Clinical Study Synopsis for Public Disclosure

These results are supplied for informational purposes only in the interest of scientific disclosure. The synopsis may include approved and non-approved uses, doses, formulations, treatment regimens and/or age groups. This information is not intended to substitute for informed medical advice. You should not use this information to diagnose or treat a health problem or disease without consulting with a Healthcare Professional. Before prescribing any product mentioned in this Register, Healthcare Professionals should always refer to the specific approved product labeling information in their country. The results from a single trial may not reflect the overall results and need to be considered in the context of the totality of the available clinical research results for a product.

1. TITLE PAGE

<table>
<tr><td colspan="4">Title
EFFICACY AND SAFETY OF CLOBETASOL PROPIONATE SHAMPOO 0.05% USED IN ASSOCIATION WITH AN ANTIFUNGAL SHAMPOO IN THE TREATMENT OF MODERATE TO SEVERE SCALP SEBORRHEIC DERMATITIS</td></tr>
<tr><td colspan="2">Project Name
Clobex® shampoo</td><td>Project Number
817</td><td>Clinical Phase
Phase IIIB</td></tr>
<tr><td colspan="2">Investigational Product
(name, formulation, concentration)
Clobex® shampoo (clobetasol propionate 0.05%)</td><td colspan="2">Comparator Products
(name, formulation, concentration)
Nizoral® shampoo (ketoconazole 2%)</td></tr>
<tr><td>Subject Population/Indication
Male or female subjects aged 18 years or older with moderate-to-severe scalp seborrheic dermatitis, at least moderate erythema, scaling and pruritus and at least 30% of the scalp area invovled</td><td>Treatment/Study Duration
-Treatment phase: 4 weeks
-Study duration: 12 weeks</td><td colspan="2">Dose
-Treatment phase
Clobex® shampoo: twice or four times weekly
Nizoral® shampoo: twice weekly
-Maintenance phase
Nizoral® shampoo: once weekly</td></tr>
<tr><td colspan="4">Design
Multi-center, investigator-blinded, randomized and controlled study in subjects with moderate-to-severe scalp seborrheic dermatitis</td></tr>
<tr><td colspan="2">Study Initiation Date
(first subject enrolled)
18/03/2009</td><td colspan="2">Study Completion/Termination Date
(last subject completed)
02/02/2010</td></tr>
<tr><td colspan="4">EUDRACT No: 2008-005217-22</td></tr>
</table>

This study was performed in compliance with Good Clinical Practice (GCP) including the archiving of essential study documents. This Clinical Study Report (CSR) complies with the International Conference on Harmonization (ICH) E3 guideline.

All data, either provided to the investigator (and study staff) or collected during the study and/or reported herein, will be regarded as confidential and proprietary in nature and will not be disclosed to any third party without Galderma's written consent.

PAGE DELETED (SIGNATURES)

2. SYNOPSIS

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis			
Investigators	**Name & location**	**Centre #**	**# Recruited subjects**	**Dates (FSI-LSO)**
		5664	6	04/09/09-22/01/10
		5487	0	N/A
		5262	0	N/A
		5447	3	29/04/09-15/01/10
		5656	16	08/04/09-25/01/10
		5024	8	28/04/09-20/01/10
		5014	7	13/10/09-14/01/10
		5140	12	23/09/09-18/01/10
		5166	28	23/03/09-19/01/10
		5077	10	22/04/09-01/02/10
		5549	22	14/04/09-22/01/10
		5488	9	17/04/09-20/01/10
		5604	19	27/04/09-29/01/10
		5523	32	24/03/09-21/01/10
		5665	16	15/04/09-28/01/10
		5288	32	18/03/09-18/01/10

NAME OF COMPANY: NAME OF FINISHED MEDICINAL PRODUCT: NAME OF ACTIVE INGREDIENT(S):	For regulatory use only	

