in the mouth	8
Gastrointestinal disorders	8

## Discussion

Pharmacy-based cohort studies can provide supplementary information on the effect and safety profile of a drug [17–19]. However, confirmatory proof of efficacy is not possible with this method. Weingärtner's [16] conclusion that patients are reliably able to document observations they make in relation to taking drugs was confirmed. In this study 94.5% of the patients reported the lozenges containing ambroxol to be well or very well tolerated. This assessment correlates closely with the satisfaction rate of 93.2%. The subjective satisfaction of the patients shown in this study agrees with the findings from the three clinical trials on the efficacy of the product [3, 4]. In these studies, too, a global assessment of efficacy was made regularly at the end of each day of observation. In two studies which each lasted three days 78 and 84% of the patients respectively rated the effect as "good" or "very good" [4]. In the third study, which ended after two days, 64% gave a positive assessment [3].

In the patient survey described here the assessment of the therapeutic success is carried out after the end of the treatment and it was up to the patient when to end the treatment. The result therefore has a greater importance for the pharmacist in his day-to-day advisory capacity.

The rapid onset of effect (within 10 minutes in 74.3% of the patients) is one of the reasons for the positive assessment of

the therapeutic result. Self-treatment of sore throat with advice from the pharmacist is suitable for the therapy of acute pharyngitis. This study shows that in Germany the pharmacist is the preferred contact for the patient in over 90% of cases. It also shows that by self-medication with lozenges containing ambroxol the patient can obtain reliable and safe relief from a sore throat.

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