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Cost per PASI-75 responder of calcipotriol plus betamethasone dipropionate cutaneous foam versus non-biologic systemic therapies for the treatment of plaque psoriasis in seven European countries

Deepak Balak[a], Jose-Manuel Carrascosa[b], Stamatis Gregoriou[c], Piergiacomo Calzavara-Pinton[d], Anthony Bewley[e], Joana Antunes[f], Martin Nyeland[g], Marta Viola[h], Laura M Sawyer[h], Lidia Becla[g]*

[a]*Department of Dermatology and Allergology, University Medical Centre Utrecht, Utrecht, the Netherlands;* [b]*Dermatology Department, Hospital Universitari Germans Trias i Pujol, Universitat Autònoma de Barcelona; IGTP, Badalona, Spain;* [c]*Department of Dermatology, National and Kapodistrian University of Athens, Faculty of Medicine, Andreas Sygros Hospital, Athens, Greece;* [d]*Dermatology Department, University of Brescia, Italy;* [e]*Barts Health NHS Trust and Queen Mary University of London, London, United Kingdom;* [f]*Serviço de Dermatologia, Hospital de Santa Maria - Centro Hospitalar Lisboa, EPE, Lisbon, Portugal;* [g]*LEO Pharma A/S, Ballerup, Denmark;* [h]*Symmetron Limited, London, United Kingdom*

*Lidia Becla, Industriparken 32, DK-2750 Ballerup, Denmark, IXDDK@leo-pharma.com

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Abstract

Purpose

To compare the short-term cost and effectiveness of calcipotriol/betamethasone dipropionate (Cal/BD) cutaneous foam against non-biologic systemics in psoriasis patients for whom oral systemic or topical therapy is considered appropriate in seven European countries.

Methods

Matching-adjusted indirect comparisons of 4-week PASI-75 responses of Cal/BD foam were performed versus 12-week responses of methotrexate, acitretin, fumaric acid esters (FAE) and 16-week responses of apremilast. Analyses took a payer perspective and included drug, physician visit and monitoring costs.

Results

In all countries, Cal/BD foam generated the lowest cost per responder (CPR). Against methotrexate, apremilast and acitretin, Cal/BD foam generated response for less than €190 in Italy, €195 in Portugal, €216 in Greece, £218 in the UK, €250 in Belgium, €319 in Spain, and €359 in the Netherlands. Relative to treatment with FAE, Cal/BD foam resulted in response for less than €298, €430, €382 and £262 in Belgium, the Netherlands, Spain and the UK, respectively. For Cal/BD foam, apremilast and FAE, total costs were driven by drug costs; for methotrexate and acitretin, by monitoring.

Conclusions

Driven by its lower costs and high response rates, Cal/BD foam is likely to be a cost-effective option over the short-term in the investigated psoriasis population.

Keywords: psoriasis; calcipotriol/betamethasone dipropionate cutaneous foam; topical therapy; systemic therapy; cost per response

Introduction

Psoriasis is a chronic, immune-mediated inflammatory condition primarily manifesting on the skin and is estimated to affect 2-3% of the world's population [1]. Plaque psoriasis symptoms negatively impact patient quality of life and are associated with a considerable economic burden [2,3]. Treatment aims to reduce the severity of skin symptoms and to improve patient quality of life.

Topical therapies are usually considered the first line option in mild to moderate psoriasis while phototherapies or oral systemic therapies are generally offered for moderate to severe disease or after failure of topical therapy. Systemic therapies are often associated with greater costs to the healthcare system than topical treatments, driven by costs of medication and monitoring [3]. Individual patient characteristics and preferences determine the choice of treatment prescribed by physicians.

A frequently used first-line topical psoriasis treatment is the fixed-dose combination of calcipotriol (Cal, 50 μg/g) and betamethasone dipropionate (BD, 0.5 mg/g). The Cal/BD combination formulation has a comparable safety profile and is more effective in treating psoriasis compared to monotherapy with either calcipotriol or betamethasone dipropionate [4-7]. A novel cutaneous foam developed for the fixed-dose Cal/BD combination has demonstrated significantly improved efficacy with a comparable safety profile when compared to Cal/BD gel and ointment [8,9], a foam vehicle [10] and Cal or BD foams alone [11].

