

Clinical Study Results of Desoximetasone Spray, 0.25% in Moderate to Severe Plaque Psoriasis

Leon Kircik MD,[a,b,c] Mark G. Lebwohl MD,[c] James Q. Del Rosso DO,[d] Jerry Bagel MD,[e] Linda Stein Gold MD,[f] Jonathan S. Weiss MD[g]

[a]Department of Dermatology, Indiana University School of Medicine, Indianapolis, IN
[b]Physicians Skin Care, PLLC, Louisville, KY
[c]Department of Dermatology, Mount Sinai School of Medicine, New York, New York
[d]Department of Dermatology, Touro University College of Osteopathic Medicine, Henderson, NV
[e]Psoriasis Treatment Center of Central New Jersey, East Windsor, NJ
[f]Director of Dermatology, Clinical Research and Division Head of Dermatology, Henry Ford Health System, Detroit and West Bloomfield, Michigan
[g]Gwinnett Clinical Research Center, Snellville, Georgia

ABSTRACT

Two Phase 3, double-blind, randomized, vehicle-controlled parallel studies evaluated the efficacy and safety of desoximetasone spray 0.25%, a super-potent topical corticosteroid, twice daily vs vehicle spray twice daily for 28 days in adult patients with moderate to severe plaque psoriasis. At baseline and throughout the study, the severity of disease for the psoriatic lesions was assessed using the Physician Global Assessment (PGA) score and a target lesion was assessed using the Total Lesion Severity Score (TLSS). A designated psoriatic plaque lesion was selected as the target lesion upon enrollment and evaluated throughout the study to determine the TLSS. To qualify for study entry, the subject needed to exhibit a PGA score of 3 (moderate) or 4 (severe) for overall disease severity, and a target lesion with an area of at least 5 cm^2 that achieved a combined score TLSS of ≥7, with a plaque elevation score of ≥3 (at least moderate). The mean % BSA affected by psoriasis ranged from 13%-17% at baseline.

In both Phase 3 studies, a statistically significantly greater percentage of subjects in the desoximetasone spray 0.25% compared to vehicle group achieved both Clinical Success and Treatment Success at Day 28. These results, which were the primary efficacy variables, demonstrated superior efficacy in the active study group for both overall improvement of plaque psoriasis (by PGA) and in the individual psoriasis lesion (by TLSS) designated at baseline as the most severely involved plaque (target lesion). Assessment of secondary efficacy variables in both Phase 3 studies showed that subjects receiving desoximetasone Spray 0.25% twice daily exhibited statistically significantly mean changes from Baseline to Day 28 in PGA, TLSS, and % BSA affected when compared to subjects receiving vehicle spray twice daily.

Tolerability and safety were assessed at all study visits. No statistically significant differences were observed between study arms and no major safety signals related to AEs were noted. No stinging and burning were reported with the spray formulation. This Class I topical corticosteroid has shown to be safe and efficacious in moderate to severe plaque psoriasis.

J Drugs Dermatol. 2013;12(12):1404-1410.

INTRODUCTION

The anti-inflammatory properties of a topically-applied corticosteroid (CS) have been well recognized since the discovery of Compound F (hydrocortisone) in 1949.[1] In 1958, dexamethasone was introduced after a search for a more metabolically stable compound with greater anti-inflammatory activity and decreased mineralocorticoid effect when given systemically. Attempts to find additional corticosteroid compounds resulted in the discovery and development of desoximetasone (16α-methyl-9 α-fluoro-Δ′-corticosterone), a derivative of dexamethasone. Animal studies confirmed the anti-inflammatory activity of desoximetasone, with the determination that the pharmacologic properties of this agent were most amenable to topical administration.

Topically applied desoximetasone was first used in Brazil in 1973. The first topical formulation of desoximetasone (0.25% cream) was approved in the United States (US) by the Food and Drug Administration (FDA) in 1977.[1] The indication was for relief of the inflammatory and pruritic manifestations of corticosteroid-responsive dermatoses, based on studies conducted in subjects

TABLE 1.