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis			
	Name & location	**Centre #**	**# Recruited subjects**	**Dates** (FSI-LSO)
		8233	16	28/09/09-29/01/10
		8236	24	25/09/09-30/01/10
		8080	4	29/10/09-02/02/10
		8261	6	24/09/09-29/01/10
		8253	20	18/09/09-28/01/10
		5493	12	04/09/09-13/01/10
		5659	12	09/09/09-18/12/09
		5658	12	10/09/09-08/01/10
Study Centers	A total of 24 centres in Belgium, France, Germany, Mexico and South Korea.			
Publication	N/A			
Clinical Phase	Phase IIIB			
Period of Study	12 weeks, including a 4-week treatment phase, a 4-week maintenance phase and a 4-week follow-up phase			
Study Objectives	The main objective of this study was to assess the efficacy and safety of different treatment regimens with clobetasol propionate shampoo 0.05% in association with ketoconazole shampoo 2% in the treatment of moderate-to-severe scalp seborrheic dermatitis (SD), in comparison with ketoconazole shampoo alone. The secondary objective of the study was to compare the efficacy and safety of clobetasol propionate shampoo 0.05% to those of ketoconazole shampoo 2%.			
Methodology	Randomized, controlled, multi-center, investigator-blinded, parallel-group comparison study			

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis
	Each group participatde in the study according to the following 3 phases, each lasting for 4 weeks: - Treatment phase: Treatment with the tested and/or comparator product according to the randomization list - Maintenance phase: Ketoconazole 2% alone, once weekly - Follow-up phase: Untreated phase During the treatment phase, subjects were randomized to one of the following treatment regimens: *C4+K2*: Clobetasol propionate 0.05% (4/week) + Ketoconazole 2% (2/week) *C2+K2*: Clobetasol propionate 0.05% (2/week) + Ketoconazole 2% (2/week) *C2*: Clobetasol propionate 0.05% (2/week) *K2*: Ketoconazole 2% (2/week)
Number of Subjects	Planned: 320 subjects (approximately 80 per treatment group) Randomized: 326 subjects (with 80-82 subjects in each treatment group)
Diagnosis, Main Inclusion Criteria	Male or female subjects aged 18 years or older, with moderate or severe scalp seborrheic dermatitis meeting specific inclusion/exclusion criteria.
Investigational Treatment: Route of Administration Dosage Regimen Mode and Frequency of Administration Batch/Formulation Number Duration of Treatment	Clobex® shampoo Topical to the scalp Clobetasol propionate 0.05% Topical to the scalp, four times or twice a week according to the randomization (C2, C2+K2 and C4+K2 groups only) 08.00891(8114016) 4 weeks *Weekly dose should not exceed 50g (50ml)*
Reference Treatment: Route of Administration Dosage Regimen Mode and Frequency of Administration Batch/Formulation Number Duration of Treatment	Nizoral® shampoo Topical to the scalp Ketoconazole 2% Topical to the scalp -Treatment phase: twice a week according to the randomization (K2, C2+K2 and C4+K2 only) -Maintenance phase: once a week (all groups) 08.00878(8EB5W00) -Treatment phase: 4 weeks -Maintenance phase: 4 weeks

