

## ABSTRACT

### Introduction

This multicenter, randomized, parallel-group, double-blind, placebo-controlled study evaluated the efficacy and safety of Mucinex® D (guaifenesin 600 mg and pseudoephedrine hydrochloride 60 mg extended-release bi-layer tablets) in providing relief of respiratory symptoms when used as adjunctive therapy to antibiotics in patients with acute respiratory infections (ARI).

### Methods

Adult patients 18-75 years, considered by the treating physician as requiring antibiotic therapy for ARI, and with a total symptom score of  $\geq 10$  based on a 0-to-3 severity rating of 10 respiratory symptoms (chest congestion, cough, thickened sputum/phlegm, runny nose, nasal congestion, sinus headache, facial pain/pressure/tenderness, post-nasal drip, sore throat and breathlessness) were prescribed an antibiotic regimen determined by the treating physician, and received Mucinex® D or a matching placebo BID for 7 days. As per study protocol, patients were taking no prior or concomitant medications for ARI. Approval was obtained from the IRB Quorum Review Inc., and written informed consent was obtained from all patients. Patients completed symptom diaries and treatment assessments twice daily and attended doctor visits on Days 4 and 8. Efficacy was assessed in intent-to-treat (ITT) and per-protocol analyses. Safety was assessed throughout the study.

### Results

Data from the 30-center ITT population (n=601; Mucinex® D=303, placebo=298) showed lower mean symptom scores with Mucinex® D vs placebo starting on Day 3 in every symptom assessed, with statistically significant improvements in total symptom score (p=0.026). Significantly more patients felt "the medication was helping during the day" on Day 2 (p=0.002) in the Mucinex® D group, and patient end-of-treatment assessments of treatment effectiveness showed a significant preference for Mucinex® D (p=0.021), as compared with placebo. The time to overall relief (no symptom worse than mild) was shorter for Mucinex® D than for placebo (p=0.038). The most common adverse events (AEs) in the Mucinex® D treatment group were insomnia (4.0%), nausea (3.6%), and headache (3.3%).

### Discussion

When used in combination with antibiotic therapy in patients with ARI, Mucinex® D was well tolerated, shortened time to relief and improved respiratory symptoms better than placebo.

## INTRODUCTION

- Acute respiratory infection (ARI) is one of the most common reasons why patients visit a physician in the United States and accounts for about 75% of all antibiotic prescriptions.<sup>1</sup>
- Excessive mucus and congestion are frequent symptoms associated with ARI, and it is important to manage these symptoms simultaneously.<sup>2-4</sup>
- The combination of antibiotics, expectorants and decongestants is quite common in the treatment of ARI,<sup>5,6</sup> with recent clinical practice guidelines for the medical management of sinusitis recognizing a role for adjunctive treatments for symptomatic relief.<sup>4</sup>
- Mucinex® D (Adams Respiratory Therapeutics, Chester, NJ, USA) is a combination of an expectorant (guaifenesin 600 mg) and a nasal decongestant (pseudoephedrine HCl 60 mg) in extended-release bi-layer tablet form, used to help loosen phlegm (mucus) and thin bronchial secretion, and to temporarily relieve nasal congestion, and sinus congestion and pressure.<sup>7</sup>
- This study was undertaken to assess the efficacy and safety of Mucinex® D compared with placebo when used for symptom relief in combination with antibiotics in patients with ARI.

## METHODS

- This was a multicenter, randomized, parallel-group, double-blind, placebo-controlled study.
- Adult patients (aged 18-75 years) with symptoms of ARI that began within 7 days of screening and a total symptom score of  $\geq 10$  based on a 0-to-3 severity rating of 10 respiratory symptoms (chest congestion, cough, thickened sputum/phlegm, runny nose, nasal congestion, sinus headache, facial pain/pressure/tenderness, post-nasal drip, sore throat, and breathlessness) considered by the treating physician as requiring antibiotic therapy for ARI were eligible for study participation. Patients taking prior or concomitant medications for ARI were excluded.
- Patients were prescribed an antibiotic regimen determined by the treating physician and were randomized to receive treatment with either Mucinex® D or matching placebo tablets twice daily for 7 days.
- Approval was obtained from the Quorum Review Inc. Institutional Review Board, and written informed consent was obtained from all patients before study entry.
- Patients completed symptom diaries and treatment assessments twice daily and attended doctor visits on Days 4 and 8. Efficacy was assessed in intent-to-treat (ITT) and per-protocol analyses. Safety was assessed throughout the study.

