Appendix I: Evidence tables – economic studies

I.1 Assessment tools

None.

I.2 Diagnostic tools for psoriatic arthritis

None.

I.3 Specialist referral for psoriatic arthritis

None.

I.4 Incidence of comorbidities in people with psoriasis

None.

I.5 Risk of skin cancer

None.

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)[10] 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

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.				
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).

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.
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*

I.7 Phototherapy

Koek MB, Sigurdsson V, van Weelden H et al. Cost effectiveness of home ultraviolet B phototherapy for psoriasis: economic evaluation of a randomised controlled trial (PLUTO study). Br Med J. 2010; 340(c1490) Ref ID: KOEK2010[1]				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CEA/CUA **Study design:** Within RCT analysis **Approach to analysis:** Pragmatic trial design; conducted from a societal perspective; outcomes measured immediately after completion of phototherapy and 12 months afterward; only first 105 of 196 trial	**Population:** Patients over 18 years with psoriasis considered eligible for phototherapy **Cohort settings:** Mean age = 41.2 / 45.0 M = 67% **Intervention 1:** Narrowband UVB (TL-01) delivered 2-3 times weekly in outpatient setting **Intervention 2:**	**Total costs* (mean per patient):** **Upon completion of phototherapy:** Intvn 1: £321 Intvn 2: £503 Incremental (2-1): £182 (CI £38 to £225, ; p=NR) **At 12m after phototherapy:** Intvn 1: £597 Intvn 2: £796 Incremental (2-1): £198 (CI £35 to £362, ; p=NR) *Indirect costs excluded from	**Primary outcome measure:** QALYs (mean per patient) **Upon completion of phototherapy:** Intvn 1: 0.0298 Intvn 2: 0.2960 Incremental (2-1): 0.0052 (CI -0.0244 to 0.0348; p=NR) **At 12m after phototherapy** Intvn 1: 1.1261 Intvn 2: 1.1528 Incremental (2-1): 0.0267 (CI -0.024 to 0.078; p=NR)	**Primary ICER (Intvn 2 vs Intvn 1):** ICER upon completion of phototherapy: £34,967 per QALY gained ICER at 12m after phototherapy: £7,432 per QALY gained Probability cost-effective: Not reported for results with direct medical costs only **Other:** £33 per addition day experiencing SAPASI 50 £12 per additional day experiencing SAPASI 75

Koek MB, Sigurdsson V, van Weelden H et al. Cost effectiveness of home ultraviolet B phototherapy for psoriasis: economic evaluation of a randomised controlled trial (PLUTO study). Br Med J. 2010; 340(c1490) Ref ID: KOEK2010[1]				
participants were followed up for 1 year; EQ-5D and SF-6D values were measured at baseline and upon completion of phototherapy and were calculated based on SAPASI, gender and employment status at 1-year follow up. **Perspective:** Dutch society **Time horizon:** After completion of phototherapy (approx 3 months); 12 months after phototherapy **Study follow-up:** 12 months following completion of phototherapy **Discounting:** Costs: none; Outcomes: none	Narrowband UVB (TL-01) delivered 3-4 times weekly at home	these results **Currency & cost year:** 2003 Dutch Euros (presented here as 2003 UK pounds‡) **Cost components incorporated:** Phototherapy, consultations with dermatologist, consultations with GP, medication	**Other outcome measures** at 12m after phototherapy **(mean):** Days experiencing SAPASI 50: Intvn 1: 210.4 Intvn 2: 216.5 Incremental (2-1): 6.1 days (CI -41.1 to 53.2; p=NR) Days experiencing SAPASI 75: Intvn 1: 111.1 Intvn 2: 127.6 Incremental (2-1): 16.5 days (CI -27.3 to 60.2; p=NR)	**Subgroup analyses:** none **Analysis of uncertainty:** Uncertainty around base case ICERs estimated using bootstrapping (1000 replications); however, the results are not presented here as they include non-medical and indirect costs 2 relevant scenario analyses performed: Using SF-6D values instead of EQ-5D: no change from base case Using invoice prices (payer perspective): intervention 1 is dominated
Data sources				
Health outcomes: The economic evaluation was conducted alongside the PLUTO study, a randomised controlled trial by Koek and colleagues[5]. Outcomes included in the economic evaluation were observed in the trial. **Quality-of-life weights:** EQ-5D and SF-6D scores were measured at baseline, after 23 irradiations and at the end of phototherapy. Utility scores were not measured during the 12 months follow-up. The authors estimated these missing scores using linear multilevel models, estimating the utility score from patients' SAPASI score, sex and employment status: EQ-5D * 100 = 89.843 – (1.428 * SAPASI) – 10.339 (only for women) + 8.341 (only when employed)				

