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# Efficacy and safety of sodium hyaluronate 0.18% (VISMED®) *vs* sodium chloride 0.9% in patients with bilateral moderate dry eye

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## Introduction

- Dry eye is a disorder of the tear film that is caused by tear deficiency or excessive tear evaporation. It is associated with symptoms of ocular discomfort, dryness, scratchiness, burning, soreness and grittiness.[1]
- Several authors[2,3] have obtained excellent results in the symptomatic treatment of this pathology with regular administration of solutions containing sodium hyaluronate.
- Sodium hyaluronate was chosen as the active compound in VISMED® because of its unique viscoelastic properties, which lubricate and protect the ocular surface. In addition, sodium hyaluronate exhibits water entrapping and mucoadhesive properties, which delay the evaporation of the product from the eye surface.
- VISMED® is a unique formulation that contains ions naturally present in the tear fluid, namely calcium, magnesium, potassium, sodium and chloride, which maintain the physiology of the cornea. It has been formulated to be hypotonic, in order to compensate for the hypertonicity of tears in patients experiencing dry eye syndrome.

## Study objective

The aim of this study was to assess the efficacy and safety of sodium hyaluronate 0.18% (VISMED®) compared with that of sodium chloride 0.9% (saline) solution in patients with bilateral moderate dry eye syndrome.

## Methods

### *Study design*

A randomized (1:1), double-masked, parallel-group, controlled, phase III trial performed in 18 centres in France.

### *Patient selection*

The intent-to-treat (ITT) population consisted of 150 patients who were diagnosed with moderate dry eye syndrome as a result of:

- Sjögren's syndrome, or
- primary hyposecretion dry eye syndrome.

### *Main inclusion criteria*

- Male and female patients aged ≥18 years.
- Experiencing at least two symptoms of bilateral dry eye, such as soreness, scratchiness, dryness, grittiness and burning, which occurred often and rated ≥40 mm on the visual analogue scale (VAS).
- With at least three out of four of the following objective parameters:
  - reduced tear volume: Schirmer test ≤10 mm wetting/5 min for each eye
  - tear film instability: break-up time (BUT) ≤10 s for each eye
  - staining with fluorescein, with a total score ≥3 for each eye
  - staining with Lissamine green, with a total score ≥3 for each eye.

### *Products and treatment*

- Sodium hyaluronate 0.18% (VISMED®) or sodium chloride 0.9% (saline).
- One drop in each eye, three times daily (i.e. every 4–5 h) or as needed for 28 days.

### *Statistical analysis*

- Primary efficacy criterion: sum of subjective symptoms on VAS.
- Co-primary efficacy criterion: objective assessment of fluorescein staining score.
- Mann–Whitney statistics (one-sided, 97.5% CI) were used to assess superiority of VISMED® over saline.

### *Procedures and assessments*

The patient procedure and assessment schedule is summarized in Table 1.

## Results

### *Patients*

The number of patients entering each stage of the study is shown in Figure 1. A total of 151 patients were randomized and received the double-blind medication (safety population). The ITT population consisted of 150 patients. The baseline demographic characteristics of patients are summarized in Table 2.

### *Safety*

- A total of 20 patients experienced adverse events (AEs) during the study: 11 (14.9%) in the VISMED® group and 9 (11.7%) in the saline group. Of these, 1 patient (1.3%) and 3 patients (4.0%) were considered to have experienced AEs that were possibly or probably related to the test product in the VISMED® and saline groups, respectively.
- Most of the AEs reported were ophthalmic disorders (9 patients, 6.0%), followed by general disorders (5 patients, 3.3%). By treatment group, the most common AE reported was burning in the VISMED® group (2 patients, 2.7%) and headache in the saline group (2 patients, 2.6%).

***Table 1:*** *Patient procedure and assessment schedule.*

| Procedures and assessments | Screening, washout | Inclusion | Follow-up, double blind | |
|---|---|---|---|---|
| | Day -12 to Day -4 Visit 1 | Day 0 Visit 2 | Day 7 Visit 3 | Day 28 Visit 4 |
| | | | VISMED® | |
| | | | Saline | |
| Verification of inclusion and exclusion criteria | X | X | | |
| Medical history and concomitant medications | X | X | X | X |
| Symptoms intensity on visual analogue scale | X | X | X | X |
| Symptoms frequency | X | X | X | X |
| Effect of symptoms on activities of daily life | X | X | X | X |
| Comfort of the eye drops | | | X | X |
| Slit lamp examination | X | X | X | X |
| Tear prism height | X | X | X | X |
| Schirmer test | X | X | X | X |
| Tear film break-up time | X | X | X | X |
| Corneal staining with fluorescein | X | X | X | X |
| Staining with Lissamine green | X | X | X | X |
| Adverse event report | X | X | X | X |

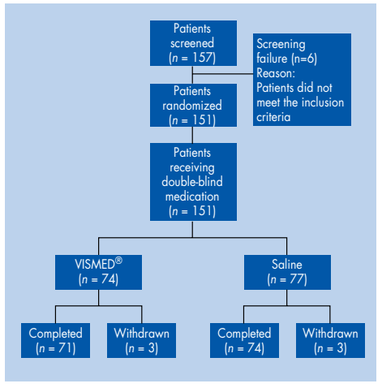


***Figure 1:*** *Study profile, all patients data set.*

***Table 2:*** *Baseline demographic characteristics, mean ± SD (ITT population).*

| Demographic characteristic | VISMED® (*n* = 73) | Saline (*n* = 77) |
|---|---|---|
| Gender (female:male) | 60:13 | 65:12 |
| Weight (kg) | 64.2 (12.1) | 64.0 (12.4) |
| Height (cm) | 161.8 (7.4) | 162.6 (7.0) |
| Age (years) | 61.4 (14.0) | 61.7 (12.5) |