## RESULTS

### Demographics

- A total of 605 patients were enrolled and randomized to study treatment (305 in the Mucinex® D group and 300 in the placebo group). Four patients did not take study medication and were not included in the safety/ITT population (2 in each group).
- The two groups were well matched with regard to baseline demographic and clinical characteristics (Table 1). Sinusitis was the most frequent diagnosis at baseline.
- Mean total symptom scores at baseline were comparable for the Mucinex® D and placebo groups (Table 1).

Table 1. Demographic and clinical characteristics (safety/ITT population)

	Mucinex® D group (N=303)	Placebo group (N=298)
<b>Age, years</b>		
Mean $\pm$ SD	40.3 $\pm$ 13.2	39.1 $\pm$ 13.8
Range	18.0-74.6	18.0-74.0
<b>Sex, n (%)</b>		
Male	120 (39.6)	103 (34.6)
Female	183 (60.4)	195 (65.4)
<b>Race, n (%)</b>		
White	274 (90.4)	275 (92.3)
Black/African American	19 (6.3)	15 (5.0)
Other	10 (3.3)	8 (2.7)
<b>Physician diagnosis (%)</b>		
Sinusitis	51.3	52.2
Bronchitis	33.4	31.0
Rhinitis	5.4	6.6
Upper respiratory infection	5.7	4.8
Pharyngitis	3.3	4.8
Unknown	0.9	0.6
<b>Most bothersome symptom, n (%)</b>		
Cough	66 (21.8)	62 (20.8)
Nasal congestion	60 (19.8)	54 (18.1)
Sinus headache	37 (12.2)	41 (13.8)
Sore throat	47 (15.5)	46 (15.4)
<b>Total symptom score (0-40)</b>		
Mean $\pm$ SD	16.6 $\pm$ 4.1	16.9 $\pm$ 4.3
Range	10-29	10-28

### Efficacy

- Significantly lower mean total symptom scores were seen in the Mucinex® D group from Day 3 onwards (p-values ranging from 0.009 to 0.044 vs placebo). Mean total symptom score at Visit 3 (Day 8) was significantly lower in the Mucinex® D group than in the placebo group (4.4 and 5.3, respectively; p=0.015).
- Mean individual symptom scores tended to be lower in the Mucinex® D group compared with the placebo group, but most differences were not statistically significant.
- The greatest effects of symptom relief in the Mucinex® D group were observed for nasal congestion and sinus headache (Figure 1).
- Median time to relief was significantly shorter in the Mucinex® D group than in the placebo group for both nasal congestion (4.75 vs 5.75 days [log rank test, p=0.015; Wilcoxon test, p=0.012]) and sinus headache (3.25 vs 4.75 days [log rank test, p=0.041; Wilcoxon test, p=0.022]) (Figure 2).
- The time to overall relief (no symptom worse than mild) was also significantly shorter in the Mucinex® D group than in the placebo group (p=0.038).
- A larger percentage of patients felt the medication was helpful during the day in the Mucinex® D group at all timepoints. Statistically significant differences between the two treatments in favor of the Mucinex® D group were observed from as early as Day 2 (67.9% versus 55.2% in the placebo group; p=0.002).
- Results of the patients' global assessment showed the mean rating for relief of symptoms at the end of the study to be significantly better in the Mucinex® D group (p=0.021). A larger proportion of patients considered the medication to be very or extremely effective in the Mucinex® D group than in the placebo group (Figure 3).
- Investigator global assessments also favored Mucinex® D, with 82.2% of investigators in the Mucinex® D group recommending study medication for future use as adjunctive therapy to antibiotics for symptom relief of ARI compared with 75.0% in the placebo group (p=0.048).

Figure 1. Mean symptom scores\* for (a) nasal congestion and (b) sinus headache (ITT population)