A recent matching-adjusted indirect comparison (MAIC) [12], showed Cal/BD foam to have better effectiveness compared to apremilast, methotrexate and acitretin and to have comparable effectiveness versus fumaric acid esters (FAE) in patients eligible for either topical or non-biologic systemic treatment. Methotrexate and acitretin are associated with

relatively low acquisition costs but require regular doctor visits and monitoring for adverse events. By comparison, treatments such as apremilast and FAE are associated with higher acquisition costs, and potentially less frequent monitoring in the case of apremilast. Cal/BD foam requires no ongoing monitoring and could be prescribed in general practice. Pharmaco-economic data on whether Cal/BD foam offers better value for money in patients who are eligible for both topical and systemic therapy is essential for optimal decision making in restricted health care budget systems.

The objective of this study is to compare the costs and effectiveness of Cal/BD foam with that of non-biologic systemic therapies in patients eligible for topical and non-biologic systemic treatment in seven European countries: Belgium, Greece, Italy, the Netherlands, Portugal, Spain and the United Kingdom.

Materials and methods

Responder rates

Response was defined as a 75% reduction in the Psoriasis Area and Severity Index score (PASI-75). The proportion of patients responding to Cal/BD foam and oral systemic therapies were derived from a recently published MAIC [12]. MAIC is a methodological approach for indirect comparisons where no appropriate common comparator is available and individual patient data (IPD) are available for at least one intervention. Here, IPD from 4 Cal/BD foam randomised controlled trials (RCTs) were matched to average study population characteristics from published studies of non-biologic systemic therapies.

A separate MAIC was available for Cal/BD foam versus each non-biologic systemic therapy. In each comparison, the IPD from pooled Cal/BD foam trials were re-weighted such that the average baseline characteristics from the Cal/BD foam treatment cohort matched those from

each comparator study (see Supplementary Table 1). As a result, the absolute responder rate of Cal/BD foam is unique for each matched comparison. The PASI-75 endpoint of the Cal/BD foam trials at week 4 were compared to the PASI-75 endpoints of the comparator trials, which were measured at week 12 for methotrexate, acitretin and FAE, and week 16 for apremilast. Results from a sensitivity analysis comparing the week 12 outcomes for Cal/BD foam (only reported in the PSO-ABLE study) [8] to the week 12 or week 16 outcomes for the non-biologic systemic therapies were also available [12].

[Table 1 near here]

Table 1 presents the MAIC results from Bewley et al., which fed into the present cost per responder analysis. These results indicate that, among patients considered for either topical or non-biologic systemic treatment, Cal/BD foam for either 4 weeks or 12 weeks is expected to generate significantly more PASI-75 responders than 12 weeks of treatment with acitretin or methotrexate or 16 weeks of treatment with apremilast. Compared to 12 weeks of therapy with FAE, the absolute responder rate for Cal/BD foam is lower over 4 weeks (42.4% vs 47.0%) and higher over 12 weeks of treatment (58.5% vs 47.0%), though the differences are not statistically significant at either time point. No comparison could be made with ciclosporin due to a lack of data [12].

Costs and health care resource use

The analysis took a payer perspective for each of the European countries and considered both drug and monitoring costs based on local databases and national guidelines. Not all non-biologic systemic therapies are available or used in all countries. For example, neither apremilast nor FAE are currently available in Portugal; FAE are also not available in Greece.

Methotrexate administered via injection is rarely used in the UK, Greece, Belgium and the Netherlands and was therefore not evaluated in these countries.

Drug costs were calculated by combining the total dose received during treatment with local drug costs obtained from published sources (see Supplementary Table 2). For Belgium and the Netherlands, the pharmacy selling price was used. In Portugal and Spain, drug costs were based on their wholesale purchase price and in Greece they were based on the reimbursed prices. In Italy, the ex-factory wholesale purchase price was used with mandatory discounts (-5%; -5%) included. Finally, list prices in the UK were taken from the National Health Service drug tariff.

The Cal/BD foam dose was estimated as a weighted average of 4-week consumption across the included Cal/BD foam RCTs [8-11]. Non-biologic systemic therapy doses were determined according to European Medicines Agency label or the trial included in the analysis and calculated for treatment duration.