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis
Non-Investigational Products to be provided for the study:	Cetaphil® shampoo Clearview™ Urine Pregnancy Test
Assessments Efficacy Variables	At each visit: • *Investigator's Global Assessment (IGA)* from 0 (completely clear) to 4 (severe) • Individual sign scores of scalp SD: *erythema* and *scaling* from 0 (none) to 3 (severe) • *Pruritus* score from 0 (none) to 3 (severe) • *Extent index* of the scalp SD (involved scalp area) from 0 (< 10%) to 4 (70-100%)
Safety Variables	At each visit: • Local tolerability assessment of *skin atrophy*, *telangiectasia* and *burning* sensation using a scale from none (0) to severe (3) • Incidence of *adverse events*
Other Variables	• Subject's quality of life questionnaires (*Skindex-29*) at baseline and at the end of the treatment phase (week 4) • *Subject's satisfaction questionnaire* at the end of the treatment phase (week 4)
Analyzed Variables	<u>*Primary efficacy variable*</u>: on the intent-to-treat (ITT) and per protocol (PP) populations • *Percent change from baseline in Total Severity Score* (*TSS*) at week 4 (the end of the treatment Phase): sum of *erythema*, *scaling* and *pruritus* <u>*Secondary efficacy variables*</u>: on the ITT population • *Percent change from baseline in TSS* at each other visit • *IGA* at each post-baseline visit*:* % of subjects across scores • *Percent change from baseline in Seborrheic Dermatitis Area and Severity Index (SDASI)* at each post-baseline visit: combined score of *erythema*, *scaling* and *extent index* • *Erythema* score at each post-baseline visit: % of subjects across scores • *Scaling* score at each post-baseline visit: % of subjects across scores • *Pruritus* score at each post-baseline visit: % of subjects across scores • *Extent index* at each post-baseline visit: % of subjects across scores

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis
	<u>*Safety variables*</u>: on the safety (APT) population • *Local tolerance worst-score* post-baseline: % of subjects across scores • Incidence of *adverse events* <u>*Other*</u>: on the ITT population (observed data) • *Skindex-29* scores at study baseline and at the end of the treatment phase (week 4) • *Subject's satisfaction questionnaire* at the end of the treatment phase (week 4)
Principal Statistical Methods	Centers considered too small were combined to create analysis-centers. The Per Protocol (PP) population consisted of all enrolled and randomized subjects, except subjects considered not evaluable due to major deviations from the protocol. The ITT population consisted of the entire population enrolled and randomized. The last observation carried forward (LOCF) method was used to impute efficacy missing values. Analysis population definitions and pooling of centers were decided before the database lock and unblinding. The primary objective of this study was to demonstrate the superiority of clobetasol propionate shampoo 0.05% associated with ketoconazole shampoo 2% in various regimens compared to ketoconazole shampoo 2% alone twice weekly, in terms of percent change in TSS at week 4/LOCF. The primary efficacy criterion was analyzed by using the Cochran-Mantel-Haenszel (CMH) statistic, stratified by center (or analysis-center) after ridit transformation with the row mean difference statistics, testing the hypothesis of equality. The p-value had to be inferior to 0.05 at week 4, in the ITT/LOCF population. PP analysis was also performed to assess the robustness of the results obtained in the ITT/LOCF population. The secondary efficacy variables, local tolerability worst-scores and questionnaires were analyzed similarly as the primary efficacy analyses in the appropriate population. Each test was two-sided, at the 0.050 significance level.

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis
	The subject disposition, demographics, baseline characteristics, raw scores of TSS, SDASI, local tolerability, and adverse events were only descriptively summarized.

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

RESULTS

	Clobetasol (4/w) Ketoconazole (2/w)	Clobetasol (2/w) Ketoconazole (2/w)	Clobetasol (2/w)	Ketoconazole (2/w)
Demography				
N	82	82	82	80
Gender, N (%)				
Male	46 (56.1)	43 (52.4)	44 (53.7)	44 (55.0)
Female	36 (43.9)	39 (47.6)	38 (46.3)	36 (45.0)
Age, year				
Mean ± SD	46.9±16.0	43.8±17.2	44.9±15.3	44.7±15.5
Race, N (%)				
Caucasian	53 (64.6)	50 (61.0)	51 (62.2)	51 (63.8)
Black	1 (1.2)	2 (2.4)	3 (3.7)	3 (3.8)
Asian	10 (12.2)	11 (13.4)	9 (11.0)	9 (11.3)
Hispanic	17 (20.7)	19 (23.2)	18 (22.0)	17 (21.3)
Other	1 (1.2)	-	1 (1.2)	-
Subject Disposition				
N	82	82	82	80
Normal completion, N (%)	76 (92.7)	74 (90.2)	76 (92.7)	74 (92.5)
Discontinued, N (%)				
Lack of Efficacy	1 (1.2)	-	1 (1.2)	-
Adverse Event	-	1 (1.2)	1 (1.2)	-
Subject Request	2 (2.4)	2 (2.4)	2 (2.4)	3 (3.8)
Protocol Violation	-	-	-	-
Lost to Follow-up	1 (1.2)	2 (2.4)	1 (1.2)	3 (3.8)
Other	1 (1.2)	2 (2.4)	1 (1.2)	-
Pregnancy	1 (1.2)	1 (1.2)	-	-
Analyzed Population				
ITT population, N (%)	82 (100)	82 (100)	82 (100)	80 (100)
PP population, N (%)	78 (95.1)	78 (95.1)	76 (92.7)	76 (95.0)
Safety population, N (%)	82 (100)	82 (100)	82 (100)	80 (100)