Overview of Pivotal Trials Evaluating the Efficacy and Safety of Desoximetasone Spray 0.25% in the Treatment of Adults with Moderate to Severe Plaque Psoriasis

Study	Study Design	Enrollment^	Study Groups (n)
Phase 2 Study (dose–finding)	28-day, double-blind, vehicle-controlled, randomized, dose- and schedule comparison (1:1:2:2:2), parallel-group study	N=151 enrolled* 148 completed 92 males 58 females Age range 22-82 years	A: desoximetasone spray, 0.05% twice daily (30) B: desoximetasone spray, 0.25% once daily (30) C: desoximetasone spray, 0.25% twice daily (30) D: vehicle spray once daily (15)** E: vehicle spray twice daily (15)**
Phase 3 Study 1	28-day, double blind, randomized, vehiclecontrolled (1:1), parallel group study	N=120 119 completed 85 males 35 females Age range 20-80 years	A: desoximetasone spray, 0.25% twice daily (60) B: vehicle spray twice daily (60)**
Phase 3 Study 2	Same as Study 1	N=120 120 completed 72 males 48 females Age range 19-41 years	Both study groups same as Study 1 (60 in active arm and 60 in vehicle arm)*

^All three studies were multicenter, completed in the United States, and preformed under the supervision of an independent contract research organization; *One subject (03-0051) was randomized to vehicle but was not dosed in the clinic and did not return for subsequent visits; #Double-blind within treatments applied at the same frequency; +391 subjects were enrolled across all three studies; 35 subjects were identified as participating in more than on study (Phase 2 dose-finding study and one of the Phase 3 studies); 33 studies participated first in DSXS-0906 and then in DSXS-0808; 2 studies participated first in DSXS-0906 and then in DSXS-0914.The time between participation ranged from 185 to 274 days (approximately 6 to 9 months); **The vehicle used in all studies was the same and contained the excipients included in the same concentrations as in desoximetasone spray and was identical in appearance and consistency to the desoximetasone spray formulation.

with psoriasis or atopic dermatitis. Topical desoximetasone formulations, which include both mid-potency and high potency TCS products depending on concentration and vehicle, are approved in over fifty countries in Europe, Asia, South America, and Africa.[2,3] In April 2013, desoximetasone spray 0.25% received FDA approval for the treatment of plaque psoriasis in adults (≥18 years of age), and is the first super-potency TCS formulation of desoximetasone.[4,5]

As the role of topical corticosteroid (TCS) therapy in the treatment of several cutaneous disorders became better defined over time, a variety of compounds and vehicle formulations emerged.[3,5,6] These CS developed for topical use are specifically glucocorticosteroids based on the central structural nucleus of hydrocortisone, or derivatives thereafter such dexamethasone.[3,5,6] Since its introduction in 1977 of desoximetasone 0.25% cream, subsequent formulations including 0.05% cream, gel and ointment have been approved. While the previous 0.25% formulations of desoximetasone are ranked as high-potency TCS, the. 0.05% formulations are ranked as mid-potency TCS.

Desoximetasone spray was formulated using a combination of ingredients designed to enhance cutaneous penetration (isopropyl myristate, isopropyl alcohol), to mitigate damage to the stratum corneum permeability barrier and provide emolliency (glyceryloleate, mineral oil), and reduce symptoms of irritation (l-menthol).[4,5] Importantly, prior to the approval of the 0.25% spray, desoximetasone has never been formulated to provide the potency required to achieve the designation of super-potent TCS.

Desoximetasone Spray 0.25% Phase 1 and 2 Studies

Four pharmacologic studies were completed to support the approval of desoximetasone spray 0.25%. A phase I vasoconstrictor assay study was completed in healthy volunteers and demonstrated that this formulation achieved super-high potency status.[2] It was also demonstrated that desoximetasone spray 0.25% does not induce photoallergy or phototoxicity, is not sensitizing, and has low potential for causing skin irritation in three additional Phase I studies. The negligible potential for inducing skin allergenicity is supported by the fact that desoximetasone is a Class C CS which exhibits the lowest potential for causing cutaneous allergy among all structural classes of TCS, calculated to be <0.2%.[7,8]