The consumption of methotrexate could not be derived from the observational study synthesised in the MAIC [13], so was calculated based on the label posology [14] and a titration period validated by clinical experts. Patients were assumed to start on 7.5 mg of methotrexate per week and escalate to 10 mg in weeks 2 and 3, to 15 mg in weeks 4 to 6, to 20 mg in weeks 7 to 10 and to 25 mg in weeks 11 and 12. This amounts to an average weekly dose of 16.9 mg for the first 12 weeks. The dose of acitretin is determined by patient weight and was derived from Chiricozzi *et al.* [15], the observational study synthesised in the MAIC. The mean dosage in this study was 25.01 mg (SD±6.79) corresponding to a mean of 0.31 mg/kg. Multiplied by the mean patient weight from the PSO-ABLE study (87 kg), the mean daily dosage was 27 mg. The dose of apremilast was 30 mg twice daily following a 5-day

titration. Dimethyl fumarate was given at a daily dose of 240 mg 3 times daily after a 9-week titration schedule.

The type and frequency of general practitioner (GP) visits, specialist dermatologist visits and monitoring tests for each therapy were based on published guidance, where available, and clinical expert opinion (see Supplementary Table 3). Baseline tests were also included as these differed across treatments. Unit costs of health care visits and laboratory tests were combined with country-specific estimates of resource use to estimate the total cost of physician visits and monitoring (see Supplementary Table 4). Liver ultrasound and biopsies for methotrexate were excluded as a very small percentage of patients are assumed to require this and such testing falls outside the first 12 weeks of therapy. All health care resource use and cost inputs were validated by local clinical experts.

Table 2 presents the total and disaggregated costs for the treatment period by country.

[Table 2 near here]

Scenario analysis

The primary analysis used 4-week costs and outcomes for Cal/BD foam and compared them to the 12-or 16-week costs and outcomes for non-biologic systemic therapies. Differences in time points reflect the use of each therapy within its label and correspond to the primary endpoints in the included trials.

Two scenarios were tested to increase comparability between topical and non-biological systemic treatment duration. In the first scenario, the results of the MAICs using the PASI-75 responder rate from week 12 for Cal/BD foam from the PSO-ABLE [8] study were combined with the mean consumption at week 12 (236.4 g) and compared to the week 12 or 16

endpoint for systemic therapies. In the second, resource use and costs for all comparators were amended to reflect only the first four weeks of treatment, including early follow-up visits and drug titration where applicable. Responder rates were unchanged from the main analysis. That is, costs reflect the first 4 weeks of treatment, but responder rates reflect 12 to 16 weeks of non-biologic systemic treatment and 4 weeks of Cal/BD foam. For inputs to these scenario analyses, see Supplementary Table 5.

Results

Among patients analysed in this study, Cal/BD foam is associated with a lower cost per PASI-75 responder than the non-biologic systemic therapies included in the analysis (Fig. 1). Note that the absolute PASI-75 response rate of Cal/BD foam depends on the matched comparison; therefore, its cost per response differs depending on the comparator.

Methotrexate has the lowest drug costs but is among the treatments associated with the highest monitoring costs. The drug costs for acitretin are higher than Cal/BD foam in the UK, Belgium, the Netherlands and Portugal and lower in Spain, Greece and Italy; however, physician visit and monitoring costs are higher across all countries. Monitoring costs for FAE are higher than for acitretin and lower than for methotrexate (except in Italy), but FAE has a considerably higher drug cost. Apremilast is the systemic with the lowest monitoring costs, but the drug itself costs more than twice as much as any other therapy over a 12- to 16-week period. Cal/BD foam has the lowest total costs, because it requires no laboratory testing at baseline and few, if any, follow-up visits. Even if all Cal/BD foam treated patients are assumed to have two specialist visits in the first 4 weeks of treatment, it remains the option with the lowest total cost across all countries.