Koek MB, Sigurdsson V, van Weelden H et al. Cost effectiveness of home ultraviolet B phototherapy for psoriasis: economic evaluation of a randomised controlled trial (PLUTO study). Br Med J. 2010; 340(c1490) Ref ID: KOEK2010[1]

SF-6D * 100 = 82.499 – (0.976 * SAPASI) – 7.939 (only for women) + 6.471 (only when employed) – (0.488 * SAPASI) (only when employed)

Cost sources: Resource use estimated within the trial through diaries recording frequency and duration of irradiation as well as frequency of visits paid to dermatologist or GP until the end of phototherapy (approx 3 months). During 12-month follow-up, participants recorded frequency of dermatologist and GP visits and occurrence and duration of newly started phototherapy in a bimonthly questionnaire. Concomitant use of psoriasis drugs (topicals and systemic therapies) was retrieved retrospectively from the participants' pharmacists. Costs of dermatologist and GP consultations were taken from the Dutch healthcare insurance board manual for costing (Oostenbrink et al. 2004). Invoice tariffs from two home care organisations were used to cost phototherapy delivered in the home. The authors note that the invoice tariffs may overestimate the real cost of home phototherapy. Costs of concomitant drugs were taken from the Dutch medication guide (Dutch Healthcare Insurance Board 2003).

Comments

Source of funding: Netherlands Organisation for Health Research and Development

Limitations: The costing perspective is one of Dutch society, thus including non-medical and indirect costs. The results presented here reflect only direct medical costs, and are therefore only a subset of those reported in the study. The time horizon is sufficient to capture health benefits of phototherapy, but it does not capture the estimated resource use or consequences for people not responding to phototherapy. The method used to estimate QALYs following completion of phototherapy is potentially less robust than having collected EQ-5D or SF-6D valuations directly from participants at 12-months follow-up.

Other:

Overall applicability*: Partially applicable **Overall quality**:** Potentially serious limitations

Abbreviations: CEA = cost-effectiveness analysis; CI = confidence interval; CUA = cost-utility analysis; ICER = incremental cost-effectiveness ratio; NR = not reported; EQ-5D = EuroQol; SF-6D = Short Form 6 dimensions ‡ Converted using 2006 Purchasing Power Parities Organisation for Economic Co-operation and Development (OECD). OECD Stat Extracts: purchasing power parities for GDP. http://stats oecd org/Index aspx?datasetcode=SNA_TABLE4 [2010 [accessed2011 Feb 24]

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

Marchetti A, Feldman SR, Kimball AB et al. Treatments for mild-to-moderate recalcitrant plaque psoriasis: expected clinical and economic outcomes for first-line and second-line care. Dermatol Online J. 2005; 11(1) Ref ID: MARCHETTI2005[2]

Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
Economic analysis: CEA **Study design:** Decision analytic model	**Population:** Patients with mild to moderate psoriasis **Cohort settings:**	**Total costs (mean per patient):** Intvn 1: £2,954 Intvn 2: £3,164 Incremental (2-1): £210	**Primary outcome measure:** Remission days (mean per patient) Intvn 1: 189.5 Intvn 2: 199.8	**Primary ICER (Intvn 2 vs Intvn 1):** ICER: £20 per additional remission day CI: NR **Other:** None

