

Calcipotriene plus betamethasone dipropionate (0.005%/0.064%) foam vs halobetasol propionate and tazarotene (0.01%/0.045%) lotion: matching-adjusted indirect comparison & US cost-per-responder analysis

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Introduction

- Fixed-combination topical treatments for plaque psoriasis provide treatment advantages via a dual mechanism of action. The combination of active pharmaceutical ingredients (API), skin penetration, bioavailability of APIs, and formulation can impact clinical efficacy.
- Additionally, adherence is impacted by length of therapy and vehicle acceptability. In the absence of head-to-head trials, a comparison of relative effectiveness between fixed-combination topical treatments is pertinent.
- Calcipotriene and betamethasone dipropionate (0.005%/0.064%, Cal/BD) foam is a fixed-combination, once-daily topical treatment of plaque psoriasis in patients 12 years of age and older.¹
- Halobetasol propionate and tazarotene (0.01%/0.045%, HP/TAZ) lotion is a fixed-combination, once-daily topical treatment of plaque psoriasis in adults.²

Objective

Conduct an anchored matching-adjusted indirect comparison (MAIC) and incremental cost per responder (ICPR) analysis using individual patient data from Cal/BD foam studies and aggregate patient characteristics and outcomes from published efficacy assessments of HP/TAZ lotion in adult patients with moderate-to-severe plaque psoriasis.

Methods

Study Selection

- Published clinical trials with sufficiently similar populations and outcomes to support indirect comparisons were identified for Cal/BD foam and HP/TAZ Lotion (Figure 1).
- Comparative studies were excluded for the following reasons: the sample size included fewer than 40 patients (this exclusion was stipulated to preserve adequate statistical power); treatment efficacy was not measured, or time points of efficacy measurements were not specified; baseline characteristics were not reported; and the mean baseline Psoriasis Area and Severity Index (PASI) or body surface area (BSA) were greater than 15.

Study Design

- MAIC 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
- Baseline characteristics for matching were selected based on clinical input and by forward selection using a logistic model, with the relevant end point (ie, treatment success) as the dependent variable and selection entry criteria, $p < 0.2$.
- Available baseline variables for matching included disease severity (PGA, BSA), quality of life, demographics, duration of psoriasis, body mass index, and history of topical treatment (Table 1).
- MAIC analysis was conducted between Cal/BD foam and HP/TAZ lotion, number-needed-to-treat (NNT) was conducted between active treatment and respective vehicle, and associated pharmacoeconomic evaluation through US incremental cost per responder analysis (ICPR).

