Calcipotriene plus betamethasone dipropionate (0.005%/0.064%) foam and apremilast: matching-adjusted indirect comparison and US cost per responder analyses

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Background

- New and effective topical treatments and systemic treatments with improved safety for the treatment of plaque psoriasis have blurred the distinction among treatment options, particularly for patients who may be considered for either topical treatment or non-biologic systemic treatment present with a broad range of symptoms and factors.
- Calcipotriene and betamethasone dipropionate 0.005%/0.064%) foam is a fixed-combination, once-daily topical treatment for adult patients with plaque psoriasis.[1]
- Apremilast is a twice-daily oral treatment for patients with moderate to severe plaque psoriasis who are candidates for phototherapy or systemic therapy.[2]
- Despite overlap in studied populations, head-to-head clinical trials and comparative analyses have not been conducted between Cal/BD foam and apremilast.

Objective

Conduct a matching-adjusted indirect comparison (MAIC) analysis to compare individual patient data from available study populations for Cal/BD foam with aggregate patient characteristics and treatment outcomes from published efficacy assessments of apremilast in adult patients with moderate plaque psoriasis.

Methodology

Study Design *(Figure 1)*

- Matching-adjusted indirect comparisons (MAICs) use individual patient data (IPD) from trials of one treatment to match baseline summary statistics reported from trials of another treatment to compare treatment outcomes across a balanced patient population.[3]
- Published clinical trials with sufficiently similar populations and outcomes to support indirect comparisons were identified for Cal/BD foam and apremilast.
- Priority baseline variables for matching included disease severity (Psoriasis Area and Severity Index, PASI, or body surface area, BSA), quality of life, demographics, duration of psoriasis, body mass index, and history of topical treatment.
- MAIC analysis was conducted between Cal/BD foam and apremilast[4] and associated economic evaluation through US cost per responder analysis.

Statistical Analysis

- Weighted analyses of response rate variables PGA and PASI 75 were conducted with IPD from pooled Cal/BD foam trials and aggregated results from the other treatment study using a logistic model and 95% confidence intervals (CIs)
- Sensitivity analyses were completed to investigate results by comparison to phase 3 PSO-ABLE Cal/BD trial data from Week 4 and Week 12.

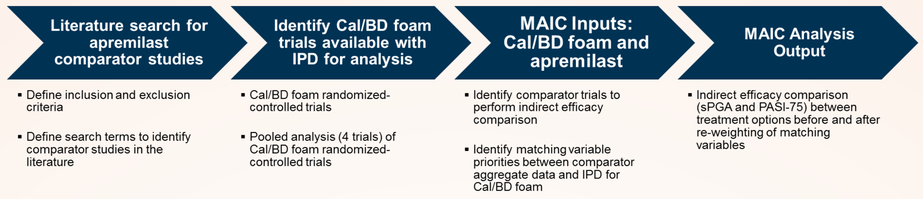

Figure 1. Methodology of MAIC analysis of Cal/BD foam and apremilast[4]

Table 1. Identification of Cal/BD foam and apremilast trials for MAIC analysis[4]

Potential matching variable (priority)	Pooled data[5-8]	UNVEIL[9]
Treatment	**Cal/BD foam**	**Apremilast**
Study design	Randomized, double-blind controlled study	Phase IV randomized study
Dosing	QD	30 mg BID
N	749	148
Sex, male (%)	470 (62.8%)	74 (50.0%)
mean Age (SD)	51.4 (14.1)	48.6 (15.4)
mean BMI (SD)	31.2 (7.2)	30.5 (7.4)
mean BSA (SD)	7.3 (6.1)	7.2 (1.6)
Years of psoriasis (SD)	16.8 (14.0)	17.5 (13.9)
mean PASI (SD)	7.3 (4.6)	8.2 (4.0)
mean DLQI (SD)	-	11.0 (6.5)
BSA X PGA (SD)	21.9 (20.5)	21.8 (5.3)
Prev. topical treatment, yes	637 (85.1%)	122 (82.4%)
Prev. syst treatment, yes	233 (31.1%)	-

BMI, body mass index; BSA, body surface area; PASI, psoriasis area and severity index; DLQI, dermatology life quality index; PGA, physician's global assessment; QD, once daily; BID, twice daily

Exclusion Criteria for Comparator Trials:

- Mean PASI or mean BSA ≥15 [suitability range 3-15] to ensure comparability between Cal/BD foam and apremilast study populations with moderate disease
- Combination therapy treatment approaches due to difficulty in isolating effect of one treatment
- No efficacy measures available limiting any comparative effectiveness comparisons
- No baseline demographics and/or disease characteristics available preventing adequate matching of study populations
- Time points of efficacy measures not specified limiting comparative efficacy comparisons

Inclusion Criteria for Comparator Trials:

- Apremilast had to be studied, over time either retrospectively or prospectively
- Manuscript languages: English, Danish, Swedish or Norwegian
- Apremilast investigated for plaque psoriasis

Comparator Trial Used in MAIC:

- Based on inclusion and exclusion criteria, and overlap of studied populations, only one study of apremilast (UNVEIL[9]) met the criteria and was included in the MAIC analysis *(Table 1)*

Results

Table 2. sPGA 0/1 efficacy response rates calculated via MAIC between Cal/BD foam and apremilast.[4]

	Pooled data[5-8]		UNVEIL[9]
Treatment	**Cal/BD foam**		**Apremilast**
	Before re-weighting	After reweighting	
Effective sample size, n	748	640	148
BMI	31.2	30.5	30.5
PASI	7.3	8.2	8.2
Previous topical treatment	85.1%	82.4%	82.4%
PGA 0/1 responder, % (95% CI)	56.4% (51.9%; 60.9%)	**52.7%** (44.9%; 60.4%)	**30.4%** (23.6%; 38.2%)
P-value (t-test)		p<0.001	

- **After matching study populations, 52.7% of patients treated with Cal/BD foam achieved sPGA 0/1 at week 4 vs. 30.4% treated with apremilast at week 16 (p<0.001).**

Table 3. PASI75 efficacy response rates calculated via MAIC between Cal/BD foam and apremilast.[4]

	Pooled data[5-8]		UNVEIL[9]
Treatment	**Cal/BD foam**		**Apremilast**
	Before re-weighting	After reweighting	
Effective sample size, n	748	651	148
Age	51.3	48.6	48.6
BMI	31.2	30.5	30.5
Previous topical treatment	85.1%	82.4%	82.4%
PASI-75 responder, % (95% CI)	**51.4%** (51.2%, 51.5%)	**51.1%** (50.5%, 51.7%)	**21.6%** (15.8%, 28.9%)
P-value (t-test)		p<0.001	

- **After matching study populations, 51.1% of patients treated with Cal/BD foam achieved PASI-75 at week 4 vs. 21.6% treated with apremilast at week 16 (p<0.001).**

Table 4. Economic evaluation of Cal/BD foam for 4 weeks and apremilast for 16 weeks for treatment of moderate plaque psoriasis through a cost per PASI-75 responder analysis.

	PASI 75	Treatment period [weeks]	Consumption per treatment period	Pack cost	# Units per Pack	Unit	Unit per pack	Price per Unit
Cal/BD foam	51.1%	4	117.1 g*	$987.09 $1974.18	1 2	60 g 60 g x 2	60-120 g	$16.45 per g
Apremilast	21.6%	16	6570 mg**	$1012.5 - 3939.71	27-60	10-30 mg	690-1800 mg	$2.19 per mg
Data Source	*MAIC (Table 2)*	*Approved FDA indication*	**4 pooled Cal/BD studies **FDA indication*	*Analysource®, accessed April 2018 (third party provider of WAC pricing data)*				

- Cost per responder analysis was conducted based on the regimens approved by the FDA using US drug pricing.
  - Apremilast dosing per treatment - 6570 mg over 16 weeks[2]
  - Cal/BD foam dosing per treatment - average consumption data in 4 phase II/III trials[5-8]; 117.1 g over 4 weeks
- Cost per treatment period was calculated by multiplying the drug WAC per unit dose (mg or g, respectively) with total dosing (apremilast) or average consumption (Cal/BD foam) over treatment period.
- Cost per PASI-75 Responder was calculated by multiplying cost per treatment period by proportion of patients achieving PASI-75, as calculated in the MAIC analysis[4].

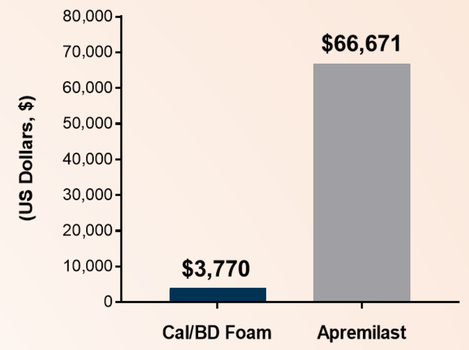

Figure 2. Average Cost Per PASI-75 Responder for Cal/BD foam and apremilast based on the MAIC analysis.

- In the US, cost per PASI-75 response Cal/BD foam is $3,770, and is lower than cost per response for apremilast ($66,671).

Limitations

- Comparative safety analyses and associated economic impact were not conducted.
- WAC prices do not reflect manufacturer rebates, are not reflective of actual spend, and are dated for April 2018.
- Time to response difference between Cal/BD foam (4 weeks) and apremilast (16 weeks) precluded use of the same treatment time horizon.
- Analyses based on clinical trials may not be generalizable to the real world.
- Imbalance in sample size exists due to applicable publications on comparator, and may not be fully addressed by methodology.
- Additional head-to-head research should be conducted to confirm the comparative efficacy findings.

Conclusions

- **This analysis used matching-adjusted indirect comparison to balance study populations in terms of baseline characteristics in a comparative efficacy and cost per responder evaluation.**
- **Results demonstrate that Cal/BD foam has higher PGA 0/1 and PASI-75 response rates and a lower cost per PASI-75 responder in the US than apremilast in adult patients with moderate plaque psoriasis.**

Acknowledgements

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