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

RESULTS

	Clobetasol (4/w) Ketoconazole (2/w)	Clobetasol (2/w) Ketoconazole (2/w)	Clobetasol (2/w)	Ketoconazole (2/w)
Baseline Disease Characteristics				
N	82	82	82	80
TSS				
Mean ± STD	7.0 ± 0.9	6.8 ± 0.9	6.9 ± 1.0	7.0 ± 0.9
IGA				
3: Moderate	63 (76.8)	65 (79.3)	68 (82.9)	62 (77.5)
4: Severe	19 (23.2)	17 (20.7)	14 (17.1)	18 (22.5)
Mean ± STD	3.2 ± 0.4	3.2 ± 0.4	3.2 ± 0.4	3.2 ± 0.4
SDASI				
Mean ± STD	13.2 ± 4.6	13.1 ± 4.7	12.8 ± 5.1	13.4 ± 4.6
Erythema				
2: Moderate	63 (76.8)	58 (70.7)	65 (79.3)	58 (72.5)
3: Severe	19 (23.2)	24 (29.3)	17 (20.7)	22 (27.5)
Mean ± STD	2.2 ± 0.4	2.3 ± 0.5	2.2 ± 0.4	2.3 ± 0.4
Scaling				
2: Moderate	48 (58.5)	63 (76.8)	56 (68.3)	48 (60.0)
3: Severe	34 (41.5)	19 (23.2)	26 (31.7)	32 (40.0)
Mean ± STD	2.4 ± 0.5	2.2 ± 0.4	2.3 ± 0.5	2.4 ± 0.5
Pruritus				
2: Moderate	51 (62.2)	58 (70.7)	49 (59.8)	55 (68.8)
3: Severe	31 (37.8)	24 (29.3)	33 (40.2)	25 (31.3)
Mean ± STD	2.4 ± 0.5	2.3 ± 0.5	2.4 ± 0.5	2.3 ± 0.5
Extent index				
2: 30% - 49%	32 (39.0)	28 (34.1)	36 (43.9)	30 (37.5)
3: 50% - 69%	35 (42.7)	39 (47.6)	29 (35.4)	33 (41.3)
4: ≥ 70%	15 (18.3)	15 (18.3)	17 (20.7)	17 (21.3)
Mean ± STD	2.8 ± 0.7	2.8 ± 0.7	2.8 ± 0.8	2.8 ± 0.8

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

RESULTS

	Clobetasol (4/w) Ketoconazole (2/w)	Clobetasol (2/w) Ketoconazole (2/w)	Clobetasol (2/w)	Ketoconazole (2/w)
Efficacy results				
TSS - median % change from baseline (ITT population)				
N	82	82	82	80
Week 4 (LOCF)	-71.4	-66.7	-66.7	-57.1
P-value vs. keto	0.001	<0.001	0.039	-
P-value vs. clobe (2/w)		0.094	-	
N	80	76	77	75
Week 8	-50.0	-62.5	-50.0	-57.1
P-value vs. keto	0.595	0.373	0.244	-
P-value vs. clobe (2/w)		0.089	-	
N	76	76	76	74
Week 12	-50.0	-50.0	-50.0	-50.0
P-value vs. keto	0.704	0.783	0.401	-
P-value vs. clobe (2/w)		0.321	-	
TSS - median % change from baseline (PP population)				
N	78	78	76	76
Week 4	-71.4	-71.4	-66.7	-57.1
P-value vs. keto	0.001	0.001	0.012	-
P-value vs. clobe (2/w)		0.181	-	
IGA (ITT population) Baseline				
N	82	82	82	80
Mean ± STD	3.2 ± 0.4	3.2 ± 0.4	3.2 ± 0.4	3.2 ± 0.4