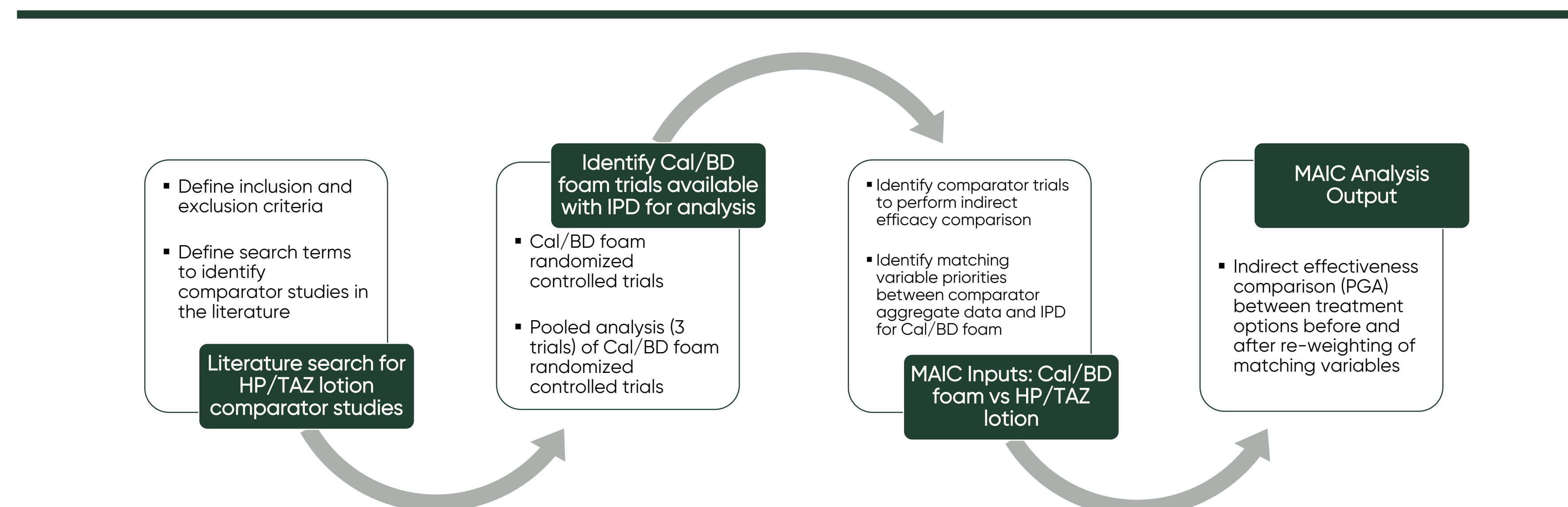


Figure 1. Methodology of MAIC analysis of Cal/BD foam and HP/TAZ lotion

Table 1. Identification of Cal/BD foam and HP/TAZ lotion trials for MAIC analysis

Potential Matching Variables	Pooled Cal/BD foam Studies			Pooled HP/TAZ Lotion Studies		
Study design	Three multicenter, randomized, double-blind, controlled studies ^{4,6}			Two multicenter, randomized, double-blind, vehicle-controlled Phase 3 studies ⁷		
Dosing	QD (4 weeks)			QD (8 weeks)		
Treatment	Cal/BD foam	Foam vehicle	All	HP/TAZ lotion	Lotion vehicle	All
N	649	199	848	276	142	418
Mean age (SD), y	52.0 (13.9)	48.0 (14.0)	51.0 (14.0)	50.0 (14.2)	51.0 (13.2)	50.3 (13.8)
Male, n (%)	417 (64.3)	108 (54.3)	525 (61.9)	175 (63.4)	97 (68.3)	272 (65.1)
White/Caucasian, n (%)	577 (88.9)	180 (90.5)	757 (89.3)	232 (84.1)	126 (88.7)	358 (85.6)
Mean BMI (SD), kg/m ²	31.3 (7.3)	31.2 (7.9)	31.2 (7.4)	-	-	-
Mean BSA (SD), %	7.4 (6.3)	7.9 (6.8)	7.5 (6.4)	6.0 (2.9)	5.7 (2.5)	5.9 (2.8)
Mean duration of psoriasis (SD), y	17.1 (14.0)	15.8 (12.5)	16.8 (13.7)	NR	NR	NR
Mean PASI (SD) score	7.2 (4.6)	7.5 (5.5)	7.3 (4.8)	NR	NR	NR
IGA, n (%)						
Mild	126 (19.4)	38 (19.1)	164 (19.3)	-	-	-
Moderate	465 (71.6)	140 (70.4)	605 (71.3)	237 (85.9)	119 (83.9)	356 (85.2)
Severe	58 (8.9)	21 (10.6)	79 (9.3)	39 (14.1)	23 (16.2)	62 (14.8)

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

Results

Table 2. Anchored MAIC evaluating PGA 'treatment success' response rates and NNT for Cal/BD foam and HP/TAZ lotion.