"As the role of topical corticosteroid (TCS) therapy in the treatment of several cutaneous disorders became better defined over time, a variety of compounds and vehicle formulations emerged"

A phase 2 study evaluated the effects of desoximetasone spray 0.25% on hypothalamic-pituitary axis (HPA) suppression in 24 adult subjects treated twice daily for 28 days.[4,5] Evaluable cortisol levels were present in 21 subjects. Evidence of HPA suppression was noted in 8.3% (1/12) of subjects with 10-15% BSA and in 22.2% (2/9) of subjects with >15% BSA. In two subjects available for follow up testing, HPA suppression reversed within 28 days after the end of treatment.[5] Plasma levels of desoximetasone were also measured in this latter study and were consistent with the low levels measured for the cream and ointment formulations.[4]

TABLE 2.

Subject Demographics					
Phase 3 Studies					
Demographic Characteristics		Study 1		Study 2	
		Desoximetasone 0.25% Spray (n=60)	Vehicle Spray (n=60)	Desoximetasone 0.25% Spray (n=60)	Vehicle Spray (n=60)
Age (years)	Mean ± SD	50.67 ± 13.86	52.55 ± 15.56	48.03 ± 14.29	53.55 ± 14.82
	Range	22-76	20-80	19-76	23-81
Gender n (%)	Female	18 (30.0%)	17 (28.3%)	23 (38.3%)	25 (41.7%)
	Male	42 (70.0%)	43 (71.7%)	37 (61.7%)	35 (58.3%)
Ethnicity n (%)	Hispanic or Latino	8 (13.3%)	8 (13.3%)	11 (18.3%)	10 (16.7%)
	Not Hispanic or Latino	52 (86.7%)	52 (86.7%)	49 (81.7%)	50 (83.3%)
Race n (%)	White	58 (96.7%)	57 (95.0%)	57 (95.0%)	56 (93.3%)
	Other	2 (3.3%)	3 (5.0%)	2 (2.3%)	4 (6.7%)
% BSA	Mean	15.6	16	17.8	15.7

*Other includes Black/African American; American Indian/Alaskan Native; Asian; Native Hawiian or Other Pacific

A Phase 2 dose-finding study of desoximetasone spray in adult subjects with moderate to severe plaque psoriasis involving ≤10% body surface area (BSA) resulted in the selection of 0.25% twice daily as the concentration and frequency of application. A total of 151 subjects were enrolled in the five-arm phase 2 dose-finding study, and a total of 240 subjects collectively in the two Phase 3 trials. Table 1 depicts the three pivotal trials, one Phase 2 trial and two Phase 3 trials, used as the basis of submission for FDA approval.

Desoximetasone Spray 0.25% Phase 3 Pivotal Study Overview

Two Phase 3 double-blind, randomized, vehicle-controlled parallel studies evaluated the efficacy and safety of desoximetasone spray 0.25% twice daily versus vehicle spray twice daily for 28 days in adult patients with moderate to severe plaque psoriasis. Demographic characteristics for the subjects entering both Phase 3 studies are presented in Table 2. Appropriate candidates for inclusion in the study had to be at least 18 years of age with a definite clinical diagnosis of stable plaque psoriasis involving ≥10% of BSA using the "Rules of Nine" and were graded in severity as moderate to severe by both overall assessment and with evaluation of a designated target lesion. The mean age of the subjects was similar across studies, ranging from 48-54 years. There was a male prevalence and most subjects were white.

At baseline and throughout the study, the severity of disease for the psoriatic lesions was assessed using the Physician Global Assessment (PGA) score and a target lesion was assessed using the Total Lesion Severity Score (TLSS), a sum of the scores assigned by the investigator on three measures used to determine target plaque severity, scaling, erythema, and plaque elevation (induration), with each of these criteria on a 6-point scale. A designated psoriatic plaque lesion was selected as the target lesion upon enrollment and evaluated throughout the study to determine the TLSS. To qualify for study entry, the subject needed to exhibit a PGA score of 3 (moderate) or 4 (severe) for overall disease severity, and a target lesion with an area of at least 5 cm^2 that achieved a combined score TLSS of ≥7, with a plaque elevation score of ≥3 (at least moderate). The mean % BSA affected by psoriasis ranged from 15%-18% at baseline. This and the other key disease characteristics at baseline, the mean PGA, TLSS, and target lesion size, are presented in Table 3. There were no clinically meaningful differences in any of the assessment values among the treatment groups.

