

<b>Study No: ZVX10001</b>																						
<b>Title :</b> Skin Safety Study of Aciclovir Cream 5% - Patch Test and Photopatch Test in Japanese Healthy Male and Female Volunteers -																						
<b>Rationale:</b> As a part of the clinical development program for a topical application product in Japan, the skin irritation potential of Aciclovir Cream 5% was investigated by human patch test and photopatch test .																						
<b>Phase:</b> I																						
<b>Study Period:</b> 17 September 2003 to 17 November 2003																						
<b>Study Design:</b> Single blind, randomized, controlled trial to examine the skin-irritation potential of the test articles along with a positive and negative control under occlusive patch condition in Japanese healthy male and female volunteers.																						
<b>Centres:</b> 1 centre in Japan																						
<b>Indication:</b> Herpes simplex																						
<b>Treatment:</b> An adequate amount of Aciclovir Cream 5%, placebo (cream base), and white petrolatum was applied to Finn-Chambers®, and the chambers were placed occlusively on the right and left sides of the upper back in each subject.																						
<b>Objectives:</b> To evaluate the skin irritation potential of Aciclovir Cream 5% by patch test and photo-patch test																						
<p><b>Statistical Methods:</b> Based on the assessment in the patch test (higher score in two assessments, 30 minutes and 24 hours after removal of study medication), the skin irritation index was calculated using the following equation.</p> <ul style="list-style-type: none"> <li>• Skin irritation index = (Sum of higher scores in two assessments/number of evaluable subjects) x 100</li> </ul> <p>Based on the assessment in the photopatch test (higher score in two assessments, 24 and 48 hours after irradiation), the skin irritation index due to photosensitivity was calculated using the same equation as for the patch test.</p> <p>Assessment Criteria in Patch Test (Criteria proposed by the patch test study group in Japan)</p> <table border="1"> <thead> <tr> <th>Reaction/Findings</th> <th>Assessment</th> <th>Score</th> </tr> </thead> <tbody> <tr> <td>No reaction</td> <td></td> <td>0</td> </tr> <tr> <td>Weak erythema</td> <td>±</td> <td>0.5</td> </tr> <tr> <td>Erythema</td> <td>+</td> <td>1</td> </tr> <tr> <td>Erythema and edema</td> <td>++</td> <td>2</td> </tr> <tr> <td>Erythema and edema and papules, or vesicles</td> <td>+++</td> <td>3</td> </tr> <tr> <td>Bullae</td> <td>++++</td> <td>4</td> </tr> </tbody> </table>		Reaction/Findings	Assessment	Score	No reaction		0	Weak erythema	±	0.5	Erythema	+	1	Erythema and edema	++	2	Erythema and edema and papules, or vesicles	+++	3	Bullae	++++	4
Reaction/Findings	Assessment	Score																				
No reaction		0																				
Weak erythema	±	0.5																				
Erythema	+	1																				
Erythema and edema	++	2																				
Erythema and edema and papules, or vesicles	+++	3																				
Bullae	++++	4																				
<b>Study Population:</b> Japanese healthy volunteers (10 males and 10 females) aged 20 to 64 years, whose BMI was 18.5 to 25.0 and who passed a medical examination were eligible for this study																						
<b>Number of Subjects:</b>																						
Planned N	20																					
Dosed N	20																					
Completed n (%)	20 (100)																					
Total Number Subjects Withdrawn N (%)	0 (0)																					
Withdrawn due to Adverse Events n (%)	0 (0)																					
Withdrawn due to Lack of Efficacy n (%)	Not applicable																					
Withdrawn for Other Reasons n (%)	0 (0)																					
<b>Demographics</b>																						
N (ITT)	20																					

Females: Males	10 : 10			
Mean Age in Years (sd)	23.9 (4.6)			
Mean Weight in Kg (sd)	58.6 (7.83)			
White n (%)	0 (0)			
Japanese n (%)	20 (100)			
<b>Skin irritation Endpoints:</b>				
• <b>Skin irritation index by patch test</b>				
Treatment	Aciclovir Cream 5%	Placebo (cream base)	White petrolatum	No-compound
Skin irritation index	57.5	50.0	0	0
<b>Skin irritation index by photopatch test</b>				
Treatment	Aciclovir Cream 5%	Placebo (cream base)	White petrolatum	No-compound
Skin irritation index	7.5	15.0	2.5	5.0
<b>Safety results (other than skin irritation reaction caused by patch test and photopatch test):</b>				
<p>Throughout the study, safety was assessed by spontaneous reporting of adverse experiences, by physician or nursing observation. In addition, medical examination by physician including direct questioning using a non-leading questionnaire and vital sign measurements were done before and, at 24, 48, 72 hours and 7 days after study drug application. Clinical laboratory tests were scheduled before and at 72 hours after study drug application. All subjects treated with study medication were included in clinical safety evaluation.</p> <p>A total of 13 AEs was reported in 8 subjects during the study. All AEs but one were mild in severity, and one AE was moderate. There were no subject withdrawals due to AEs. The most commonly reported AE was adhesive plaster sensitivity. All AEs but one were considered not related to study medication. All AEs resolved or diminished by the end of the study.</p>				
<b>Adverse Events:</b>				
N (ITT)	20			
No. subjects with AEs n (%)	8 (40)			
Adhesive plaster sensitivity	4 (20)			
Itching	2 (10)			
Urticaria pressure	1 (5)			
Application site pruritus	1 (5)			
Epigastric pain	1 (5)			
Stomachache	1 (5)			
Uric acid high	1 (5)			
Eosinophil percentage increased	1 (5)			
<b>Serious Adverse Events, n (%):</b>				
No serious Adverse Events occurred during the study				
<b>Conclusions:</b> AEs were reported by 8/20 subjects in this study. There were no SAEs reported in this study.				
<b>Publications:</b> No publication				

Updated: 22Oct08