Treatment	Pooled Data		HP/TAZ lotion (+vehicle) ⁷
	Cal/BD foam (+vehicle) ^{4,6}	Before re-weighting	
Effective sample size, n	649 (+199)	586	276 (+142)
Baseline PGA, %			
Moderate	71.3%	85.2%	85.2%
Severe	9.3%	14.8%	14.8%
BSA	7.5%	5.9%	5.9%
Male, n (%)	61.9%	65.1%	65.1%
White/Caucasian at baseline, %	89.3%	85.6%	85.6%
Active	48.5%	55.7%	40.6%
PGA Treatment success rate (95% CI)	(41.2%, 55.9%)	(52.3%, 59.1%)	(34.8%, 46.4%)
Vehicle	5.0%	4.3%	9.9%
PGA Treatment success rate (95% CI)	(4.4%, 5.7%)	(3.5%, 5.1%)	(5.0%, 14.8%)
Active - Vehicle	43.5%	51.4%	30.7%
Difference in PGA success rates (95% CI)	(36.5%, 50.5%)	(47.6%, 55.2%)	(23.1%, 38.3%)
Anchored MAIC			
Difference in PGA success rates between Cal/BD foam & HP/TAZ lotion (95% CI; P-value)			20.7% (12.2%, 29.1%; P<.001)
Number needed to treat (NNT) relative to vehicle - Cal/BD foam vs HP/TAZ lotion			1.9 vs 3.3

PGA, physicians' global assessment; BSA, body surface area; MAIC, matching adjusted indirect comparison

Table 3. Economic evaluation of Cal/BD foam for 4 weeks and HP/TAZ lotion for 8 weeks for treatment of moderate plaque psoriasis through a cost per PGA 'treatment success' responder analysis.

	No units/pack	Grams per unit	Unit cost per pack (WAC) [a]	Cost per gram	Treatment period [weeks]	Quantity used per treatment period	Anchored MAIC: PGA 0/1 (4 vs. 8 weeks)	ICPR per PGA 0/1 responder [b]
Cal/BD Foam	1	60 gm	\$1050	\$17.50	4	117.1 gm*	51.4%	\$3988
HP/TAZ Lotion	1	100 gm	\$825	\$8.25	8	234.2 gm**	30.7%	\$6294

- Incremental cost per responder analysis was based on the FDA Prescribing Information^{1,2} and anchored MAIC analysis using US Wholesale Acquisition Cost (WAC) drug pricing from June 2019 (Analysource®).
- Cost per treatment period was calculated by multiplying the per gram drug WAC with the average consumption of study drug over treatment period of 4 weeks and 8 weeks, respectively, assuming equal weekly consumption rates.
- The estimated incremental cost per responder (ICPR) was calculated by multiplying the NNT by the overall drug costs throughout the treatment period and corresponds to the additional cost to achieve 1 additional responder for each of the treatments vs vehicle (Table 3).
- The incremental cost per PGA 0/1 responder relative to vehicle for Cal/BD foam was \$3988 and is 37% lower compared with HP/TAZ lotion (\$6294) (Figure 2).