Subjects who were eligible to participate in the study based on the inclusion and exclusion criteria and who consented to proceed were enrolled at baseline (Day 1) and returned to the study center at Day 7, Day 14, and Day 28 (end of study). Education was given by study staff to subjects on proper use of study medication with instructions to spray the study medication directly to all affected areas and rub in gently and completely twice-daily for 28 days. Study medication was to be applied in the morning and evening approximately 12 hours apart. Subjects returned to the clinic for assessment of signs and symptoms of psoriasis, adverse events, update all concomitant medications, and to evaluate compliance with the subject and their dosing diary.

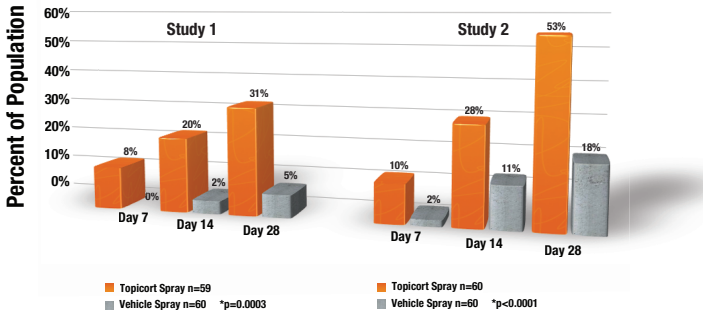
Desoximetasone Spray 0.25% Phase 3 Study Assessments and Analyses

The primary endpoint based on PGA score was the proportion of subjects in each treatment group who were considered a

TABLE 3.

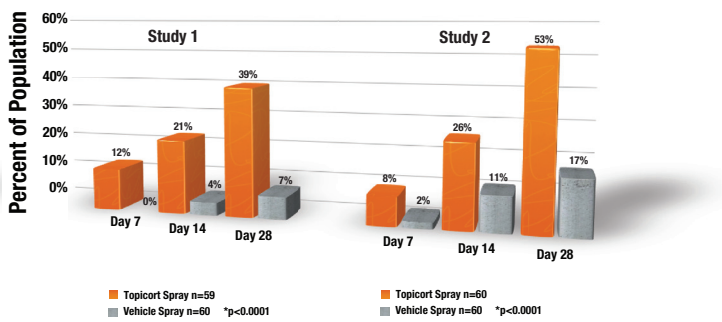
Severity and Extent of Disease at Baseline: All Subjects									
	Study 1		Study 2			Study 1		Study 2	
PGA	Desoxi	Vehicle	Desoxi	Vehicle	Target Lesion Size	Desoxi	Vehicle	Desoxi	Vehicle
	n=60	n=60	n=60	n=60		n=60	n=60	n=60	n=60
0 (Clear)	0	0	0	0	Mean	41.52	38.02	50.34	57.42
1 (Almost Clear)	0	0	0	0	Minimum	6	5	6	6
2 (Mild)	0	0	0	0	Maximum	209	196	651	565
3 (Moderate)	45 (75%)	44 (73%)	38 (63%)	40 (67%)					
4 (Severe)	15 (25%)	16 (27%)	22 (37%)	19 (32%)					
5 (Very Severe)	0	0	0	1 (2%)					
% BSA					TLSS Score				
Mean	15.58	16	17.78	15.67	Mean	9.52	9.35	10.03	10.02
Median	12	11	12	11	Minimum	7	7	7	7
Minimum	10	10	10	10	Maximum	15	12	14	15
Maximum	60	70	86	70					

FIGURE 1. Clinical success.



Clinical Success is defined as a Physician Global Assessment (PGA) Score of 0 (clear) or 1 (almost clear) at Day 28

FIGURE 1. TLSS assessment.