In comparison with methotrexate, apremilast and acitretin, the cost per response for Cal/BD foam ranged from €216 (€109.54/0.508) in Greece to €359 (€182.16/0.508) in the Netherlands. The cost per PASI-75 response of oral methotrexate, on the other hand, ranged from €480 (€160.83/0.335) in Italy to £1,865 (£624.90/0.335) in the UK. In Italy, Portugal and Spain, where methotrexate is available in injection form, the costs per response were €675, €1,136 and €1,241, respectively. For acitretin, the cost per response was as low as €560 (€177.55/0.317) in Greece and up to €1,735 (€549.84/0.317) in the Netherlands. Apremilast was universally associated with the highest cost per responder, ranging from approximately €9,500 (€2,052.52/0.216) in Greece to more than €15,600 (€3,387.53/0.216) in Spain. Cal/BD foam had a higher cost per response when compared with FAE (from €228 [€96.76/0.424] in Italy to €382 [€162.17/0.424] in Spain) than when compared to other oral systemic treatments due to the lower expected responder rate generated in the MAIC. However, the cost to generate a PASI-75 responder is substantially greater for FAE than Cal/BD foam, ranging from around €1,800 (€852.46/0.470) in Italy to nearly €2,600 (€1,216.75/0.470) in the Netherlands.

[Table 3 near here]

In the first scenario analysis, presented in Table 3, where Cal/BD foam was assumed to be used for 12 weeks instead of four, both total costs and the proportions of responders increased, though at different rates. The costs increased proportionally more than the responder rate, resulting in an increase to the cost per PASI-75 response for Cal/BD foam; however, it remained substantially lower than all comparator non-biologic systemic therapies in all markets.

In the second scenario, the total costs for non-biologic systemic therapies decreased substantially when drug and health care resource use estimates were restricted to just the first

four weeks of treatment. In this conservative scenario, Cal/BD foam treatment was less costly than all comparators and remained the treatment with the lowest cost per PASI-75 response in all markets. Neither scenario showed the conclusions of the main analysis to be sensitive to reasonable variation in cost or efficacy assumptions.

Discussion

This study compared the relative effectiveness and costs of treatment with Cal/BD foam versus non-biologic systemic therapies in seven European countries. The cost per responder analysis applied country-specific costs and resource use and combined it with PASI-75 response rates from a recently published MAIC analysis, which evaluated Cal/BD foam and non-biologic systemic therapies in a population of patients eligible for topical and non-biologic systemic therapies [12].

There is a clear distinction between patients with mild and severe psoriasis in terms of both symptoms and treatment received: topical therapy is the preferred treatment for mild patients, while the latter require systemic treatment. Additionally, there is an ill-defined group of psoriasis patients that falls in the middle of this spectrum, which is the target population for our study. This patient population is clinically heterogenous, and there is no consensus on their treatment. Determining the best value treatment for these patients, whilst tailoring care to individual patient needs and preferences, may lead to the consideration of a number of treatments and modalities. This cost per responder analysis demonstrated that Cal/BD foam is consistently associated with better or comparable response rates at a lower total cost than methotrexate, acitretin, apremilast and FAE.

Older non-biologic systemic therapies (methotrexate, acitretin and FAE) are associated with high rates of discontinuation, driven largely by adverse events and the inconvenience of

treatment monitoring [16-18]. Psoriasis patients are a group with significant comorbidities [19] and the risk of hepatotoxicity with methotrexate therapy is increased among patients with obesity, diabetes or pre-existing liver conditions [20]. Topical treatment alternatives such as Cal/BD foam minimise the risk of additional comorbidities associated with conventional systemic therapies that have costs that were not accounted for in this analysis. Of course, the presence of a co-morbidity such as psoriatic arthritis would favour systemic therapy over topical treatments regardless of the severity of plaque psoriasis. Hence, the optimal type of treatment (e.g. topical, phototherapy or systemic treatment) will vary by individual, and the prescribing physician will need to consider disease activity, co-morbidities and patient preference, among others.

Frequent monitoring visits for systemic therapies are not only inconvenient but can cost the patient a great deal in terms of travel and time away from work or family. The payer perspective adopted in this analysis does not capture these costs and does not reflect differences in access observed in the countries included. For example, in an archipelagic country like Greece, patients living on small islands may not have access to specialist or laboratory care and might need to travel to seek such services.

Furthermore, while some studies assessing patients' compliance report that relative to systemic treatments, topical therapies are associated lower treatment adherence [21-23], others report the opposite [6,24]. Both patient- and drug-related factors contribute to non-adherence to topical therapy, including but not limited to, side-effects, time for application and "messiness" of the drug [6]. Cal/BD foam is greatly preferred to topical ointments and creams due to its ease of application and lack of mess [25].

