# Clinical Study Synopsis for Public Disclosure

This clinical study synopsis is provided in line with **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

The synopsis - which is part of the clinical study report - had been prepared in accordance with best practice and applicable legal and regulatory requirements at the time of study completion.

The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups; it has not necessarily been submitted to regulatory authorities.

A synopsis is not intended to provide a comprehensive analysis of all data currently available regarding a particular drug. More current information regarding a drug is available in the approved labeling information which may vary from country to country.

Additional information on this study and the drug concerned may be provided upon request based on **Boehringer Ingelheim's *Policy on Transparency and Publication of Clinical Study Data***.

| | | | |
|---|---|---|---|
| **Name of company:**<br>Boehringer Ingelheim | | **Tabulated Trial Report** | Boehringer Ingelheim |
| **Name of finished product:**<br>Not applicable | | **EudraCT No.:**<br>2009-016370-32 | |
| **Name of active ingredient:**<br>BI 671800 | | **Page:**<br>1 of 4 | **Synopsis No.:** |
| **Module:** | | **Volume:** | |
| **Report date:**<br>01 JUN 2012 | **Trial No. / U No.:**<br>1268.7 /<br>U12-1590-01 | **Dates of trial:**<br>16 SEP 2010 – 14 OCT 2010 | **Date of revision:**<br>Not applicable |



| | |
|---|---|
| **Title of trial:** | A phase I trial to investigate the metabolism and pharmacokinetics of an open-label single dose of 400 mg [$^{14}$C]BI 671800 HEA administered as an oral solution of the choline salt in healthy male volunteers |
| **Principal Investigator:** | [redacted] |
| **Trial site:** | [redacted], USA |
| **Publication (reference):** | Data of this study have not been published. |
| **Clinical phase:** | I |
| **Objectives:** | The primary objective was to determine the basic pharmacokinetics of BI 671800, its major metabolite BI 600957, and $^{14}$C-radioactivity including mass balance, excretion pathways, and metabolism following a single oral dose of 400 mg [$^{14}$C]BI 671800 to healthy male volunteers.<br>The secondary objective was to assess the safety and tolerability following a single oral dose of 400 mg [$^{14}$C]BI 671800 to healthy male volunteers. |
| **Methodology:** | This was an open-label absorption, metabolism, and excretion study. One group of 8 healthy male subjects received a single oral dose of 400 mg [$^{14}$C]BI 671800. |
| **No. of subjects:** | |
| **planned:** | Entered: 8 |
| **actual:** | Entered: 8 treated: 8 analysed (for primary endpoint): 8 |
| **Diagnosis and main criteria for inclusion:** | Healthy male volunteers, age 18 to 55 years with a body mass index of 18 to 30 kg/m$^2$, were eligible for this trial. |
| **Test product:** | Oral solution of [$^{14}$C]BI 671800 |
| **dose:** | 400 mg/10 mL containing approximately 100 µCi $^{14}$C-radioactivity |
| **mode of admin.:** | Oral administration with 240 mL water in the fasted state |
| **batch no.:** | BI 671800 HEA: B093000581<br>[$^{14}$C]BI 671800 HEA: MH-101804-091-1 |

| | | | |
|---|---|---|---|
| **Name of company:** Boehringer Ingelheim | | **Tabulated Trial Report** | Boehringer Ingelheim |
| **Name of finished product:** Not applicable | | **EudraCT No.:** 2009-016370-32 | |
| **Name of active ingredient:** BI 671800 | | **Page:** 2 of 4 | **Synopsis No.:** |
| **Module:** | | **Volume:** | |
| **Report date:** 01 JUN 2012 | **Trial No. / U No.:** 1268.7 / U12-1590-01 | **Dates of trial:** 16 SEP 2010 – 14 OCT 2010 | **Date of revision:** Not applicable |



| | |
|---|---|
| **Reference product:** | Not applicable |
| **Duration of treatment:** | One day (single dose) |
| **Criteria for evaluation:** | |
| **Pharmacokinetics:** | *Primary endpoints*<br>• Individual concentration-time profiles of $^{14}$C-radioactivity in whole blood, plasma, urine, and faeces<br>• Individual concentration-time profiles of BI 671800 and BI 600957 in plasma and urine<br>• Rate and extent of excretion and mass balance of total $^{14}$C-radioactivity in urine and faeces<br>• Elucidation of metabolite structures and identification of major metabolites in plasma, urine, and faeces (if feasible) in comparison with various animal species (reported separately)<br>• $C_{blood\ cells}/C_{plasma}$ ratio of $^{14}$C-radioactivity<br>• Estimation of pharmacokinetic (PK) parameters ($C_{max}$, $t_{max}$, $AUC_{0-tz}$, $AUC_{0-\infty}$, $\lambda_z$, $t_{½}$, $MRT_{po}$, CL/F, $V_z/F$, $Ae_{0-tz}$, $fe_{0-tz}$, $Ae_{faeces,0-tz}$, $fe_{faeces,0-tz}$, $CL_{R,t1-t2}$) using non-compartmental methods from:<br>  • concentrations of BI 671800 and BI 600957 in plasma and urine<br>  • concentrations of $^{14}$C-radioactivity in whole blood, plasma, urine, and faeces |
| **Safety:** | Adverse events, clinical laboratory tests, vital signs (blood pressure and pulse rate), 12-lead electrocardiogram (ECG), physical examination, and assessment of tolerability by investigator |
| **Statistical methods:** | Descriptive statistics were calculated. |