Marchetti A, Feldman SR, Kimball AB et al. Treatments for mild-to-moderate recalcitrant plaque psoriasis: expected clinical and economic outcomes for first-line and second-line care. Dermatol Online J. 2005; 11(1) Ref ID: MARCHETTI2005[2]				
Approach to analysis: **Perspective:** US third party payer **Time horizon:** 1 year **Treatment effect duration:** Intervention specific treatment effect duration Broadband UVB: 3m PUVA: 5.5m **Discounting:** Costs: NA; Outcomes: NA	Start age = not reported M = not reported **Intervention 1:** Broadband UVB (2 times/wk for 8 wks followed by once every 3 wks for 12 wks) **Intervention 2:** PUVA (2 times/wk for 14 wks followed by once every 3 wks for 22 wks)	(CI NR; p=NR) **Currency & cost year:** 2003 US dollars (presented here as 2003 UK pounds‡) **Cost components incorporated:** Acquisition cost of intervention, administration costs, follow-up costs, cost of adverse events	Incremental (2-1): 10.3 (CI NR; p=NR) **Other outcome measures (mean):** None	**Subgroup analyses:** None **Analysis of uncertainty:** No sensitivity analyses were reported.
Data sources				
Health outcomes: Clinical outcomes were computed using published data on probabilities for superior response (defined as a ≥75% improvement in the physical signs and smptoms of disease) and probabilities of relapse as well as the duration of remission. Days spent in remission were the ultimate measure of effect. Single studies served as the source of effectiveness for each intervention. Iest and colleagues[6] was used to inform the effectiveness of broadband UVB and Lauharanta and colleagues [7] was used for PUVA. Koo and colleagues was used to inform the duration of treatment effect. Incidences of specific adverse events were taken from several different sources. **Quality-of-life weights:** NA **Cost sources:** Total costs for drugs were based on their wholesale acquisition cost from the *2003 Drug Topics Red Book*. Costs for clinical procedures such as administration of phototherapy and screening and monitoring were based on Medicare 2003 reimbursement rates (no reference cited).				
Comments				
Source of funding: NR **Limitations:** The study was based on clinical practice in the United States, and although costs were based on Medicare reimbursement rates, it is unclear how applicable this would be to practice in the UK NHS. The study used the outcome of mean total 'remission days' instead of the NICE preferred measure of QALYs. The treatment effect estimates were based on an unadjusted indirect comparison from an unsystematic review of the evidence instead of meta-analysis or network meta-analyses based on a systematic review. No sensitivity analysis was reported. There is no cost-effectiveness threshold for 'additional remission days' by which to judge the cost-effectiveness of interventions. **Other:**				
Overall applicability*: Partially applicable **Overall quality**:** Very serious limitations				

Abbreviations: CEA = cost-effectiveness analysis; CI = confidence interval; CUA = cost-utility analysis; ICER = incremental cost-effectiveness ratio; NR = not reported; ‡ Converted using 2006 Purchasing Power Parities Organisation for Economic Co-operation and Development (OECD). OECD Stat Extracts: purchasing power parities for GDP. http://stats oecd org/Index aspx?datasetcode=SNA_TABLE4 [2010 [accessed2011 Feb 24]
** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*

