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| NAME OF COMPANY<br>ASTRA HÄSSLE AB<br><br>TRADE NAME(S)<br><br>NAMES OF ACTIVE INGREDIENT(S) INN<br>H 199/18 and quinidine | **Clinical Study Synopsis**<br>REFERENCE IN THE DOSSIER<br>VOLUME<br><br>REF. NUMBER<br>PAGE | (FOR NATIONAL AUTHORITY USE ONLY)<br><br>STUDY CODE SH-QBE-0005<br>REPORT NO. SH-QBE-0005 |
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TITLE OF THE STUDY

# PHARMACOKINETICS OF QUINIDINE WITH AND WITHOUT CO-ADMINISTRATION OF H 199/18 SODIUM IN HEALTHY VOLUNTEERS

## STUDY CENTRE

Quintiles AB, Islandsgatan 2, S-753 18, Uppsala, Sweden
(former PMC Drug Study Unit AB)

## STUDY PERIOD

April 27 - June 19, 1995

## CLINICAL PHASE

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## OBJECTIVES

The primary objective was to study the pharmacokinetics of quinidine sulphate and the formation of one of its active metabolites, 3-hydroxyquinidine, after a single oral dose during repeated oral administration of H 199/18 or placebo in healthy subjects.

## STUDY DESIGN

The study was performed as a double-blind, randomised, two-way cross-over trial in which each subject received 30 mg H 199/18 given orally as its corresponding sodium salt in a solution or placebo solution once daily for 6 days. On day 5 a single dose of 400 mg quinidine sulphate was administered orally.

## NUMBER OF SUBJECTS

Twelve healthy male subjects were included in the study.

**DIAGNOSIS AND CRITERIA FOR INCLUSION**

*Inclusion criteria*: male, 20 - 40 years of age, normal laboratory and physical findings prior to the study entry and signed informed consent.

**INVESTIGATIONAL PRODUCT**

Thirty mg H 199/18 (batch No. H 1103-1-2-1)or placebo (batch No. H 1163-1-1-1) was given as an oral solution once daily for 6 days and 400 mg quinidine sulphate (commercially available) was administered orally as a tablet on day 5.

**REFERENCE DRUG**

Placebo (batch No. H 1163-1-1-1)

**DURATION OF TREATMENT**

Six days

**ASSESSMENT METHODS**

H 199/18 or placebo was given orally to the subjects for 6 days. Quindinine was given to the subjects as tablets on day 5. Plasma concentrations of H 199/18 (days 1 and 5), quinidine and hydroxyquinidine (day 5) were analysed.

**STATISTICAL METHODS**

A mixed analysis of variance model was used. The result was stated as 95% confidence intervals for the mean ratios and p-values for the corresponding tests. Descriptive statistic was performed in all kinetic variables

**SUMMARY OF RESULTS**

The area under the plasma drug concentration-time curve from time 0 to infinity (AUC) of quinidine (60 µmol*h/L) during treatment with H 199/18 was similar to that during placebo treatment (53 µmol*h/L) with p-value= 0.08. The AUC of hydroxyquinidine (10 µmol*h/) during treatment with H 199/18 was also similar to that during placebo treatment (10 µmol*h/) with p-value= 0.77.

The AUC after H 199/18 oral administration was higher (7.1 µmol*h/L) on day 5 compared to day 1 (2.7 µmol*h/L).

Repeated doses of H 199/18 together with single dose of quinidine were well tolerated.

**DATE:** 1997-04-11