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

RESULTS

	Clobetasol (4/w) Ketoconazole (2/w)	Clobetasol (2/w) Ketoconazole (2/w)	Clobetasol (2/w)	Ketoconazole (2/w)
Week 4 (LOCF)				
N	82	82	82	80
Mean ± STD	1.3 ± 1.0	1.2 ± 1.0	1.4 ± 1.0	1.7 ± 1.1
P-value vs. keto	0.063	0.011	0.108	-
P-value vs. clobe (2/w)		0.281	-	
Week 8				
N	80	76	77	75
Mean ± STD	1.6 ± 1.1	1.4 ± 0.9	1.7 ± 1.1	1.5 ± 1.2
P-value vs. keto	0.587	0.233	0.311	-
P-value vs. clobe (2/w)		0.070	-	
Week 12				
N	76	76	76	74
Mean ± STD	1.8 ± 1.2	1.7 ± 1.1	1.9 ± 1.1	1.6 ± 1.2
P-value vs. keto	0.552	0.966	0.279	-
P-value vs. clobe (2/w)		0.381	-	
SDASI - median % change from baseline (ITT population)				
N	82	82	82	80
Week 4 (LOCF)	-88.2	-90.3	-85.0	-80.0
P-value vs. keto	0.016	0.003	0.108	-
P-value vs. clobe (2/w)		0.094	-	
N	80	76	77	75
Week 8	-83.3	-84.2	-75.0	-87.5
P-value vs. keto	0.871	0.204	0.285	-
P-value vs. clobe (2/w)		0.047	-	

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

RESULTS

	Clobetasol (4/w) Ketoconazole (2/w)	Clobetasol (2/w) Ketoconazole (2/w)	Clobetasol (2/w)	Ketoconazole (2/w)
N	76	76	76	74
Week 12	-75.0	-75.0	-75.0	-84.2
P-value vs. keto	0.607	0.955	0.273	-
P-value vs. clobe (2/w)		0.336	-	
Erythema (ITT population)				
Baseline				
N	82	82	82	80
Mean ± STD	2.2 ± 0.4	2.3 ± 0.5	2.2 ± 0.4	2.3 ± 0.4
Week 4 (LOCF)				
N	82	82	82	80
Mean ± STD	0.8 ± 0.7	0.8 ± 0.8	0.9 ± 0.9	1.1 ± 1.0
P-value vs. keto	0.015	0.010	0.077	-
P-value vs. clobe (2/w)		0.631	-	
Week 8				
N	80	76	77	75
Mean ± STD	0.9 ± 0.8	0.9 ± 0.8	1.0 ± 0.9	0.9 ± 0.9
P-value vs. keto	0.801	0.686	0.622	-
P-value vs. clobe (2/w)		0.246	-	
Week 12				
N	76	76	76	74
Mean ± STD	1.0 ± 0.9	1.0 ± 0.9	1.1 ± 0.8	1.0 ± 0.9
P-value vs. keto	0.701	0.839	0.511	-
P-value vs. clobe (2/w)		0.355	-	

