## Sponsor

Novartis Consumer Health, SA

## Generic Drug Name

Xylometazoline Hydrochloride

## Trial Indication(s)

For the symptomatic relief of nasal congestion due to colds, hayfever or other allergic rhinitis, sinusitis.

## Protocol Number

OTCS-CE-301

## Protocol Title

A double-blind, randomized, parallel group, placebo controlled study, evaluating the decongestant effect, time to onset, duration of effect and impact on sleep and general well-being of Otrivin F2 in subjects with a common cold.

## Clinical Trial Phase

Phase IV

## Study Start/End Dates

06 Mar 2007 to 28 Mar 2007

## Reason for Termination

Not applicable.

## Study Design/Methodology

This was a single-centre, double-blind, placebo-controlled, randomized (1:1), parallel group study to investigate different aspects of the decongestant effect of Xylometazoline nasal spray and a series of exploratory variables, such as the effect of Otrivin® nasal spray on common cold and sleep.

## Centers

1 center in 1 country: United Kingdom

## Objectives:

## Primary objective(s)

The primary objective was to evaluate the decongestant effect of Xylometazoline in subjects with common cold compared to placebo treatment by means of rhinomanometry.

## Secondary objective(s)

- Secondary objectives were to measure the peak subjective effect, time to onset of subjective relief of nasal obstruction and duration of relief of nasal obstruction by objective measures of nasal obstruction.

- In addition, any effects on sleep, tiredness, general well-being and smell/taste were studied as exploratory variables with a daily diary

## Test Product (s), Dose(s), and Mode(s) of Administration

Xylometazoline 1.0mg/mL metered dose nasal spray; 0.140 g delivered per actuation. One actuation three times daily.

## Statistical Methods

Analyzes of the primary efficacy parameter were conducted for the ITT and PPS. The analysis of the ITT was considered the primary efficacy analysis. There were no differences in the ITT and PPS population in this study since there were no exclusions from the PPS. The analysis of upper airway conductance at 1 hour was conducted by fitting an ANCOVA using treatment as a factor and the baseline NAR as a covariate.

Time to Onset of Subjective Relief of Nasal Obstruction, Time to Subjective Peak Relief of Nasal Obstruction, Time to Resolution of Subjective Measures of Common Cold Symptoms, Time to 50 on the VAS and Time to 30 on the VAS were analyzed using Wilcoxon survival techniques. Peak Relief of Nasal Obstruction for each of the two treatment groups was compared by fitting an ANCOVA using treatment as a factor and the baseline NAR as a covariate. Duration of Relief of Nasal Obstruction was compared for each of the two treatment groups at each time point by fitting an ANCOVA using treatment as a factor and the baseline NAR as a covariate.

For each variable, the Subjective Measure of Common Cold Symptoms was compared for each of the two treatment groups on each day by fitting an ANCOVA to the change from baseline using treatment as a factor and the baseline NAR as a covariate. Descriptive statistics for the Subjective Measures of Sleep, Tiredness, Daily Activities, General Well-Being and Smell and for the General Questions on Treatment were presented for each variable. For each variable, the two treatment groups were compared at each time point by fitting an ANCOVA to the change from baseline using treatment as a factor and the baseline NAR as a covariate. Treatment groups were compared for the VAS score at each time point by fitting an ANOVA using treatment as a factor and the baseline nasal conductance as a covariate.

## Study Population: Key Inclusion/Exclusion Criteria

**Inclusion Criteria:**

- Over 18 years
- Have had moderate common cold symptoms for less than 36 hours.

**Exclusion Criteria:**

- Congested/runny nose for more than two continuous weeks in the previous 12 months
- Deviated septum or nasal polyps
- Recent use of antibiotics
- Recent sinusitis

Other protocol-defined inclusion/exclusion criteria may apply.