Pearce DJ, Nelson AA, Fleischer AB et al. The cost-effectiveness and cost of treatment failures associated with systemic psoriasis therapies. J Dermatol Treat. 2006; 17(1):29-37. Ref ID: PEARCE2006[3]				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CEA **Study design:** Simple decision model **Approach to analysis:** Performed an unadjusted indirect comparison to estimate the mean effectiveness (defined as the proportion of patients achieving a PASI75 or total body clearance) of interventions; calculated costs for each intervention; combined costs and outcomes into a cost per additional 1% achieving PASI 75 **Perspective:** US third-party payer	**Population:** Patients with moderate to severe psoriasis **Cohort settings:** Mean age range = 41 to 46 yrs M percent range = 61% to 83% **Intervention 1:** Acitretin (25 mg/day) **Intervention 2:** Cyclosporine (400 mg/day) **Intervention 3:** Methotrexate (15 mg/week) **Intervention 4:** Narrowband UVB(3 times/wk) **Intervention 5:** PUVA (3 times / wk; 40 mg methosoxalen with each treatment)	**Total costs (mean per patient):** Intvn 1: £910 Intvn 2: £1,580 Intvn 3: £280 Intvn 4: £1,704 Intvn 5: £2,514 **Currency & cost year:** 2003 US dollars (presented here as 2003 UK pounds‡) **Cost components incorporated:** Acquisition cost of intervention, administration costs, screening and monitoring costs	**Primary outcome measure:** Proportion achieving PASI75 or total body clearance Intvn 1: 52% Intvn 2: 83% Intvn 3: 70% Intvn 4: 72% Intvn 5: 84% **Other outcome measures (mean):** None	**Primary ICER** **Intvn 2 vs Intvn 3** (Cyclosporine vs Methotrexate)**:** £100 per additional 1% achieving PASI 75 or total body clearance **Intvn 5 vs Intvn 2** (PUVA vs Cyclosporine)**:** £934 per additional 1% achieving PASI75 or total body clearance Acitretin was dominated by Methotrexate and Narrowband UVB was dominated by Cyclosporine. **Other:** None **Subgroup analyses:** None **Analysis of uncertainty:** The authors performed a deterministic sensitivity analysis varying efficacies by a factor of ± 5%. The results of this sensitivity analysis are not reported in such a way as to determine their likely effect on the basecase results.

Pearce DJ, Nelson AA, Fleischer AB et al. The cost-effectiveness and cost of treatment failures associated with systemic psoriasis therapies. J Dermatol Treat. 2006; 17(1):29-37. Ref ID: PEARCE2006[3]				
Time horizon: 12 weeks **Treatment effect duration:** NA **Discounting:** Costs: NA; Outcomes: NA				
Data sources				
Health outcomes: Effectiveness for each intervention (defined as the percentage of patients achieving PASI75 for systemic therapies or total body clearance for phototherapy) was estimated through a systematic review of randomised trial evidence. A weighted average proportion was calculated for each intervention by pooling the results of relevant trial arms (e.g. an unadjusted indirect comparison). **Quality-of-life weights:** NA **Cost sources:** Total costs for drugs were based on their wholesale acquisition cost from the *2003 Drug Topics Red Book*. Costs for clinical procedures such as administration of phototherapy and screening and monitoring were based on Medicare 2003 reimbursement rates (no reference cited). For drugs prescribed based on weight, the authors assumed a patient weight of 80 kg.				
Comments				
Source of funding: Galderma Laboratories **Limitations:** The study was based on clinical practice in the United States, and although costs were based on Medicare reimbursement rates, it is unclear how applicable this would be to practice in the UK NHS. The study used the outcome of proportion achieving a PASI75 or total body clearance instead of the NICE preferred measure of QALYs. The treatment effect estimates were based on an unadjusted indirect comparison instead of meta-analysis or network meta-analyses. The time horizon of the analysis is 12 weeks, potentially too short to observe the full effectiveness of some interventions and insufficient to judge the longer term outcomes of treatment. Costs associated with treatment failures are ignored. There is no cost-effectiveness threshold for 'additional 1% achieving PASI75 or total body clearance' by which to judge the cost-effectiveness of interventions. The study was funded by Galderma Laboratories, but they are not makers of any of the compared interventions. **Other:**				
Overall applicability*: Partially applicable **Overall quality**:** Very serious limitations				

Abbreviations: CEA = cost-effectiveness analysis; CI = confidence interval; CUA = cost-utility analysis; ICER = incremental cost-effectiveness ratio; NR = not reported; ‡ Converted using 2006 Purchasing Power Parities Organisation for Economic Co-operation and Development (OECD). OECD Stat Extracts: purchasing power parities for GDP. http://stats oecd org/Index aspx?datasetcode=SNA_TABLE4 [2010 [accessed2011 Feb 24]

