

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.

<b>Study No.:</b> ZVC111449			
<b>Title:</b> Bioequivalence study of Aciclovir cream 5% - Bioequivalence study of Aciclovir cream between Current and New formulation in Japanese Healthy volunteers - Clinical Pharmacology study			
<b>Rationale:</b> Aciclovir Cream 5% has been on the market as ZOVIRAX® Cream 5% for the herpes simplex treatment. This time, new formulation partially modified the current formulation has been developed. Based on the "Guideline for Bioequivalence Studies of Generic Products" and "Guideline for Bioequivalence Studies of Local dermal applied Generic Products," this study was planned to investigate the Bioequivalence of the Current and the New formulation using the residual amount of Aciclovir in the keratin layer of the epidermis after single dermal application.			
<b>Phase:</b> I			
<b>Study Period:</b> 4 April 2008 – 5 August 2008			
<b>Study Design:</b> This study was consisted of three parts, the Blank test (Obtaining blank epidermal stratum corneum), the Pre-test and the Main test. The Pre-test and the Main test were Open, cross-over, single application study.			
<b>Centres:</b> A single center in Japan.			
<b>Indication:</b> herpes simplex treatment			
<b>Treatment:</b> The Current and the New formulation were randomly applied to the right side or left side of their back. 100mg of both formulation were applied to the pre-defined position. The amount of its application was determined based on the actual usage of the cream.			
<b>Objectives:</b> Primary: To show bioequivalence between the Current and the New formulation of Aciclovir cream 5% after single dermal application in keratin layer of the epidermis in healthy Japanese Subjects Secondary: To investigate the safety and tolerability of the New and the Current formulation of Aciclovir Cream 5% following single topical application in healthy Japanese male subjects			
<b>Statistical Methods:</b> This study investigated the Bioequivalence of the Current and the New formulation Aciclovir cream 5% using the residual amount of Aciclovir in the keratin layer of the epidermis after single dermal application.			
<b>Study Population:</b> Healthy Japanese male subjects, age 20 to 55 years, inclusive			
<b>Number of Subjects:</b>	<b>Blank test</b>	<b>Pre-test</b>	<b>Main test</b>
Planned, N	3	6	18
Randomised, N	3	6	18
Completed, n (%)	3 (100)	6 (100)	18 (100)
Total Number Subjects Withdrawn, N (%)	0 (0)	0 (0)	0 (0)
Withdrawn due to Adverse Events n (%)	0 (0)	0 (0)	0 (0)
Withdrawn due to Lack of Efficacy n (%)	0 (0)	0 (0)	0 (0)
Withdrawn for other reasons n (%)	0 (0)	0 (0)	0 (0)
<b>Demographics</b>	<b>Blank test</b>	<b>Pre-test</b>	<b>Main test</b>
N (ITT)	3	6	18
Females: Males	0 : 3	0 : 6	0 : 18
Mean Age, years (SD)	26.3±10.12	26.0±7.13	28.8±7.01

Japanese, n (%)	3 (100)	6 (100)	18 (100)
<b>PK Results:</b>			
<p><b>Pre-test :</b> After four parts of dermal application of the Current and the Test formulation of Aciclovir cream 5% to 6 healthy male Japanese volunteers in the Pre-test, amount of Aciclovir in keratin layer of the epidermis were measured at 2, 4, 6 and 8 hours after application. The amount was the highest at 8 hour. The geometric mean ratio of Aciclovir amount between the Current and the Test formulation at 8 hour was 0.892, and corresponding CV was 16.62%.  Referred to the above results, required number of volunteers in the Main test was calculated to be 8 to 18 assuming true geometric mean ratio to be 0.9 and CV to be 15 to 25%, and was calculated to be 9 to 20 assuming true geometric mean ratio to be 0.892 and CV to be 15 to 25%, respectively.  Based on the above investigation, the duration of cream application in the Main test was determined to be 8 hour, the number of volunteers to show the bioequivalence was determined to be 18 and the number of application site was determined to be two (one each for the Current and the New formulation).</p>			
<p><b>Main test :</b> After dermal application of the Current and the Test formulation of Aciclovir cream 5% each to 1 sites to 18 healthy male Japanese volunteers in the Main test, 90% confidence interval of geometric mean ratio of Aciclovir amount between the Current and the Test formulation at 8 hour was 0.732 to 1.039, included within the bioequivalency criterion of 0.70 to 1.43 determined in "Guid eline for Bioequivalence Studies of Local dermal applied Generic Products."  Based on the above results, the Current and the New formulation of Aciclovir cream 5% was judged to be bioequivalent.</p>			
<b>Safety Results:</b> AE were assessed from at first hospitalization to post-study screen (additional/follow-up examination).			
	<b>Pre-test N=6</b>	<b>Main test N=18</b>	
<b>Most Frequent Adverse Events – On-Therapy</b>	<b>n (%)</b>	<b>n (%)</b>	
Subjects with any AE(s), n(%)	3 (50)	2 (11)	
White blood cell decreased	1 (17)	0 (0)	
Blood amylase increased	1 (17)	0 (0)	
Protein total decreased	2 (33)	1 (6)	
Red blood cell count decreased	0 (0)	1 (6)	
Haemoglobin decreased	0 (0)	1 (6)	
Haematocrit decreased	0 (0)	1 (6)	
<b>Serious Adverse Events - On-Therapy</b>			
<b>n (%) [n considered by the investigator to be related to study medication]</b>			
	<b>Pre-test N=6</b>	<b>Main test N=18</b>	
Subjects with non-fatal SAEs, n (%)	0 (0)	0 (0)	
Subjects with fatal SAEs, n (%)	0 (0)	0 (0)	
<b>Conclusion:</b>			
<p>The Current and the New formulation of Aciclovir cream 5% was bioequivalent.  •Single dermal applications of the Current and the New Aciclovir cream 5% to healthy male volunteers were safe and tolerable.</p>			
<b>Publications:</b> No publication			