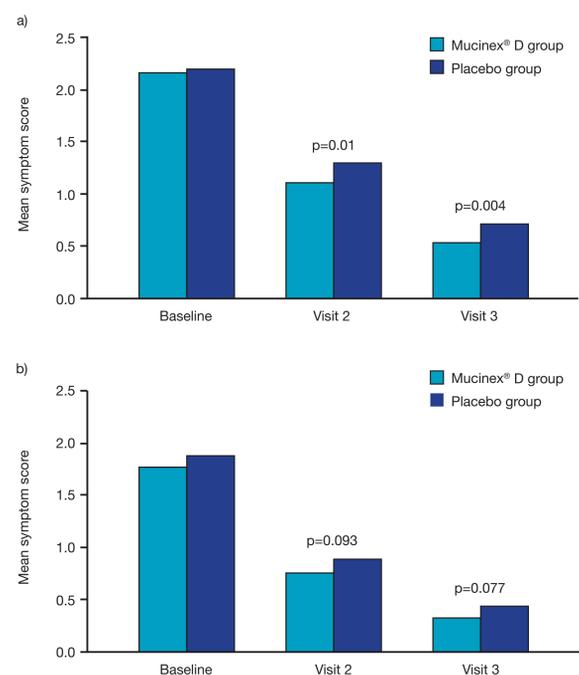


Figure 2. Proportion of patients achieving significant relief of (a) nasal congestion and (b) sinus headache (ITT population)

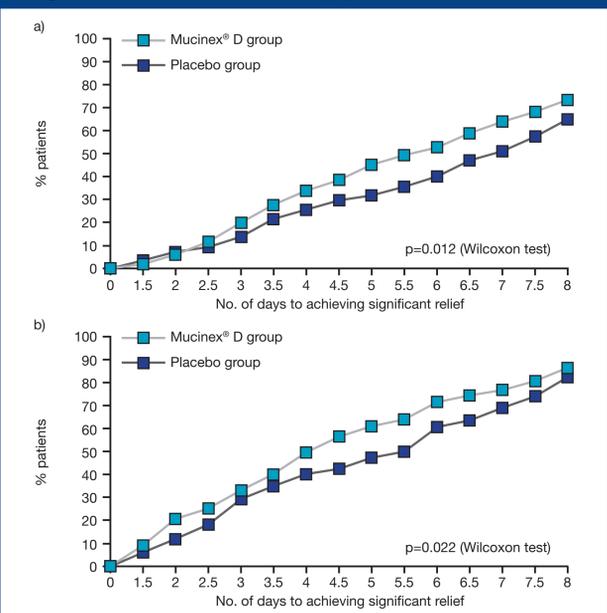
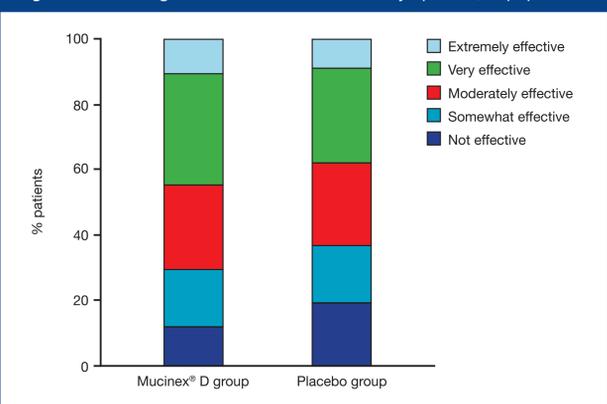


Figure 3. Patients' global assessment for relief of symptoms (ITT population)



### Safety

- Treatment with Mucinex® D was well tolerated (Table 2). The most common adverse events (AEs) in the Mucinex® D group were insomnia (4.0%), nausea (3.6%), and headache (3.3%).

Table 2. Summary of treatment-emergent AEs (safety/ITT population)

Adverse event	No. of patients (%)	
	Mucinex® D group (N=303)	Placebo group (N=298)
Any AE	58 (19.1)	36 (12.1)
Treatment-related AE	30 (9.9)	17 (5.7)
Severe AE	10 (3.3)	6 (2.0)
AE leading to discontinuation	15 (5.0)	8 (2.7)

- The incidence of AEs considered related to study medication was 9.9% in the Mucinex® D group and 5.7% in the placebo group.
- AEs resulted in treatment discontinuation in 15 patients in the Mucinex® D group (5.0%) and 8 patients in the placebo group (2.7%). The most frequently reported AE leading to treatment discontinuation was insomnia (7 patients in the Mucinex® D group [2.3%] and 2 patients in the placebo group [0.7%]).
- No serious AEs or deaths were reported in either treatment group during this study.

## CONCLUSIONS

- Treatment with Mucinex® D for 7 days as adjunctive therapy to antibiotics in patients with ARI shortened the time to relief and improved respiratory symptoms better than placebo, with most marked effects seen for nasal congestion and sinus headache.
- Patient and investigator global assessments of treatment efficacy significantly favored Mucinex® D over placebo.
- Treatment with Mucinex® D was well tolerated and there were no unexpected safety findings in this study.
- Mucinex® D as an adjunct to antibiotics addresses the importance of managing symptoms in the acute treatment of ARI.

## REFERENCES

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