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

I.8 Phototherapy combined with acitretin

Pearce DJ, Nelson AA, Fleischer AB et al. The cost-effectiveness and cost of treatment failures associated with systemic psoriasis therapies. J Dermatol Treat. 2006; 17(1):29-37. Ref ID: PEARCE2006[1]				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: CEA **Study design:** Simple decision model **Approach to analysis:** Performed an unadjusted indirect comparison to estimate the mean effectiveness (defined as the proportion of patients achieving a PASI75 or total body clearance) of interventions; calculated costs for each intervention; combined costs and outcomes into a cost per additional 1% achieving PASI 75 **Perspective:** US third-party payer **Time horizon:** 12 weeks	**Population:** Patients with moderate to severe psoriasis **Cohort settings:** Mean age range = 41 to 46 yrs M percent range = 61% to 83% **Intervention 1:** Acitretin (25 mg/day) **Intervention 2:** Cyclosporine (400 mg/day) **Intervention 3:** Methotrexate (15 mg/week) **Intervention 4:** Narrowband UVB(3 times/wk) **Intervention 5:** PUVA (3 times / wk; 40 mg methosoxalen with each treatment)	**Total costs (mean per patient):** Intvn 1: £910 Intvn 2: £1,580 Intvn 3: £280 Intvn 4: £1,704 Intvn 5: £2,514 **Currency & cost year:** 2003 US dollars (presented here as 2003 UK pounds‡) **Cost components incorporated:** Acquisition cost of intervention, administration costs, screening and monitoring costs	**Primary outcome measure:** Proportion achieving PASI75 or total body clearance Intvn 1: 52% Intvn 2: 83% Intvn 3: 70% Intvn 4: 72% Intvn 5: 84% **Other outcome measures (mean):** None	**Primary ICER** **Intvn 2 vs Intvn 3** (Cyclosporine vs Methotrexate): £100 per additional 1% achieving PASI 75 or total body clearance **Intvn 5 vs Intvn 2** (PUVA vs Cyclosporine): £934 per additional 1% achieving PASI75 or total body clearance Acitretin was dominated by Methotrexate and Narrowband UVB was dominated by Cyclosporine. **Other:** None **Subgroup analyses:** None **Analysis of uncertainty:** The authors performed a deterministic sensitivity analysis varying efficacies by a factor of ± 5%. The results of this sensitivity analysis are not reported in such a way as to determine their likely effect on the basecase results.

Pearce DJ, Nelson AA, Fleischer AB et al. The cost-effectiveness and cost of treatment failures associated with systemic psoriasis therapies. J Dermatol Treat. 2006; 17(1):29-37. Ref ID: PEARCE2006[1]				
Treatment effect duration: NA **Discounting:** Costs: NA; Outcomes: NA				
Data sources				
Health outcomes: Effectiveness for each intervention (defined as the percentage of patients achieving PASI75 for systemic therapies or total body clearance for phototherapy) was estimated through a systematic review of randomised trial evidence. A weighted average proportion was calculated for each intervention by pooling the results of relevant trial arms (e.g. an unadjusted indirect comparison). **Quality-of-life weights:** NA **Cost sources:** Total costs for drugs were based on their wholesale acquisition cost from the *2003 Drug Topics Red Book*. Costs for clinical procedures such as administration of phototherapy and screening and monitoring were based on Medicare 2003 reimbursement rates (no reference cited). For drugs prescribed based on weight, the authors assumed a patient weight of 80 kg.				
Comments				
Source of funding: Galderma Laboratories **Limitations:** The study was based on clinical practice in the United States, and although costs were based on Medicare reimbursement rates, it is unclear how applicable this would be to practice in the UK NHS. The study used the outcome of proportion achieving a PASI75 or total body clearance instead of the NICE preferred measure of QALYs. The treatment effect estimates were based on an unadjusted indirect comparison instead of meta-analysis or network meta-analyses. The time horizon of the analysis is 12 weeks, potentially too short to observe the full effectiveness of some interventions and insufficient to judge the longer term outcomes of treatment. Costs associated with treatment failures are ignored. There is no cost-effectiveness threshold for 'additional 1% achieving PASI75 or total body clearance' by which to judge the cost-effectiveness of interventions. The study was funded by Galderma Laboratories, but they are not makers of any of the compared interventions. **Other:**				
Overall applicability*: Partially applicable **Overall quality**:** Very serious limitations				

I.9 Dithranol, coal tar and vitamin D and vitamin D analogues combined with phototherapy

None.