Guidelines for psoriasis tend to group ill-defined moderate psoriasis patients with the more severe population, and this group can receive any form of therapy as first line, including

phototherapy, biologics, and systemics [26]. However, patients may have contra-indications to systemic agents or may be reluctant to initiate systemic therapy. Given the enhanced efficacy of the novel Cal/BD foam formulation at a relatively lower cost, it may be beneficial for physicians to consider Cal/BD foam prior to starting a systemic therapy in patients who are eligible for both topical and systemic therapy. For this category of psoriasis patients, optimal use of an effective topical treatment can be of clinical value, reducing or delaying escalation to potentially more aggressive treatments, such as systemic therapy [27]. Finally, our study findings support that Cal/BD foam may represent a cost-effective solution ensuring pharmacoeconomic value in addition to clinical benefit.

Strengths and Limitations

The study and its results should be interpreted in the context of certain strengths and limitations. This is the first analysis to compare the costs and effectiveness of Cal/BD foam to non-biologic systemic therapies in a population of patients who could be considered for either. This was enabled by a published MAIC analysis, which took advantage of patient-level data to account for differences in populations between Cal/BD foam clinical trials and studies of non-biologic systemic therapies, thus enabling comparisons not yet made in head-to-head trials or in network meta-analyses [12]. Though data were available for methotrexate [13], acitretin [15], apremilast [28] and FAE [29], no studies provided sufficient data about ciclosporin and therefore it could not be included in the cost per responder comparison presented here. The studies in the MAIC were not all RCTs, thus the results could be confounded by unobserved differences between patient populations. Indeed, MAIC methods can only account for known confounders or differences in patient populations that are measured and reported. Only a well-controlled head-to-head RCT can avoid this unobserved confounding.

The main limitation of this study is the comparison across different time points, though these are in line with the label usage for each treatment. Cal/BD foam is recommended for a 4-week flare treatment, while systemic therapies are intended for longer-term treatment and they take a longer time (12-16 weeks) to achieve maximal effect. Though the main analysis compared the 4-week costs and outcomes of Cal/BD foam to 12- and 16-week costs and outcomes of non-biologic systemic therapies, the results were not sensitive to variation in the duration of the treatment period. Cal/BD foam was still associated with the lowest cost per PASI-75 response when the treatment period was extended to 12 weeks, though this technically falls outside of its label usage. The analysis has focused on short-term effectiveness as data on the use of Cal/BD foam over the long-term, that is beyond 12 weeks, is limited.

Cal/BD cost was also the lowest in a conservative scenario where the costs of non-biologic systemic therapies were restricted to the first 4 weeks, but the effects were held at rates observed after the full 12- or 16-week period. The main properties of Cal/BD foam, namely that it could be effective in eligible patients, requires no monitoring and can be prescribed in primary care, outweigh the high monitoring and follow-up costs for methotrexate and acitretin and the high acquisition costs for apremilast and FAE.

Though there have been many advances in psoriasis treatment made over the last few decades, many systemic therapies are costly and leave some needs unmet. This cost per responder analysis demonstrated that Cal/BD foam, used over 4-12 weeks, can generate more PASI-75 responders than apremilast, acitretin and methotrexate and a comparable proportion of responders to FAE at a lower total cost in patients eligible for either topical or systemic treatment. These results indicate a potential economic benefit of Cal/BD foam and supports its use before considering a switch to oral systemic therapies in suitable patients.

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Declaration of interest statement

Deepak Balak is a consultant/speaker for AbbVie, Almirall, Celgene, Janssen, LEO Pharma, Novartis, Sanofi-Genzyme, and has received research grants from LEO Pharma. Jose-Manuel Carrascosa has participated as invited speaker, advisor and principal and site investigator in clinical trials for Abbvie, Almirall, Celgene, Gebro, Janssen, LEO Pharma, Lilly, Novartis and Pfizer. Piergiacomo Calzavara-Pinton has served as an advisory board member for Abbvie, Almirall, Galderma, LEO Pharma, Meda, Pierre Fabre, and Sanofi. Stamatis Gregoriou and Joana Antunes have been invited speakers for LEO Pharma. Antony Bewley declared no conflict of interest. Martin Nyeland was an employee of LEO Pharma at the time the analysis was undertaken. Marta Viola and Laura Sawyer are employed by Symmetron Limited, which received funding from LEO Pharma for this research. Lidia Becla is an employee of LEO Pharma.