Treatment Success is defined as a Total Lesion Severity Score (TLSS) for the target lesion of 0 (clear) or 1 (almost clear) for each of the individual measures of severity (erthema, scaling, and plaque elevation) at Day 28.
The lesion selected for the target lesion was the most severe, with an area of at least 5cm² and a plaque elevation score of at least 3 (moderate). The TLSS scale for each of the three measures is 0 (clear); 1 (almost clear); 2 (mild); 3 (moderate); 4 (severe); 5 (very severe).

Clinical Success at Day 28 based on PGA score. The following definitions were used to determine treatment outcome:

Clinical Success PGA score of 0 (clear) or 1 (almost clear)

Clinical Failure PGA score >1 or insufficient therapeutic response

An insufficient therapeutic response was recorded if the investigator noted worsening of psoriasis in a subject at any time during the study or if a subject did not complete the study because of lack of treatment effect, including being provided an alternative medication or therapy for treatment of the psoriasis.

The primary endpoint based on TLSS was the proportion of subjects in each treatment group who were considered a Treatment Success for the target lesion at Day 28. The following definitions were used to determine the treatment outcome, with insufficient therapeutic response recorded as noted above for PGA:

Treatment Success TLSS of 0 (clear) or 1 (almost clear) for each of three individual signs: erythema, scaling, and plaque elevation

Treatment Failure TLSS >1 for any of the individual signs or insufficient therapeutic response

TABLE 4.

Secondary Efficacy Endpoint: Change from Baseline in PGA, TLSS, and BSA			
Secondary Efficacy Analysis at Day 28: Study 1			
Parameter (ITT)	Desoximetasone 0.025% Spray (n=59) Mean ± SD	Vehicle (n=60) Mean ± SD	*P*-value
Mean Change from Baseline in TLSS	4.73 ± 3.08	1.93 ± 1.96	<0.0001
Mean Change from Baseline in PGA	1.14 ± 0.9	0.50 ± 0.68	<0.0001
Mean Change from Baseline in % BSA Affected	2.24 ± 3.79	0.37 ± 2.05	0.0011
Secondary Efficacy Analysis at Day 28: Study 2			
Parameter (ITT)	Desoximetasone 0.025% Spray (n=60) Mean ± SD	Vehicle (n=60) Mean ± SD	*P*-value
Mean Change from Baseline in TLSS	6.18 ± 3.13	3.02 ± 2.97	<0.0001
Mean Change from Baseline in PGA	1.73 ± 1.06	0.85 ± 0.94	<0.0001
Mean Change from Baseline in % BSA Affected	3.47 ± 4.74	1.27 ± 4.23	0.0083

According to the Statistical Analysis Plan (SAP) for each study, the primary and secondary efficacy analyses were to be based on an intent-to-treat (ITT) population, defined as subjects who were exposed to study medication. Subjects who withdrew for lack of effect were to be considered a Clinical Failure or Treatment Failure regardless of their PGA or target lesion scores at the last visit. Those who withdrew from either study for reasons other than lack of effect were to be retained in the ITT population and analyzed with the LOCF. Interim missing data were excluded from analyses with no imputation.

The primary efficacy variables, as defined prospectively in the protocols, were Clinical Success and Treatment Success based on the PGA score and the TLSS, respectively.

Primary and Secondary Efficacy Results

In both Phase 3 studies, a statistically significantly greater percentage of subjects in the desoximetasone spray 0.25% compared to vehicle group achieved both Clinical Success and Treatment Success at Day 28 (Figures 1 and 2). These results, which were the primary efficacy variables, demonstrated superior efficacy in the active study group for both overall improvement of plaque psoriasis (by PGA) and in the individual psoriasis lesion (by TLSS) designated at baseline as the most severely involved plaque (target lesion).

Assessment of secondary efficacy variables in both Phase 3 studies showed that subjects receiving desoximetasone Spray 0.25% twice daily exhibited statistically significantly mean changes from Baseline to Day 28 in PGA, TLSS, and % BSA affected when compared to subjects receiving vehicle spray twice daily (Table 4).

