Appendix I: Evidence Tables – Economic Studies

I.6 Topicals

I.6.1 Psoriasis of the trunk and limbs

D. M. Ashcroft, A. Li Wan Po, H. C. Williams, and C. E. Griffiths. Cost-effectiveness analysis of topical calcipotriol versus short-contact dithranol: In the treatment of mild to moderate plaque psoriasis. Pharmacoeconomics 18 (5):469-476, 2000.				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CEA **Study design:** Decision Tree analytic model **Perspective:** UK, NHS payer perspective **Time horizon:** 12 weeks (and 1 year in sensitivity analysis) **Treatment effect duration:** up to 1 year **Discounting:** N/A	**Population:** Patients with mild to moderate plaque psoriasis **Cohort settings:** Start age = NR M = NR **Intervention 1:** Calcipotriol applied twice daily (estimated weekly dosage of 34.2g). The efficacy used in the base case was 0.608. **Intervention 2:** Dithrocream 2% applied once daily (estimate weekly dosage of 17.1g/wk). The efficacy used in the base case was 0.496	**Total costs (mean per patient):** Intvn 1:£96.03 Intvn 2: £ 30.35 Incremental: £64.68 **Currency & cost year:** 2000 UK sterling **Cost components incorporated:** Only direct cost of treatment included. No account for treatment failures.	**Primary outcome measure:** **Success rate:** Intvn 1: 0.608 Intvn 2:0.496 Incremental: 0.112 **Successful days (Success rate*treatment duration):** Intvn 1: 51.07 Intvn 2: 41.66 Incremental: 9.04	**Cost effectiveness ratio:** £577.50 per success **Analysis of uncertainty:** Limited one way deterministic sensitivity analysis undertaken using one alternative cost and efficacy rate for both treatments. Where calcipotriol had increased efficacy (0.784) the cost effectiveness ratio= £244.58 per success Where dithranol had increased efficacy (0.542) the cost effectiveness ratio= £980.00 per success Where the cost of calcipotriol increased to £100, the cost effectiveness ratio= £612.95 per success Where the cost of dithranol increased to £36 and £59.12, the cost effectiveness ratio= £535.98 per success and £329.55 per success respectively. A 1 year time horizon was also explored: Total costs – 1 year horizon (mean per patient): Intvn 1:£164.94; Intvn 2: £ 126.25 Incremental: £38.66 Successful days – over 1 year horizon: Intvn 1: 116.32; Intvn 2:114.38 Incremental: £1.94 days Cost effectiveness ratio: £19.93 per successful day
Data sources				
Health outcomes: A head to head RCT(n=306){Wall, 1998 WALL1998 /id} and trial abstract (n=171) {Lister R.K, 1997 313 /id}				

D. M. Ashcroft, A. Li Wan Po, H. C. Williams, and C. E. Griffiths. Cost-effectiveness analysis of topical calcipotriol versus short-contact dithranol: In the treatment of mild to moderate plaque psoriasis. Pharmacoeconomics 18 (5):469-476, 2000.
Quality-of-life weights: N/A **Cost sources:** Only direct unit cost of treatment considered, using the source: Monthly Index of Medical Specialities.
Comments
Source of funding: Research grant from Boots Healthcare International. **Limitations:** Unclear if best estimates of resource use, treatment effect and cost were used. Limited sensitivity analysis. Does not account for treatment failures and long term consequences of treatment. No quality of life assessment performed. **Other:**
Overall applicability*: Partially applicable Overall quality: Potentially Serious Limitations.**

Bottomley JM, Auland ME, Morais J et al. Cost-effectiveness of the two-compound formulation calcipotriol and betamethasone dipropionate compared with commonly used topical treatments in the management of moderately severe plaque psoriasis in Scotland. Curr Med Res Opin. 2007; 23(8):1887-1901.				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CUA **Study design:** Decision analytic model **Perspective:** Scottish NHS **Time horizon:** 1 year **Discounting:** N/A (less than 1 year)	**Population:** Patients with moderately severe plaque psoriasis **Cohort settings:** Start age = NA M = NA **Intervention 1:** Dovobet once daily (4 weeks) → same **Intervention 2:** Calcipotriol once daily (4 weeks) → Betamethasone dipropionate daily (4 weeks) **Intervention 3:**	**Cost components incorporated**: Topical treatment, GP consultation, Specialist outpatient consultation, course of phototherapy **Total costs (mean):** Intervention 1: £453.52 Intervention 2: £591.48 Intervention 3: £550.18 Intervention 4: £586.37 Intervention 5: £729.93 **Currency & cost year:** 2006-2007 UK pounds	**Health outcomes incorporated:** Proportion achieving PASI-75 response; relapse **Primary outcome measure (QALYs):** Intervention 1: 0.857 Intervention 2: 0.844 Intervention 3: 0.846 Intervention 4: 0.0845 Intervention 5: 0.839	**Base case ICERs:** Intervention 1 dominated all other treatments **Analysis of uncertainty** The results were sensitive to changes in the cost second-line treatment with phototherapy, cost of Dovobet, baseline utility and utility enjoyed whilst on the phototherapy waiting list. Cost of phototherapy: Dovobet cost-effective up to £400 for phototherapy; Dovobet dominant when phototherapy >£400. Cost of Dovobet: If patients used maximum dose (100 g per week), ICER relative to other comparators ranged from £11,000 to £32,000 per QALY gained.