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

RESULTS

	Clobetasol (4/w) Ketoconazole (2/w)	Clobetasol (2/w) Ketoconazole (2/w)	Clobetasol (2/w)	Ketoconazole (2/w)
Scaling (ITT population)				
Baseline				
N	82	82	82	80
Mean ± STD	2.4 ± 0.5	2.2 ± 0.4	2.3 ± 0.5	2.4 ± 0.5
Week 4 (LOCF)				
N	82	82	82	80
Mean ± STD	0.8 ± 0.8	0.8 ± 0.8	1.0 ± 0.8	1.2 ± 1.0
P-value vs. keto	0.021	0.003	0.259	-
P-value vs. clobe (2/w)		0.016	-	
Week 8				
N	80	76	77	75
Mean ± STD	1.2 ± 1.0	1.1 ± 0.8	1.3 ± 0.8	1.2 ± 1.0
P-value vs. keto	0.773	0.381	0.349	-
P-value vs. clobe (2/w)		0.105	-	
Week 12				
N	76	76	76	74
Mean ± STD	1.4 ± 1.0	1.2 ± 0.8	1.5 ± 1.0	1.3 ± 1.0
P-value vs. keto	0.414	0.737	0.164	-
P-value vs. clobe (2/w)		0.061	-	
Pruritus (ITT population)				
Baseline				
N	82	82	82	80
Mean ± STD	2.4 ± 0.5	2.3 ± 0.5	2.4 ± 0.5	2.3 ± 0.5

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

RESULTS

	Clobetasol (4/w) Ketoconazole (2/w)	Clobetasol (2/w) Ketoconazole (2/w)	Clobetasol (2/w)	Ketoconazole (2/w)
Week 4 (LOCF)				
N	82	82	82	80
Mean ± STD	0.6 ± 0.8	0.6 ± 0.8	0.8 ± 0.8	1.0 ± 0.9
P-value vs. keto	0.010	0.001	0.167	-
P-value vs. clobe (2/w)		0.052	-	
Week 8				
N	80	76	77	75
Mean ± STD	1.0 ± 0.9	0.8 ± 0.8	1.2 ± 0.9	0.9 ± 0.9
P-value vs. keto	0.458	0.392	0.089	-
P-value vs. clobe (2/w)		0.012	-	
Week 12				
N	76	76	76	74
Mean ± STD	1.2 ± 1.0	1.0 ± 0.9	1.2 ± 0.9	1.0 ± 0.9
P-value vs. keto	0.488	0.785	0.202	-
P-value vs. clobe (2/w)		0.152	-	
Extent index (ITT population)				
Baseline				
N	82	82	82	80
Mean ± STD	2.8 ± 0.7	2.8 ± 0.7	2.8 ± 0.8	2.8 ± 0.8
Week 4 (LOCF)				
N	82	82	82	80
Mean ± STD	1.0 ± 0.9	1.0 ± 1.1	1.2 ± 1.1	1.4 ± 1.2
P-value vs. keto	0.047	0.017	0.211	-
P-value vs. clobe (2/w)		0.256	-	

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

RESULTS

	Clobetasol (4/w) Ketoconazole (2/w)	Clobetasol (2/w) Ketoconazole (2/w)	Clobetasol (2/w)	Ketoconazole (2/w)
Week 8				
N	80	76	77	75
Mean ± STD	1.3 ± 1.0	1.1 ± 1.0	1.5 ± 1.2	1.3 ± 1.2
P-value vs. keto	0.955	0.279	0.345	-
P-value vs. clobe (2/w)		0.034	-	
Week 12				
N	76	76	76	74
Mean ± STD	1.5 ± 1.2	1.4 ± 1.0	1.6 ± 1.2	1.3 ± 1.1
P-value vs. keto	0.820	0.803	0.219	-
P-value vs. clobe (2/w)		0.329	-	
Safety results				
Local Tolerability (Safety population)				
N	81	81	79	79
Skin atrophy				
Worsening from baseline				
No, N (%)	81 (100)	81 (100)	79 (100)	79 (100)
Maximum score of worsening	-	-	-	-
Telangiectasia				
Worsening from baseline				
No, N (%)	79 (97.5)	78 (96.3)	78 (98.7)	78 (98.7)
Yes, N (%)	2 (2.5)	3 (3.7)	1 (1.3)	1 (1.3)
P-value vs. keto	0.575	0.291	1.000	-
P-value vs. clobe (2/w)		0.291	-	
Maximum score of worsening, N				
1: Mild	2	3	1	1