Safety and Tolerability Results

Tolerability and safety were assessed at all study visits. In one study which included a total of 120 subjects, 38 subjects reported a total of 69 adverse events (AEs), with 35 AEs noted in the active treatment group, and 34 reported by subjects in the vehicle group.[2] Among the 120 study subjects in the other pivotal study, 21 subjects reported a total of 34 adverse events. Of these events, 16 were reported by actively treated subjects and 18 were noted by vehicle-treated subjects.[42] Some of these AEs were determined to be unrelated to study medication, while others, especially application site reactions, were often determined as possibly, probably, or definitely related to study treatment.

Detailed summaries of AEs are from the Phase 3 studies are depicted in Tables 5-6.[4,5] No statistically significant differences were observed between study arms and no major safety signals related to AEs were noted. No stinging or burning was reported in any subject throughout the study.

A total of 24 subjects discontinued from the two Phase 3 studies. Overall, comparable proportions of subjects discontinued from the both the active and vehicle groups within each study and across both studies. Overall, three subjects withdrew for insufficient therapeutic response and were considered a Clinical Failure or Treatment Failure regardless of their PGA or target lesion scores at the last visit. Two subjects who ran out of study medication had BSA values of 14% and 30% at Baseline.

DISCUSSION

Desoximetasone spray 0.25% used twice daily for 28 days proved to be effective and safe for the treatment of adults with moderate to severe plaque psoriasis. The % BSA required for inclusion was markedly higher in this study than in other studies of super-potent TCS agents. In both Phase 3 studies with desoximetasone spray 0.25%, the inclusion criteria mandated ≥10% BSA, with the mean % BSA at baseline (study entry) ranging from 15.58%-17.78%.

TABLE 5.

AE Summary

	Study 1			Study 2		
	Desoxi Spray	Vehicle	Total	Desoxi Spray	Vehicle	Total
Safety Population	**n = 60**	**n = 60**	**N = 60**	**n = 60**	**n = 60**	**N = 60**
Number of Patients with AE (n, % Total Safety)	17 (28.33%)	21 (35.00%)	38 (31.67%)	9 (15.00%)	12 (20.00%)	21 (17.50%)
Number of AEs Reported (n, % Total Reported)	35 (50.72%)	34 (49.28%)	69 (100.00%)	16 (47.06%)	18 (52.94%)	34 (100.00%)
Number of Patientswith SAE	0	0	0	0	0	0
Number of Patients Discontinued due to AE	1	2	3	1	2	*3*
Number of Patients Discontinued due to SAE	0	0	0	0	0	0
Number of Deaths	0	0	0	0	0	0
Total (n, % AEs/ Number Patients	35	34	69	16	18	34

TABLE 6.

AE Subject Analyses

Percent of Subjects with at Least One Adverse Reaction (possible, probable, or definitely related to the treatment)

	Study 1		Study 2	
	Desoxi 0.025% Spray (n=60)	Vehicle Spray (n=60)	Desoxi 0.025% Spray (n=60)	Vehicle Spray (n=60)
Application-site dryness	2.4%	3.0%	-	0.6%
Application-site irritation	-	1.2%	2.4%	1.8%
Application-site pruritus	1.8%	3.0%	-	-
Application-site erythema	-	1.2%	-	-
Application-site pain	-	-	-	1.2%
Application-site rash	-	0.6%	-	-
Insomnia	-	-	-	0.6%
Folliculitis	-	-	0.6%	-
Psoriasis	0.6%	0.6%	-	0.6%
Skin ulcer	0.6%	-	-	-

What can be gleaned from the study design that may potentially be clinically relevant? Super-potent TCS remain as a central component of the treatment armamentarium for plaque psoriasis including all ranges of severity.[9-12] However, judicious use with an appreciation of both their therapeutic benefits and limitations is vital in order to achieve successful treatment outcomes, including understanding of how to manage vehicle selection, potency, and the specific disease state being treated. In the case of plaque psoriasis, dermatology providers have learned to utilize agents with higher potency ranking to optimize initial control and then to adjust treatment based on the clinical response.[9-12]