### *Efficacy*

Primary analysis

- Patients receiving VISMED® exhibited a greater per cent change from baseline for symptoms intensity on VAS than those in the saline group at Day 7 (-19.85% and -16.17%, respectively) and Day 28 (-33.98% and -31.23%, respectively) (Figure 2). The difference between VISMED® and saline was almost statistically significant at Day 7 ($p = 0.0300$) and not at Day 28 ($p = 0.1337$).
- VISMED® showed a per cent change from baseline for total fluorescein score that was greater than that seen in the saline group at Day 7 (-27.03% and -20.19%, respectively) and Day 28 (-43.44% and -30.21%, respectively) (Figure 3). The difference between VISMED® and saline was almost statistically significant at Day 7 ($p = 0.0546$) and Day 28 ($p = 0.0279$).

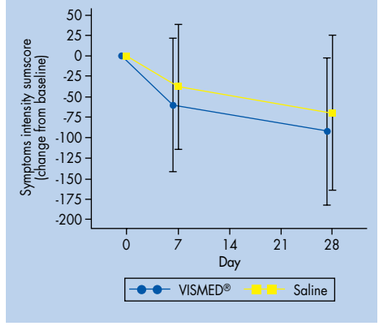


***Figure 2:*** *Symptoms intensity on VAS, change from baseline, mean ± SD (ITT population).*

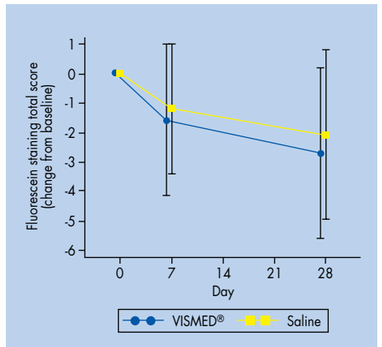


***Figure 3:*** *Fluorescein staining score, change from baseline, mean ± SD (ITT population).*

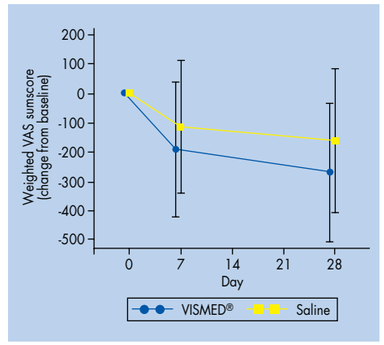


***Figure 4:*** *Composite index of symptoms intensity and frequency, change from baseline, mean ± SD (ITT population).*

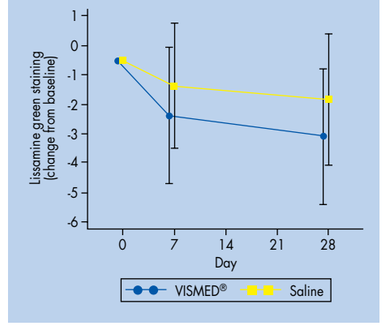


***Figure 5:*** *Lissamine green staining score, change from baseline, mean ± SD (ITT population).*

Secondary analysis

- At Day 28, VISMED® produced a significantly ($p = 0.0222$) better reduction in the composite index of symptoms intensity and frequency compared with saline (62% and 54%, respectively) (Figure 4).
- The score for Lissamine green staining indicated a significant difference between groups in favour of VISMED® at Day 7 ($p = 0.0013$) and Day 28 ($p = 0.0007$) (Figure 5).
- The effect of symptoms on the activities of daily life was significantly lower in the VISMED® group compared with the saline group at Day 7 ($p = 0.0235$) and Day 28 ($p = 0.0053$) (Figure 6).
- At Day 28, the comfort of the eye drop was significantly ($p = 0.0158$) better in patients treated with VISMED® than in patients who received saline (Figure 7).
- The reduction in fluorescein staining score also tended to be better in the VISMED® group than in the saline group at Day 7 ($p = 0.0546$) and Day 28 ($p = 0.0279$).
- There were no differences in tear volume and tear film BUT between the two groups.

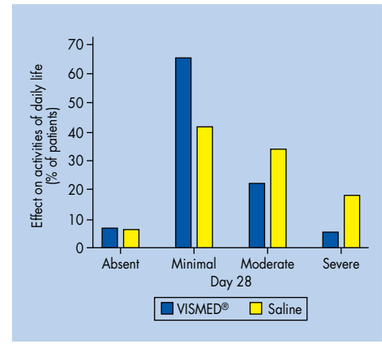


***Figure 6:*** *Effect of symptoms on the activities of daily life, frequency count at Day 28 (ITT population).*

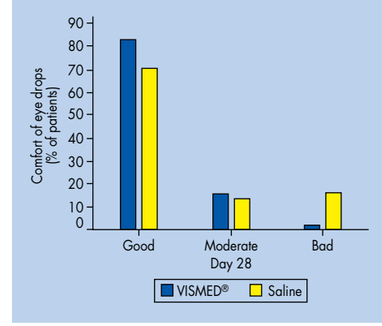


***Figure 7:*** *Comfort of the eye drops, frequency count at Day 28 (ITT population).*

## Conclusions

- Treatment with VISMED® resulted in a low incidence of AEs and was well tolerated.
- VISMED®, administered topically to the eye three or four times daily (i.e. every 4–5h) for 28 days, was effective in reducing subjective symptoms intensity on VAS and objective corneal staining with fluorescein.
- VISMED® was efficient in improving scores of symptoms frequency, composite index of symptoms intensity on VAS and frequency, effect of symptoms on activities of daily life, comfort of the eye drops and staining with Lissamine green.

## References

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