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

RESULTS

	Clobetasol (4/w) Ketoconazole (2/w)	Clobetasol (2/w) Ketoconazole (2/w)	Clobetasol (2/w)	Ketoconazole (2/w)
Burning				
Worsening from baseline	77 (95.1)	73 (90.1)	71 (89.9)	68 (86.1)
No, N (%)	4 (4.9)	8 (9.9)	8 (10.1)	11 (13.9)
Yes, N (%)	0.043	0.462	0.468	-
P-value vs. keto		0.923	-	
P-value vs. clobe (2/w)				
Maximum score of worsening, N				
1: Mild	2	7	7	8
2: Moderate	1	1	-	3
3: Severe	1	-	1	-
Adverse events (Safety population)				
Number of AEs				
All AEs	39	41	35	32
Related AEs	5	8	4	2
All dermatologic AEs	6	9	5	4
Related dermatologic AEs	3	5	3	2
All serious AEs	1	0	1	0
Related serious AEs	0	0	0	0
AEs leading to discontinuation	0	1	1	0

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

RESULTS

	Clobetasol (4/w) Ketoconazole (2/w)	Clobetasol (2/w) Ketoconazole (2/w)	Clobetasol (2/w)	Ketoconazole (2/w)
Number (%) of subjects with AEs				
All AEs	23 (28.0)	27 (32.9)	29 (35.4)	20 (25.0)
Related AEs	4 (4.9)	6 (7.3)	4 (4.9)	2 (2.5)
All dermatologic AEs	5 (6.1)	8 (9.8)	5 (6.1)	4 (5.0)
Related dermatologic AEs	3 (3.7)	4 (4.9)	3 (3.7)	2 (2.5)
All serious AEs	1 (1.2)	0 (0)	1 (1.2)	0 (0)
Related serious AEs	0 (0)	0 (0)	0 (0)	0 (0)
AEs leading to discontinuation	0 (0)	1 (1.2)	1 (1.2)	0 (0)

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

NARRATIVE SUMMARY

Study Design

This was a multi-center, investigator-blinded, randomized and controlled study of 12 weeks in subjects with moderate or severe scalp seborrheic dermatitis. The primary objective of this study was to assess the efficacy and safety of clobetasol shampoo in association with ketoconazole shampoo compared with ketoconazole shampoo monotherapy in the treatment of scalp SD. The secondary objective was to compare the efficacy of clobetasol shampoo to that of the ketoconazole shampoo. The study consisted of three phases, each lasting 4 weeks. During the treatment phase, subjects were randomized to receive ketoconazole shampoo twice weekly (K2), clobetasol shampoo twice weekly (C2), clobetasol twice weekly alternating with ketoconazole twice weekly (C2+K2) or clobetasol four times weekly alternating with ketoconazole twice weekly (C4+K2). During the maintenance phase, all subjects received ketoconazole shampoo once weekly. During the follow-up phase, subject did not receive any treatment. There were five visits in total, occurring at baseline, weeks 2, 4, 8 and 12.

Eligible subjects were 18 years or older, with moderate or severe scalp seborrheic dermatitis, at least moderate erythema, scaling and pruritus, and having at least 30% of their scalp area involved in the disease.

Study Population

A total of 326 subjects were randomized into the study, with 82 subjects in each clobetasol-containing group and 80 subjects in the K2 group. Subject disposition and baseline disease characteristics were similar among the four groups. Overall, 92.0% of total subjects reported normal study completion, with the most frequent reasons for study discontinuation being “lost to follow up” and “subject’s request”. At baseline, a majority of subjects had moderate scalp seborrheic dermatitis, as well as moderate erythema, scaling and pruritus. The mean total severity score (TSS; sum of erythema, scaling and pruritus score) was 6.9 on the scale from 0 to 9.