As many subjects with ≥10% BSA are considered candidates for systemic therapies such as biologic agents, the subject may be transitioned if necessary to such a therapy after completion of the initial course with desoximetasone spray 0.25% used for up to 4 weeks.[4,9] Additionally, the spray vehicle is an invaluable tool for the treatment of large body surface, as well as hair-bearing areas such as the scalp and difficult to reach areas. More specifically, twice daily application of desoximetasone spray 0.25% was shown to be significantly superior to the vehicle and well-tolerated. There were no statistically significant differences between the adverse events reported in active and vehicle arms and no burning or stinging was reported.

CONCLUSION

Desoximetasone spray 0.25% is a super-potent TCS formulation that has the potential based on clinical studies to be a valuable addition to the treatment armamentarium for plaque psoriasis. Ultimately, it is important that safety considerations be taken into account with all therapies, thus necessitating education on the proper use and application, frequency, duration, and follow-up when desoximetasone spray 0.25% is prescribed.

ACKNOWLEDGMENTS

The authors would like to acknowledge the clinical investigators who participated in the desoximetasone spray, 0.25% pivotal studies including John Fitzgerald Adams MD, Barbara Bopp MD, Robert Brown MD, Alicia Bucko DO JD, Michael Buhalo MD, Zoe Draelos MD, Scott Geunther MD,

Karl Heine MD, David Horowitz MD, Terry Jones MD, David James Kerr MD, Russell Mader MD, Jose Edward Mendez DO, Christopher Moeller MD, Edward John Primka MD, John Proffitt MD, Stephen Schleicher MD, Harry Sharata MD, Allan Soo MD, and Dow Stough MD.

DISCLOSURES

Drs. Kircik, Lebwohl, Del Rosso, Bagel, Stein Gold, and Weiss are consultants to Taro Pharmaceuticals.

REFERENCES

1. Sulzberger MB, Witten VH. Effect of topically applied compound F in selected dermatoses. *J Invest Dermatol*. 1952;19:101-102.
2. Data on file, Taro Pharmaceuticals Inc.
3. Hengge UR. Topical corticosteroids. In: Gaspari AA, Tyring SK, Eds. Clinical and Basic Immunodermatology, Springer-Verlag, London, United Kingdom, 2008, pp. 561-577.
4. Topicort Spray Package Insert
5. Warner MR, Camisa C. Topical corticosteroids. In: Wolverton SE, Ed. Comprehensive Dermatologic Drug Therapy, 2nd Edition, Saunders-Elsevier, Philadelphia, USA, 2007, pp 595-624.
6. Del Rosso J, Friedlander SF. Corticosteroids: options in the era of steroid sparing therapy. J *Am Acad Dermatol*. 2005;53:850-858.
7. Brown F, Wilkinson SM. Effective prescribing in steroid allergy: Controversies and cross-reactions. *Clin Derm*. 2011;29:287-294.
8. BaeckM, Marot L, Nicolas JF, et al. Allergic hypersensitivity to topical and systemic corticosteroids: a review. *Allergy*. 2009;64:978-994.
9. Zeichner JA, Lebwohl MG, Menter A, et al. Optimizing topical therapies for treating psoriasis: a consensus conference. *Cutis*. 2010;86(3 Suppl):5-31.
10. Samarasekera EJ, Sawyer L, Wonderling D, et al. Topical therapies for the treatment of plaque psoriasis: systematic review and network meta-analyses. *Br J Dermatol*. 2013;168(5):954-967.
11. Mason AR, Mason J, Cork M, Dooley G, et al. Topical treatments for chronic plaque psoriasis. Cochrane Database Syst Rev. 2013 Mar 28;3:CD005028. doi: .1002/14651858.CD005028.pub3.
12. Hsu S, Papp KA, Lebwohl MG, et al. Consensus guidelines for the management of plaque psoriasis. *Arch Dermatol*. 2012;148(1):95-102

AUTHOR CORRESPONDENCE

Leon Kircik MD
E-mail:.....wedoderm@yahoo.com