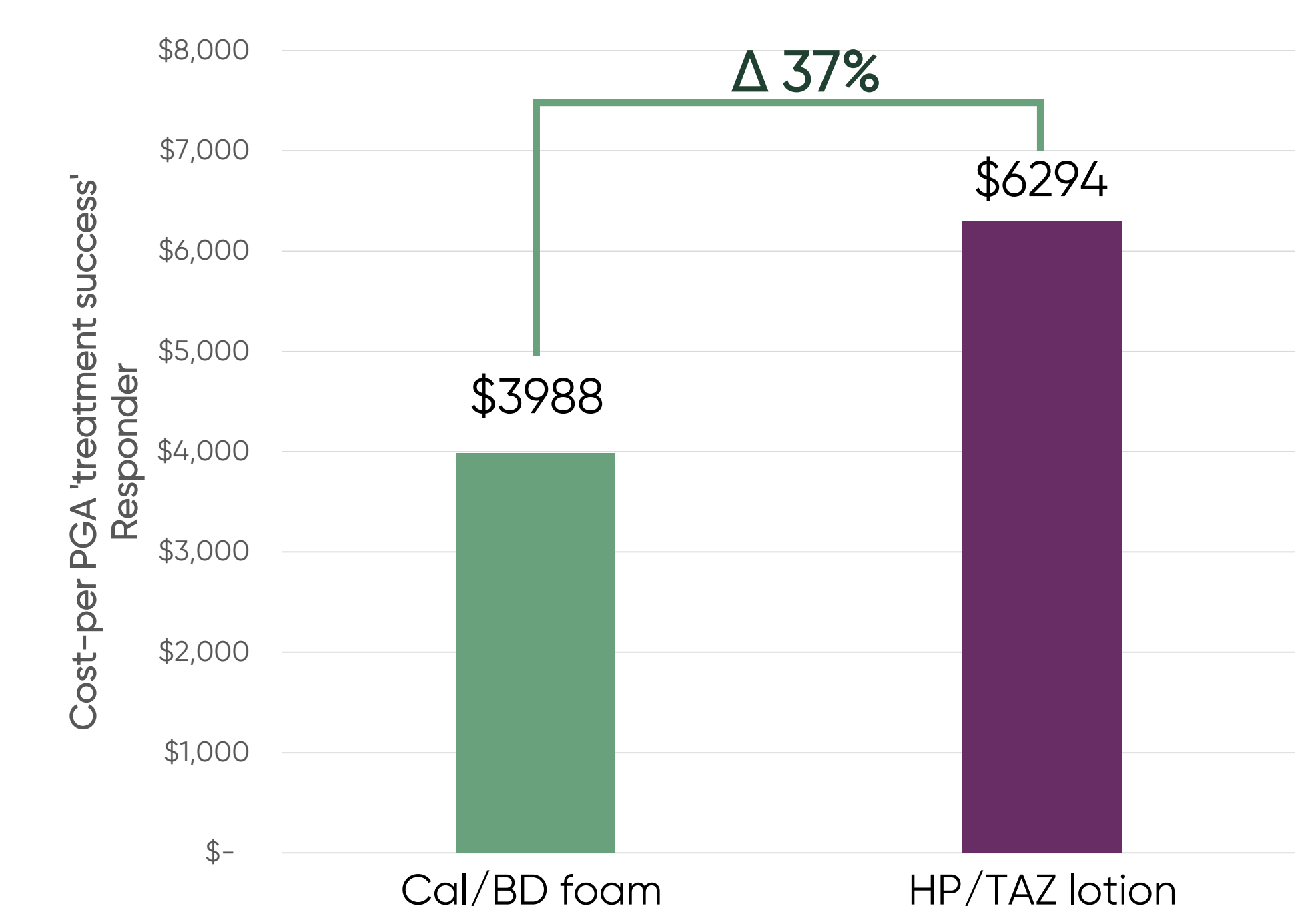


Figure 2. Average Cost Per PGA Responder for Cal/BD foam and HP/TAZ lotion based on the anchored MAIC analysis.

Limitations

- Observed (e.g. patient randomization) and unobserved (e.g. vehicle) cross-trial differences may not be accounted for in the analysis
- 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 June 2019.
- Time to response difference between Cal/BD foam (4 weeks)¹ and HP/TAZ lotion (8 weeks)².
- Imbalance in sample size exists due to applicable publications on comparator, and may not be fully addressed by methodology.
- Analyses based on clinical trials may not be generalizable to the real world.
- Additional head-to-head research should be conducted to confirm these comparative effectiveness findings.

Conclusions

- This analysis used an anchored MAIC to balance baseline characteristics of study populations in an indirect, comparative effectiveness evaluation of two fixed-combination topical treatments for plaque psoriasis.
- Evaluation demonstrates that Cal/BD foam treatment has statistically greater difference in PGA 0/1 response rates, a lower cost per PGA 0/1 responder, and quicker treatment response than HP/TAZ lotion in adult patients with moderate-to-severe plaque psoriasis.

Acknowledgements

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Disclosures

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