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Tables

Table 1. Proportion of PASI-75 responders with Cal/BD foam vs non-biologic systemic therapies

		Methotrexate (12 weeks)	Apremilast (16 weeks)	Acitretin (12 weeks)	Fumaric acid esters (12 weeks)
Systemic therapy	PASI-75	33.5%	21.6%	31.7%	47.0%
	(95% CI)	(27.2, 39.8)	(15.8, 28.9)	(17.5, 46.0)	(37.9, 56.1)
Cal/BD foam (4 weeks)	PASI-75	50.8%	51.1%	50.9%	42.4%
	(95% CI)	(50.3, 51.3)	(50.5, 51.7)	(50.1, 51.6)	(35.0, 50.2)
	p value	<0.001	<0.001	0.009	0.451
Cal/BD foam (12 weeks)	PASI-75	59.8%	60.4%	77.5%	58.5%
	(95% CI)	(52.2, 66.8)	(50.5, 69.5)	(66.8, 85.6)	(47.9, 68.4)
	p value	<0.001	<0.001	<0.001	0.11

Source: Bewley *et al.* 2018 [12] **Note:** p values are for Cal/BD foam vs systemic therapy. **Abbreviations:** Cal/BD, calcipotriol and betamethasone dipropionate; CI, confidence interval.

Table 2. Drug consumption and healthcare costs in seven European countries

		Cal/BD foam (4 weeks)	MTX oral (12 weeks)	MTX injection (12 weeks)	Apremilast (16 weeks)	Acitretin (12 weeks)	Fumaric acid esters (12 weeks)
	Total drug consumption	117.1 g	202.5 mg	202.5 mg	6570 mg	2268 mg	34020 mg
Belgium costs	Drug (PSP)	€93.82	€21.79	N/A	€3,156.01	€175.31	€806.28
	Physician	€32.58	€233.88	N/A	€65.16	€65.16	€90.59
	Monitoring	€0.00	€103.60	N/A	€0.00	€41.33	€41.57
	Total	**€126.40**	**€359.26**	**N/A**	**€3,221.17**	**€281.79**	**€938.44**
Greece costs	Drug (reimbursed price)	€89.54	€5.52	N/A	€2,012.89	€64.83	N/A
	Physician	€20.00	€40.00	N/A	€20.00	€20.00	N/A
	Monitoring	€0.00	€180.42	N/A	€19.63	€92.73	N/A
	Total	**€109.54**	**€225.94**	**N/A**	**€2,052.52**	**€177.56**	**N/A**
Italy costs	Drug (ex-factory price)	€69.56	€9.78	€74.93	€3,018.86	€57.74	€670.91
	Physician	€27.20	€81.60	€81.60	€68.00	€81.60	€81.60
	Monitoring	€0.00	€69.45	€69.45	€78.05	€72.85	€99.95
	Total	**€96.76**	**€160.83**	**€225.98**	**€3,164.91**	**€212.19**	**€852.46**
Netherlands costs	Drug (PSP)	€91.16	€13.45	N/A	€3,027.95	€133.06	€791.13
	Physician	€91.00	€364.00	N/A	€182.00	€364.00	€364.00
	Monitoring	€0.00	€113.66	N/A	€38.08	€52.78	€61.63
	Total	**€182.16**	**€491.11**	**N/A**	**€3,248.03**	**€549.84**	**€1,216.75**
Portugal costs	Drug (WPP)	€65.09	€4.70	€198.50	N/A	€79.12	N/A
	Physician	€34.10	€127.10	€127.10	N/A	€96.10	N/A
	Monitoring	€0.00	€54.83	€54.83	N/A	€38.02	N/A
	Total	**€99.19**	**€186.63**	**€380.43**	**N/A**	**€213.24**	**N/A**
Spain costs	Drug (WPP)	€69.85	€4.12	€120.20	€3,265.36	€54.43	€637.35
	Physician	€92.32	€124.80	€124.80	€92.32	€92.32	€129.92
	Monitoring	€0.00	€170.64	€170.64	€29.85	€53.38	€64.56
	Total	**€162.17**	**€299.56**	**€415.64**	**€3,387.53**	**€200.13**	**€831.83**
UK costs	Drug (drug tariff price)	£77.44	£9.14	N/A	£2,190.18	£86.74	£667.80
	Physician	£33.50	£502.70	N/A	£301.62	£201.08	£301.62
	Monitoring	£0.00	£113.06	N/A	£60.19	£87.85	£88.49
	Total	**£110.94**	**£624.90**	**N/A**	**£2,551.99**	**£375.67**	**£1,057.91**

