

DRUG PRODUCT	H 199/18 capsule	<h2>Synopsis</h2> <p>REFERRING TO PART OF THE DOSSIER</p>	<p>(FOR NATIONAL AUTHORITY USE ONLY)</p>
DRUG SUBSTANCE	H 199/18		
DOCUMENT NO.	SH-QBE-0021		
VERSION NO.	01		
STUDY CODE	SH-QBE-0021		
DATE	27 April, 1999		

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**An efficacy and safety study of H 199/18 20 mg vs. omeprazole in the management of patients with gastroesophageal reflux symptoms without macroscopic esophagitis - A multicentre study**

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**STUDY CENTRE(S)**

Multicentre study including 65 centres in Denmark, Finland, Norway and Sweden

**PUBLICATION (REFERENCE)**

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**STUDY PERIOD**

- DATE OF FIRST ENROLMENT      September 29, 1997
- DATE OF LAST COMPLETED      May 7, 1998

**PHASE OF DEVELOPMENT**

III A

**OBJECTIVES**

Primary:

- To compare the efficacy of 4 weeks' (visit 3) treatment with either H 199/18 20 mg o.m. (once daily) or omeprazole 20 mg o.m., on complete resolution of heartburn as assessed by the investigator.

Secondary:

- To compare the efficacy of 2 weeks' (visit 2) treatment with either H 199/18 20 mg o.m. or omeprazole 20 mg o.m., on complete resolution of heartburn as assessed by the investigator.
- To compare the efficacy of 4 weeks' treatment with either H 199/18 20 mg o.m. or omeprazole 20 mg o.m., on relief of heartburn as assessed by the patient with a diary card.
- To compare the treatment groups with regard to Overall Treatment Evaluation (OTE).
- To compare the treatment groups with regard to other GERD symptoms.
- To evaluate the safety and tolerability of H 199/18.

## **STUDY DESIGN**

Double-blind, randomised and parallel group study with H 199/18 20 mg or omeprazole 20 mg.

## **DIAGNOSIS AND MAIN CRITERIA FOR INCLUSION**

Presence of heartburn as main symptom with normal endoscopy, at least 6 months' history of episodes of heartburn, female or male 18-80 years of age, signed informed consent.

## **TEST PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION**

H 199/18 capsule, 20 mg once daily, batch number: H 1189-04-01-03.

## **COMPARATOR PRODUCT, BATCH NUMBER, DOSAGE AND MODE OF ADMINISTRATION**

Omeprazole capsule, 20 mg once daily, batch number: H 0431-13-05-06.

## **DURATION OF TREATMENT**

Four weeks of double-blind treatment.

## **MAIN VARIABLE(S):**

### **EFFICACY**

The primary variable was complete resolution of heartburn defined as no days with heartburn episodes during the last 7 days prior to visit 3. Secondary variables were complete resolution of heartburn at visit 2 and adequate control of heartburn at visit 3. Further secondary variables were relief of heartburn as assessed by diary cards, OTE and relief of other GERD symptoms.

### **SAFETY**

Adverse events (AE), laboratory assessments and vital signs.

## **STATISTICAL METHODS**

The two treatment groups were compared regarding the primary variable, using a Mantel-Haenszel Chi-Square test with stratification based on countries. (H 199/18 20 mg versus omeprazole 20 mg).

Dichotomised secondary variables were analysed by a Mantel-Haenszel Chi-Square test stratified by country (complete resolution of heartburn, adequate control of heartburn) or by baseline score (regurgitation, dysphagia). The number of days until the first day without heartburn and the number of days until the first 7-day period without heartburn were analysed by a log rank test. The percentage of time without heartburn during the study period was analysed by a one-way ANOVA. The score of the OTE questionnaire was analysed by a Mann-Whitney test.

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The primary variable was analysed using both an intention to treat (ITT) and a per protocol (PP) approach. Secondary variables were analysed using an ITT approach only. An “All patients randomised” analysis was also performed and the results of this analysis are presented in Section 14.4 in the body of the report.

patients

	<b>H 199/18 20 mg</b>	<b>Ome 20 mg</b>	<b>Total</b>
No. planned	330	330	660
No. randomised and treated	336	334	670 <sup>*)</sup>
Males/Females	175/161	168/166	343/327
Mean age (range)	48.5 (19-79)	48.5 (20-79)	48.5 (19-79)
No. analysed for efficacy	336	334	670
No. analysed for safety	336	334	670
No. completed (visit 3)	328	322	650

<sup>\*)</sup> 671 patients were randomised. One patient was randomised but not treated.

## SUMMARY

### EFFICACY RESULTS

The proportion of patients with complete resolution of heartburn after four weeks is shown in Table 1. The difference between the treatment groups is not statistically significant, as shown in Table 2.

**Table 1. Proportion of patients with complete resolution of heartburn, defined as no heartburn during the last 7 days prior to visit 3, estimates and 95% exact confidence intervals.**

Treatment	Estimate	Lower limit	Upper limit
ITT			
H 20	61.9% (208/336)	56.5%	67.1%
O 20	59.6% (199/334)	54.1%	64.9%
PP			
H 20	62.6% (189/302)	56.9%	68.1%
O 20	59.6% (171/287)	53.7%	65.3%

**Table 2. Difference between H 199/18 20 mg and omeprazole 20 mg in proportion of patients with complete resolution of heartburn at visit 3, estimates, 95% confidence intervals and Mantel-Haenszel test stratified by country.**

	Estimate	Lower limit	Upper limit	M-H Chi-Square	p-value
ITT					
H 20 - O 20	2.3%	-5.1%	9.7%	0.36	0.549
PP					
H 20 - O 20	3.0%	-4.9%	10.9%	0.50	0.478

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**SAFETY RESULTS**

Both treatments were safe and well tolerated with a low frequency of reported AEs and SAEs. The frequency and distribution of AEs during the study were similar for the two treatments H 199/18 20 mg and omeprazole 20 mg. The laboratory profiles were very similar for the two treatments with small deviations during the study period.

**DATE OF THE REPORT**

27 April, 1999