## Participant Flow Table

| No. Subjects Screened | No. Subjects Randomized | No. Subjects Exposed | No. Subjects Completed* | No. Subjects Discontinued |
|---|---|---|---|---|
| 78 | 66 | 61 | 61 | 0 |

** Includes a total of 6 subjects who completed Visit 3 of the study but were later found to have finished treatment on a study day when symptoms of nasal congestion were still present.*

## Baseline Characteristics

### Demographic summary by treatment group

| | Otrivin® 0.1% | Vehicle Reference |
|---|---|---|
| Age (yr) | | |
| mean ± SD | 20.0 (1.6) | 20.9 (5.2) |
| Median | 20 | 20 |
| 20-<40 | 29 | 31 |
| 40-<60 | 0 | 1 |
| 60-<75 | 0 | 0 |
| >75 | 0 | 0 |
| Sex - n(%) | | |
| Male | 11 (37.9%) | 12 (37.5%) |
| Female | 18 (62.1%) | 20 (62.5%) |
| Race - n(%) | | |
| Black | 0 (0%) | 0 (0%) |
| Caucasian | 28 (96.6%) | 29 (90.6%) |
| Oriental | 1 (3.4) | 2 (6.3%) |
| Other | 0 (0%) | 1 (3.1%) |

## Summary of Efficacy

### Primary Outcome Result(s)

**Upper Airway Conductance at 1h ($cm^3$/sec)- intent to treat population**

| | |
|---|---|
| Otrivin® (LS Mean): 384.23 | LS Mean Difference: 157.82 (p < 0.0001) |
| Reference (LS Mean): 226.42 | |

### Secondary Outcome Result(s)

**Time to Onset of Subjective Relief of Nasal Obstruction (mins) - intent to treat population**

| | |
|---|---|
| Otrivin® (median): 1.7 | Difference: 0.2 (p = 0.6474) |
| Reference (median): 1.5 | |

**Subjective Peak Relief of Nasal Obstruction (VAS Score) - intent to treat population**

| | |
|---|---|
| Otrivin® (LS Mean): 20.7 mm | LS Mean Difference: -10.8 (p = 0.0298) |
| Reference (LS Mean): 31.5 mm | |

**Development of Subjective Relief of Nasal Obstruction for the first 30 minutes after dosing- intent to treat population**

| | |
|---|---|
| Otrivin® | p < 0.02 |
| Reference | |

Otrivin® had significantly less subjective symptoms between 5 and 30 minutes post dosing compared with the vehicle reference.

## Duration of Objective Relief of Nasal Obstruction (hours) - intent to treat population

| |
|---|
| 10h |

(defined as the last time point at which pδ0.05 when comparing the difference in LS mean Nasal Conductance for each treatment at each time point).

## Duration of Clinical Relief of Nasal Obstruction (hours) - intent to treat population

| |
|---|
| 12h |

(defined as the last measured time point at which nasal conductance is > published limit for clinical relief (i.e. > 250 $cm^3$/sec)

## Time to Subjective Peak Relief of Nasal Obstruction (min) - intent to treat population

| | |
|---|---|
| Otrivin® (median): 30 | Difference: 0 (p = 0.7336) |
| Reference (median): 30 | |

## Subjective Measure of Common Cold Symptoms - intent to treat population

| | |
|---|---|
| Otrivin® | p < 0.05 |
| Reference | |

Significant differences between treatments in Overall Symptoms (day 1), Blocked Nose (day 1 & 2), Sore Throat and Ear ache (day 1).

## Summary of Safety

## Safety Results

### Serious Adverse Events by System Organ Class

There were no serious adverse events reported.

### Number (%) of subjects with most frequent AEs

| | Otrivin® n (%) | Vehicle Reference n (%) |
|---|---|---|
| **Subjects Studied** | | |
| total no. of subjects | 29 | 32 |
| total no. with an AE | 7 (24.1%) | 9 (28.1%) |
| **Adverse Events** | | |
| Head ache | 1 (3.4%) | 4 (12.5%) |
| Period pain | 3 (10.3%) | 0 |
| Epistaxis | 1 (3.4%) | 1 (3.1%) |
| Cough | 1 (3.4%) | 1 (3.1%) |
| Back ache | 0 | 1 (3.1%) |
| Cystitis | 1 (3.4%) | 0 |
| Migraine | 0 | 1 (3.1%) |
| Nausea | 0 | 1 (3.1%) |
| Neck ache | 0 | 1 (3.1%) |
| Sore eyes | 0 | 1 (3.1%) |
| Toothache | 1 (3.4%) | 0 |

* AEs are listed by frequency

## Date of Clinical Trial Report

31-July-2007