Efficacy Results

The primary efficacy endpoint of the study was the percent change from baseline in TSS at week 4 (the end of the treatment phase). Both C2+K2 and C4+K2 provided significantly greater efficacy than K2 in reducing TSS at week 4 (median percent reduction from baseline: 66.7% and 71.4% vs. 57.1%; both $P<.05$). They had an early onset of action, with significantly superior efficacy compared to K2 observed at week 2 (both $P<.05$). C2 was also significantly more efficacious than K2 ($P<.05$) at week 4, although no significant difference between C2+K2 and C2 was observed. Taken together, the three clobetasol-

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

containing regimens (C2, C2+K2 and C4+K2) were significantly more efficacious than ketoconazole monotherapy in reducing TSS.

Similarly, the three clobetasol-containing regimens, especially C2+K2, were more efficacious than ketoconazole monotherapy in decreasing other global severity scores and all individual disease scores. After 4 weeks of treatment with C2+K2, 60.9% of subjects reported their SD being “completely clear” or “almost clear”, compared to 50.1% with K2 ($P<.05$). The percentage of subject in the group of C2+K2 who reported none or mild erythema, scaling or pruritus was 85.4%, 86.6% and 86.6%, respectively, compared to 66.3%, 63.8% and 76.3% with K2 (all $P<.05$).

During the maintenance phase when all subjects received once weekly ketoconazole shampoo, a slight worsening of the disease was observed in the groups receiving C2 or C4+K2 during the treatment phase; while the efficacy obtained in the treatment of C2+K2 or K2 remained stable. Overall, the subjects receiving C2+K2 followed by once weekly ketoconazole reported the highest efficacy at week 8, one month after cessation of the acute treatment.

During the follow-up phase when subjects received no active treatment, no obvious worsening of the disease was observed and similarly good efficacy was reported for all 4 groups.

In summary, the C2+K2 combination regime provided significantly greater efficacy compared with K2 in the treatment of scalp SD. Moreover, the high efficacy obtained in this acute combination therapy could be maintained with the once weekly ketoconazole shampoo therapy for at least one month.

Safety Results

Overall, the safety and local tolerability of the four regimens were similar.

A total of 16 subjects (4.9%) reported 19 treatment-related AEs, a majority of which were of dermatological nature and mild in severity. Only 1 related AE led to study discontinuation (pruritus in the C2+K2 group). Two serious AEs were reported during the study, 1 for the C2 group (upper limb fracture) and 1 for the C4+K2 group (angina pectoris), none of which being related to the treatments.

During the 12-week study period, no treatment induced skin atrophy. Only 3 subjects, two in the C2+K2 group and one in the K2 group, had telangiectasia appearing during the study and persisting at study completion. All were mild in intensity, with two appearing during the follow-up phase (1 subject with C2+K2 and 1 subject with K2) and the other appearing at week 2. Slightly more subjects from the K2 group (11 subjects) reported post-baseline worsening of burning than from other groups (8, 8 and 4 for C2, C2+K2 and C4+K2, respectively).

NAME OF COMPANY:	For regulatory use only	
NAME OF FINISHED MEDICINAL PRODUCT:		
NAME OF ACTIVE INGREDIENT(S):		

Title	Efficacy and Safety of Clobetasol Propionate Shampoo 0.05% Used in Association with an Antifungal Shampoo in the Treatment of Moderate to Severe Scalp Seborrheic Dermatitis

Conclusions

The results of this study suggested that adding clobetasol shampoo twice weekly to the ketoconazole therapy led to a significantly greater efficacy in the treatment of moderate-to-severe scalp seborrheic dermatitis. This study also confirmed the previously demonstrated treatment efficacy of clobetasol shampoo alone. The short-contact clobetasol shampoo was safe and well-tolerated either alone or in combination with ketoconazole. The additional benefit obtained in the twice weekly clobetasol alternating with twice weekly ketoconazole regimen could be subsequently maintained with the once weekly ketoconazole shampoo application, leading to a high and sustained efficacy for at least 3 months.