The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

**Study No:** C93-077

**Title:** A study to investigate the relative bioavailability of ondansetron syrup and Zofran tablets 4 mg

**Rationale:** Ondansetron has been approved in a number of countries as an antiemetic. A syrup formulation of ondansetron was developed for use in subjects who may have found swallowing tablets difficult. The primary target population was paediatric patients although it was thought that adults, especially the elderly, would also benefit. This study in healthy volunteers was conducted to demonstrate bioequivalence between syrup and tablet formulations.

**Phase:** I

**Study Period:** 17 January 1994 – 24 January 1994

**Study Design:** Open label, single dose, randomised, two-way, cross-over study.

**Centres:** One centre in Germany

**Indication:** None.

**Treatment:** The two treatments in this study were:
- Ondansetron syrup 4 mg/5 mL,
- Ondansetron tablet 4 mg.

There was a 7 day washout interval between dosing occasions.

**Objectives:** The objective of this study was to demonstrate that the ondansetron syrup 4 mg/5 mL was bioequivalent to ondansetron tablets 4 mg.

**Statistical Methods:** The following parameters were derived from plasma ondansetron concentration data: maximum measured plasma ondansetron concentration (Cmax); time of the sample in which Cmax was measured (tmax); area under the curve of plasma ondansetron concentration versus time extrapolated to infinite time (AUC∞); terminal elimination rate constant for ondansetron in plasma (λz) and the corresponding terminal plasma half-life (t½).

Linear least regression was used to determine λz, using logarithmically transformed points in the terminal phase. The pharmacokinetic values AUC∞, Cmax and t½ were analysed using analysis of variance allowing for effects owing to subjects, periods and treatments. A log transformation was applied to the data in order to satisfy the constant variance assumption for the analysis of variance. Geometric mean values for each of the parameters were calculated for each treatment, together with 95% confidence intervals. Estimates of the ratio of ondansetron syrup to ondansetron tablet were produced, along with their associated 90% confidence intervals and tested for significance. Bioequivalence was declared if the 90% confidence intervals for the treatment comparison (ondansetron syrup 4 mg/5 mL to ondansetron tablets 4 mg), in relation to Cmax and AUC∞, were completely contained within the interval (80%, 125%). Values of tmax were compared using Koch’s non-parametric method for two-period crossovers, based on the Wilcoxon Rank Sum test. An estimate of the median difference between the treatments, together with a 90% confidence interval was calculated.

All subjects were included in the safety analysis, which consisted of summary statistics only.

**Study Population:** Sixteen healthy male volunteers aged between 18 and 50 years. Subjects who had allergic reactions to medications, clinical abnormalities during the physical examination or a case history considered unsuitable for the study were excluded.

**Number of Subjects:**

<table>
<thead>
<tr>
<th>Planned N</th>
<th>16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dosed N</td>
<td>16</td>
</tr>
<tr>
<td>Completed n (%)</td>
<td>16 (100)</td>
</tr>
<tr>
<td>Total Number Subjects Withdrawn N (%)</td>
<td>0</td>
</tr>
<tr>
<td>Withdrawn due to Adverse Events n (%)</td>
<td>0</td>
</tr>
<tr>
<td>Withdrawn due to Lack of Efficacy n (%)</td>
<td>0</td>
</tr>
<tr>
<td>Withdrawn for Other Reasons n (%)</td>
<td>0</td>
</tr>
</tbody>
</table>

**Demographics**

<p>| N (ITT) | 16 |</p>
<table>
<thead>
<tr>
<th>Females: Males</th>
<th>0 : 16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median Age in Years (range)</td>
<td>30 (22, 43)</td>
</tr>
<tr>
<td>Median Weight in kg (range)</td>
<td>74.5 (62.0, 90.0)</td>
</tr>
<tr>
<td>Caucasian n %</td>
<td>15 (94)</td>
</tr>
</tbody>
</table>

**Pharmacokinetic Endpoints**: A summary of pharmacokinetic parameters for ondansetron with a statistical analysis is presented in the following table. Bioequivalence between the two formulations of ondansetron syrup 4 mg/5 mL and ondansetron tablets 4 mg was demonstrated.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Treatment</th>
<th>Estimate</th>
<th>95% CI</th>
<th>Mean ratio</th>
<th>90% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC∞ (ng.h/mL)</td>
<td>A</td>
<td>48.8</td>
<td>43.3, 54.9</td>
<td>105%</td>
<td>91%, 120%</td>
<td>0.573</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>46.6</td>
<td>41.4, 52.5</td>
<td>41.4, 52.5</td>
<td>41.4, 52.5</td>
<td></td>
</tr>
<tr>
<td>Cmax (ng/mL)</td>
<td>A</td>
<td>7.42</td>
<td>6.57, 8.38</td>
<td>95%</td>
<td>82%, 109%</td>
<td>0.521</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>7.82</td>
<td>6.92, 8.83</td>
<td>6.92, 8.83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>tmax (h)</td>
<td>A</td>
<td>2.00</td>
<td>1.00, 5.00</td>
<td>0.00</td>
<td>-0.50, 0.50</td>
<td>0.872</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>2.00</td>
<td>1.00, 5.00</td>
<td>1.00, 5.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td>t½ (h)</td>
<td>A</td>
<td>3.75</td>
<td>3.29, 4.27</td>
<td>96%</td>
<td>83%, 112%</td>
<td>0.663</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>3.89</td>
<td>3.42, 4.43</td>
<td>3.42, 4.43</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Treatment A = ondansetron syrup 4 mg/5 mL; Treatment B = ondansetron tablets 4mg.
Data are presented as geometric means and 95% confidence intervals except tmax, which is presented as median and range. The mean ratio is presented as the ratio of treatment A to treatment B with the 90% confidence intervals with the exception of tmax, which is presented as the median difference with the 90% confidence intervals.

**Safety results:**

<table>
<thead>
<tr>
<th>Adverse Events:</th>
<th>Ondansetron syrup 4 mg/5 mL</th>
<th>Ondansetron tablet 4 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (safety)</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>No. subjects with AEs n (%)</td>
<td>3 (19)</td>
<td>5 (31)</td>
</tr>
<tr>
<td>Most Frequent AEs: number of observations (number of subjects) %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache n (%)</td>
<td>3 (19)</td>
<td>5 (31)</td>
</tr>
</tbody>
</table>

**Serious Adverse Events:**
No. Subjects with SAEs 0 0

**Publications:**


Date Updated: 28-Nov-2005