Abbreviations: Cal/BD, calcipotriol and betamethasone dipropionate; MTX, methotrexate; N/A, Not applicable; PSP, pharmacy selling price; WPP, wholesale purchase price

Note: N/A indicates where the drug was not included in the analysis for a given country because it is either not used or not available locally

Table 3. Cost per PASI-75 responder for Cal/BD foam compared to non-biologic systemic therapies when treatment duration is varied in alternative scenarios 1 and 2

		Cost per PASI-75 responder								
Country	**Scenario**	**Cal/BD foam**	**MTX oral**	**MTX injection**	**Cal/BD foam**	**Apremilast**	**Cal/BD foam**	**Acitretin**	**Cal/BD foam**	**Fumaric acid esters**
Belgium	SA1	€371	€1,072	N/A	€368	€14,913	€286	€889	€379	€1,997
	SA2	€249	€697	N/A	€247	€3,771	€248	€370	€298	€451
Greece	SA1	€336	€674	N/A	€332	€9,502	€259	€560	N/A	N/A
	SA2	€216	€546	N/A	€214	€2,482	€215	€424	N/A	N/A
Italy	SA1	€280	€480	€675	€278	€14,652	€216	€669	€287	€1,814
	SA2	€190	€272	€313	€189	€3,880	€190	€347	€228	€452
Netherlands	SA1	€460	€1,466	N/A	€455	€15,037	€355	€1,735	€470	€2,589
	SA2	€359	€1,127	N/A	€356	€4,001	€358	€1,121	€430	€689
Portugal	SA1	€277	€557	€1,136	N/A	N/A	€214	€673	N/A	N/A
	SA2	€195	€417	€539	N/A	N/A	€195	€376	N/A	N/A
Spain	SA1	€ 390	€ 894	€ 1,241	€ 386	€ 15,683	€ 301	€ 631	€ 399	€ 1,770
	SA2	€ 319	€ 754	€ 827	€ 317	€ 4,144	€ 319	€ 330	€ 382	€ 408
UK	SA1	£317	£1,865	N/A	£314	£11,815	£245	£1,185	£325	£2,251
	SA2	£218	£1,184	N/A	£217	£3,661	£218	£615	£262	£824

Abbreviations: Cal/BD, calcipotriol and betamethasone dipropionate; SA, scenario analysis; MTX, methotrexate; N/A, Not applicable

Note: SA1 used 12-week costs and effects for Cal/BD foam; SA2 used 4-week costs and 12- or 16-week effects for non-biologic systemic therapies; N/A indicates where the drug was not included in the analysis for that specific country

Figures Legends

Figure 1. Cost per PASI-75 responder for 4-week Cal/BD foam compared to methotrexate (12 weeks), apremilast (16 weeks), acitretin and fumaric acid esters (12 weeks) in the seven European countries.

a. Belgium

b. Greece

c. Italy

d. The Netherlands

e. Portugal

f. Spain

g. United Kingdom

NOTES: Apremilast cost-per-responder bars exceed scale, value is indicated on top of bar. Analyses carried out versus comparators recommended for use in each country, as reflected in graphic. Cost-per-responder for Cal/BD foam varies due to differences in the individual analyses carried out per pairwise comparison. Acitretin was identified as a comparator at the time of the analysis for Greece (b) but is now temporarily not available: the results are still displayed for completeness. Abbreviations: Cal/BD, calcipotriol and betamethasone dipropionate; FAE, fumaric acid esters; MTX, methotrexate; NA, comparison not applicable as comparator not recommended for use in country.