Bottomley JM, Auland ME, Morais J et al. Cost-effectiveness of the two-compound formulation calcipotriol and betamethasone dipropionate compared with commonly used topical treatments in the management of moderately severe plaque psoriasis in Scotland. Curr Med Res Opin. 2007; 23(8):1887-1901.				
	Calcipotriol twice daily (4 weeks) → Betamethasone dipropionate daily (4 weeks) **Intervention 4:** Betamethasone dipropionate daily (4 weeks) → Calcipotriol once daily (4 weeks) **Intervention 5:** Concurrent calcipotriol (morning) and Betamethasone dipropionate (evening) (4 weeks) → same			Baseline utility: When baseline utility fell below 0.725, ICER for Dovobet >£20,000. Utility on waiting list: If utility was >0.875, ICER for Dovobet >£20,000.

Data sources

Health outcomes: Absolute risk parameters were derived from an unadjusted indirect comparison of the five topical therapies from seven randomised trials, six published (Guenther 2002, Kaufmann 2002, Kragballe 2004, Ortonne 2004, Papp 2003, Douglas 2002) and one unpublished (Study MCB 9302). The response data for each treatment was derived from the relevant treatment arms from included trials. Weighted means of the number of responders (PASI ≥75) and non-responders (PASI <75) were calculated for each treatment. Response data for second-line phototherapy was taken from Dawe 1998. Risk of relapse was informed by expert consensus, and set at 20%. The probability of response was assumed to be independent of previous treatments.

Quality-of-life weights:

Guenther 2002 derived utility values in the RCT using EQ-5D enabling utilities to be defined for patients of responder and non-responder health states at 4 weeks. Mean utility at baseline was 0.8 and mean utility gain associated with PASI ≥75 was 0.09 and with PASI <75 was 0.07.The utility for time spent on the waiting list for phototherapy was equal to baseline, 0.8. Baseline utility was varied in a one way sensitivity analysis.

Cost sources:

Costs of alternative topical treatments were based on reported mean quantities of study drug used by patients in the RCTs at the end of 4-week treatment periods. These were converted into the cheapest combination of the number of packs of medication required. Referral required one visit to the GP and one initial specialist outpatient visit. Costs of medicines were taken from the Monthly Index of Medical Specialties Feb 2007. Costs of GP consultation were taken from PSSRU 2006. Costs of outpatient visits were taken from Scotland Health Service Costs 2006 reports 045 and 046. Due to a lack of data, the cost of phototherapy (£701) was estimated based on one

Bottomley JM, Auland ME, Morais J et al. Cost-effectiveness of the two-compound formulation calcipotriol and betamethasone dipropionate compared with commonly used topical treatments in the management of moderately severe plaque psoriasis in Scotland. Curr Med Res Opin. 2007; 23(8):1887-1901.
consultant outpatient assessment followed by 20 sessions in a dermatology outpatient centre supervised by a nurse.
Comments
Source of funding: Funded by LEO Pharma, makers of Dovobet. ; **Limitations:** Treatment effects were derived from an unadjusted indirect comparison, a method which breaks randomisation and tends to generate overly precise estimates of relative efficacy. **Other:** Is it really reasonable to offer Dovobet as a second-line treatment if it has failed to produce a response as an initial treatment?
Overall applicability*: Directly applicable Overall quality: Potentially serious limitations**

Oh PI, Gupta AK, Einarson TR et al. Calcipotriol in the treatment of psoriasis of limited severity: pharacoeconomic evaluation. J Cutan Med Surg. 1997; 2(1):7-15. Ref ID: OH1997

Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
Economic analysis: CUA **Study design:** Decision analytic model. 3 pair wise comparisons were made against BMV+CAL. A secondary analysis explored second line treatments where BMV failed. **Perspective:** Canadian	**Population:** Patients with psoriasis of limited extent that had previously been treated with betamethasone. **Cohort settings:** Start age = M = **Intervention 1:** BMV (0.1%), 45g per week, switching to CAL 45g per week for 6 weeks if unsuccessful. **Intervention 2:** BMV (0.1%), 60g per week for 6 weeks, then 45g per week for rest of year if successful or CLO (0.05%) at 50g per week for 2 weeks if unsuccessful **Intervention 3:** BMV (0.1%), 60g per week for 6 weeks, then 45g per week for rest of year if successful or CLO (0.05%) at 50g per	**Cost components incorporated**: Included the cost of UVB and PUVA in treatment failure. **Total costs (mean):** Intervention 1: $587 Intervention 2: $406 Intervention 3: $499 Intervention 4: $591 Intervention 1B: $1485 Intervention 2B: $1481 Intervention 3B: $1395	**Health outcomes incorporated:** Proportion achieving PASI-75 response; relapse **Primary outcome measure (QALYs):** Intervention 1: 0.8174 Intervention 2: 0.8125 Intervention 3: 0.8029 Intervention 4: 0.7933 Intervention 1B: 0.8165 Intervention 2B: 0.7748 Intervention 3B: 0.8047	**Basecase ICERs:** Intervention 1 vs. 2: $37,755 Intervention 1 vs. 3: $6,345 Intervention 1 vs. 4: subject to dominance Intervention 1B vs. 2B:$96 Intervention 1B vs. 3B: $7258 **Analysis of uncertainty** The results were sensitive to changes in the cost and quantity of calcipotriol used, if the amount of calcipotriol reduced from 45g to 30.6g, the calcipotriol strategy (intervention 1) was dominant (less costly and more effective).

Oh PI, Gupta AK, Einarson TR et al. Calcipotriol in the treatment of psoriasis of limited severity: pharacoeconomic evaluation. J Cutan Med Surg. 1997; 2(1):7-15. Ref ID: OH1997				
Government payer perspective. **Time horizon:** 1 year **Discounting:** N/A (less than 1 year)	week for 4 weeks if unsuccessful **Intervention 4:** BMV (0.1%), 60g per week for 6 weeks, then 45g per week for rest of year if successful or CLO (0.05%) at 50g per week for 6 weeks if unsuccessful **Secondary analysis for patients that have failed BV** **Intervention 1B:** CAL **Intervention 2B:** BD **Intervention 3B:** F (0.05%) Success defined as sufficient improvement to allow dosage of drug to be reduced to 75% of initial dosage of drug. Failure defined as persistence of symptoms over 6 weeks such that a change in treatment regimen was required. UVB and PUVA were end of line treatments for any strategy that failed.	**Currency & cost year:** 1995 Canadian dollars		Analysis also sensitive to utility associated with side effects of F, whereby if patients on F and CAL had similar associated utility, F became the dominant strategy.
Data sources				
Health outcomes: Efficacy rates derived from meta-analysis, including studies from 1976 to 1994, including randomised, open, single/double blinded studies whose subjects had a defined diagnosis of plaque-type psoriasis or psoriasis vulgaris. Authors focused on studies which addressed “mild” to “mild to moderate” disease. Event rates of each drug were pooled using the DerSimonian and Laird method **Quality-of-life weights:** Based on 30 interviewees with psoriasis (respondents of an educational ad) using standard gamble technique. **Cost sources:** Costs of topical corticosteroids were obtained from the Ontario Drug Benefit Formulary (1995) and the cost of physician fees, laboratory tests and UVB therapy were obtained from the OHIP Fee Schedule (1992), and Leo Laboratory in the case of calcipotriol. The cost of PUVA was estimated from Sander et al (1993). Costs of failure and relapse estimated using resource use responses of an expert panel.				

Oh PI, Gupta AK, Einarson TR et al. Calcipotriol in the treatment of psoriasis of limited severity: pharacoeconomic evaluation. J Cutan Med Surg. 1997; 2(1):7-15. Ref ID: OH1997	
Comments	
Source of funding: Funded by LEO Pharma, makers of Dovobet. ; **Limitations:** Relatively old estimates of cost and treatment effect, unclear if best estimates of resource use used (expert opinion used), did not include all comparators in the review question, limited deterministic sensitivity analysis **Other:**	
Overall applicability*: Directly applicable Overall quality: Potentially serious limitations**	

Abbreviations: AE = adverse event; BD=twice daily; BDP= betamethasone dipropionate; BMV = betamethasone valerate; CAL = Calcipotriol; CLO =Clobetasol propionate; CI = confidence interval; CUA = cost-utility analysis; F = Fluocinonide; ICER=incremental cost effectiveness ratio; NA= not applicable; NHS= National Health Service; NR = not reported; RCT = randomised control trial, OD=once daily; PUVA=psoralen + UVA treatment; TCF gel=two compound formulation gel; QALY=Quality adjusted life year
** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*

I.6.2 Psoriasis of the scalp

A. G. Affleck, J. M. Bottomley, M. E. Auland, P. Jackson, and Jacob Ryttov. Cost effectiveness of the two-compound formulation calcipotriol and betamethasone dipropionate gel in the treatment of scalp psoriasis in Scotland. Curr.Med.Res.Opin. 27 (1):269-284, 2011.

Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
Economic analysis: CUA **Study design:** Decision analytic model **Approach to analysis:** Hypothetical patients move through the model, trying up to 3 topical treatments, with transitions defined by response to treatment and relapse following	**Population:** Patients with moderately severe scalp psoriasis **Intervention strategies:** 1: TCF→ BMV BD→ Capasal OD 2: TCF→ Calc BD→ Capasal OD 3: BMV BD→ Calc+Polytar→ TCF 4: Calc OD→ Calc BD→ Capasal OD 5: BMV BD→ Calc OD→ Calc+BDP 6: BDP OD→ Calc BD→ Capasal OD 7: Calc OD→ TCF→ BMV BD	**Cost components incorporated:** (list cost components incorporated) Cost components incorporated: Topical treatments, GP consultation, Specialist outpatient consultation **Total costs (mean):** 6: 224.61 11: 230.57 1: 230.89 7: 249.03	**Health outcomes incorporated:** Proportion achieving Investigator Global Assessment of controlled disease defined as 'absence of disease/clear' or ' very mild disease/minimal'; proportion not achieving controlled disease; skin-related adverse events; relapse **Primary outcome measure (QALYs):**	**Base case:** Strategy 6 (BDP OD – Calcipotriol BD – Capasal OD) is least cost. Strategy 11 (BMV BD – Calcipotriol+BDP – TCF) is second least costly and most effective with an ICER of £3,725 compared to strategy 6. **Subgroup analyses:** NR **Analysis of uncertainty:** Deterministic sensitivity analyses were run for several variables, including the effectiveness of TCF gel, the incidence of skin AEs, the

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discontinuation of treatment **Perspective:** Scottish NHS **Time horizon:** 1 year **Treatment effect duration:** 8 weeks or until relapse **Discounting:** N/A (less than 1 year)	8: Calc+Polytar → BMV BD → TCF 9: BMV BD → Calc OD → Calc BD 10: Calc BD → TCF → BMV BD 11: BMV BD → Calc+BDP → TCF 12: BMV BD → Calc+Polytar→ Capasal OD	3: 251.17 2: 254.19 5: 255.29 10: 256.32 8: 258.61 12: 284.37 9: 285.31 4: 311.73 **Currency & cost year:** 2009-2010 UK Pounds	6: 0.7835 11: 0.7851 1: 0.7847 7: 0.7846 3: 0.7839 2: 0.7843 5: 0.7832 10: 0.7842 8: 0.7837 12: 0.7809 9: 0.7815 4: 0.7807	decrement in utility associated with skin AEs, the risk of relapse following steroids and the consequences of treatment failure The results of these sensitivity analyses were reported in a way that makes them impossible to interpret. It is unclear what effect variation of these variables has on the results of the incremental analysis.
Data sources				
Health outcomes: Response rates and incidence of skin AE were derived from indirect pair wise comparison of data from 12 RCTs and a survey of 500 Scottish GPs. Outcome was defined by the Investigator Global Assessment (IGA) after 4 weeks. **Quality-of-life weights:** Baseline and 8-week SF-36 scores from Ortonne and colleagues (2009) were computed to SF-6D scores and utilities using a method described by Brazier and colleagues (2002). The 4-week utility gain used in the model was determined in a post-hoc analysis. Utility decrement for experiencing skin adverse events (lesional/perilesional events) was calculated as 0.0108 based on data from the same trial. **Cost sources:** Costs of topical treatments were based on reported mean quantities of study drug used by patients in the RCTs at the end of 4-week treatment periods. These were converted into the cheapest combination of the number of packs of medication required. No data was available to inform estimates of non-fixed/concurrent combination of calcipotriol and BDP, so conservative assumptions were made regarding number of packs used in the 4-week cycle. Probabilities of patient management after failure of 3 topicals estimated through a survey of Scottish health professionals. Cost of topicals from the Monthly Index of Medical Specialties (MIMS) 2010. Cost of GP consultations from Curtis and Netten 2009 (PSSRU). Cost of specialist outpatient visits from Specialty costs and activity outpatient treatments by specialty by hospital 043X (2008-09).				

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Comments
Source of funding: Funded by LEO Pharma, makers of Dovobet. ; **Limitations:** Excluded costs of treatment failures, limited deterministic sensitivity analysis with limited presentation of results, incorrect presentation of incremental analysis, unclear if best estimates of treatment effect used (indirect comparison and expert opinion used); **Other:** only applies to scalp psoriasis patients
Overall applicability*: Directly applicable Overall quality: Potentially serious limitations**

Abbreviations: CCA = cost-consequence analysis; CEA = cost-effectiveness analysis; CI = confidence interval; CUA = cost-utility analysis; d/a deterministic analysis ICER = incremental cost-effectiveness ratio; NR = not reported

** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*