| | | | |
|---|---|---|---|
| **Name of company:** Boehringer Ingelheim | | **Tabulated Trial Report** | Boehringer Ingelheim |
| **Name of finished product:** Not applicable | | **EudraCT No.:** 2009-016370-32 | |
| **Name of active ingredient:** BI 671800 | | **Page:** 3 of 4 | **Synopsis No.:** |
| **Module:** | | **Volume:** | |
| **Report date:** 01 JUN 2012 | **Trial No. / U No.:** 1268.7 / U12-1590-01 | **Dates of trial:** 16 SEP 2010 – 14 OCT 2010 | **Date of revision:** Not applicable |



**SUMMARY – CONCLUSIONS:**

**Pharmacokinetics results:**

Eight healthy male volunteers ranging in age from 21 to 52 years old were entered in this trial. The body mass index of the subjects ranged from 23.2 to 29.0 kg/m$^2$. All subjects were treated and completed the trial as planned. No important protocol violations were reported.

After administration of a single oral dose of 400 mg [$^{14}$C]BI 671800 HEA in healthy volunteers, radioactivity was rapidly absorbed, with a $t_{max}$ of 1.00 h. BI 671800 accounted for almost all plasma radioactivity at $t_{max}$, but became a progressively smaller proportion thereafter. The plasma half-life of radioactivity (47.4 h) was considerably longer than that of BI 671800 (6.82 h). Comparison of $AUC_{0-\infty}$ data showed that BI 671800 accounted for less than 25% of the radioactivity. Similarly, the $AUC_{0-\infty}$ and $C_{max}$ of BI 600957 were significantly lower than the corresponding values for total radioactivity. These data indicate that the major portion of plasma radioactivity consisted of one or more metabolites of BI 671800 which were cleared more slowly than either BI 671800 or BI 600957.

Concentrations of radioactivity were consistently lower in blood than in plasma – the mean blood/plasma concentration ratio was 0.4 to 0.5 – and the half-life of radioactivity in blood was about half the value in plasma. Mean red blood cell/plasma concentration ratios ranged from 0.00 to 0.0405, indicating very low association of radioactivity with red blood cells.

Almost all (94.5%) of the radioactive dose was excreted in urine (54.6%) and faeces (39.9%) within 7 days. The majority of radioactivity in urine was accounted for by glucuronide and glycine conjugates of trifluoromethylbenzoic acid, the product of amide hydrolysis; BI 671800 or its disproportionate human metabolite, BI 600957, accounted for only a small percentage of the radioactivity in urine.

| | | | |
|---|---|---|---|
| **Name of company:**<br>Boehringer Ingelheim | | **Tabulated Trial Report** | Boehringer Ingelheim |
| **Name of finished product:**<br>Not applicable | | **EudraCT No.:**<br>2009-016370-32 | |
| **Name of active ingredient:**<br>BI 671800 | | **Page:**<br>4 of 4 | **Synopsis No.:** |
| **Module:** | | **Volume:** | |
| **Report date:**<br>01 JUN 2012 | **Trial No. / U No.:**<br>1268.7 /<br>U12-1590-01 | **Dates of trial:**<br>16 SEP 2010 – 14 OCT 2010 | **Date of revision:**<br>Not applicable |



**Safety results:**

All 8 subjects were treated with a single dose of 400 mg [$^{14}$C]BI 671800 HEA.

Adverse events were reported in 5 subjects (62.5%). The most frequently reported adverse events during the treatment period were related to venipuncture (haemorrhage, haematoma, and pain) in a total of 3 subjects (37.5%). No serious adverse events were reported. The investigator considered headache and nausea in 1 subject possibly related to the study medication. All adverse events were of mild intensity.

Global tolerability was good in all subjects and there were no signficant findings in clinical laboratory values, vital signs, or ECG.

**Conclusions:**

After administrationof a single oral dose of 400 mg [$^{14}$C]BI 671800 HEA in healthy volunteers, radioactivity was rapidly absorbed, with a $t_{max}$ of 1.00 h. The major portion of plasma radioactivity consisted of one or more metabolites of BI 671800 which were cleared more slowly than either BI 671800 or BI 600957. Association of radioactivity with red blood cells was very low. Almost all the radioactive dose was excreted in urine and faeces. The majority of radioactivity in urine was accounted for by glucuronide and glycine conjugates of trifluoromethylbenzoic acid. Single doses of 400 mg [$^{14}$C]BI 671800 HEA were well tolerated in healthy male volunteers.