I.10 Systemic therapy

Opmeer BC, Heydendael VMR, de Borgie CAJM et al. Costs of treatment in patients with moderate to severe plaque psoriasis: economic analysis in a randomized controlled comparison of methotrexate and cyclosporine. *Arch Dermatol.* 2004; 140(6):685-690. Ref ID: OPMEER2004				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: Cost minimisation analysis **Study design:** Trial-based analysis **Approach to analysis:** Assumed equal efficacy between methotrexate and ciclosporin and used prospectively collected resource data to compare costs of 16-week treatment and 36-week follow-up. **Perspective:** Dutch society (but only direct medical costs reported here) **Time horizon:** 1 year (16 weeks treatment; 36 weeks follow-up) **Treatment effect duration:** NA **Discounting:** NA	**Population:** Patients with moderate to severe plaque psoriasis **Cohort settings:** Mean age = 41.6 (13) MTX; 38.3 (12.4) Cyclosp M = 65% MTX; 69% Cyclosp **Intervention 1:** Methotrexate, 16 weeks treatment **Intervention 2:** Ciclosporin, 16 weeks treatment	**Total costs (mean per patient):** Intvn 1: £1,934 Intvn 2: £2,410 Incremental(2-1): -£476 (CI NR; p=NR) **Currency & cost year:** 1999 Dutch Euros (presented here as 1999 UK pounds‡) **Cost components incorporated:** Medication, outpatient visits, comedication during follow-up, diagnostic and laboratory tests, additional visits to health care providers. *Direct non-medical and indirect costs were reported but have been excluded from the data reported here	**Primary outcome measure:** Effectiveness between treatments assumed to be equal	**Cost minimisation analysis** (If effectiveness of methotrexate and ciclosporin is equal): Methotrexate has lower overall costs; therefore, methotrexate is cost-saving compared to ciclosporin. **Analysis of uncertainty:** Visual inspection of box and whisker plots indicates that costs accrued during treatment were significantly different between strategies, but this did not hold during 36 weeks follow-up.

Opmeer BC, Heydendael VMR, de Borgie CAJM et al. Costs of treatment in patients with moderate to severe plaque psoriasis: economic analysis in a randomized controlled comparison of methotrexate and cyclosporine. *Arch Dermatol.* 2004; 140(6):685-690. Ref ID: OPMEER2004
Data sources
Health outcomes: Analysis was performed prospectively as part of the RCT comparing methotrexate and ciclosporin conducted by Heydendael 2003[9]. **Quality-of-life weights:** NA **Cost sources:** Resource data was collected prospectively as part of the RCT. Patients were seen every other week during the first month and every 4 weeks in the subsequent 12 weeks of treatment and 36 weeks of follow-up. Clinical (PASI), functional (SF-36) and economic (resource utilisation) outcomes were measured at each visit. Unit prices were based on previous estimates[11], Dutch pharmaceutical cost listings, guideline prices and national tariffs.
Comments
Source of funding: Dutch Health Insurance Board **Limitations:** Short time horizon (1 year); relatively old cost estimates (1999/2000); no sensitivity analysis reported; costing perspective is Dutch society: some uncertainty about applicability of Dutch estimates of resource use and unit costs; cost-minimisation method **Other:**
Overall applicability*: Partially applicable **Overall quality**:** Potentially serious limitations

Abbreviations: NR = not reported ‡ Converted using 2006 Purchasing Power Parities Organisation for Economic Co-operation and Development (OECD). OECD Stat Extracts: purchasing power parities for GDP. http://stats oecd org/Index aspx?datasetcode=SNA_TABLE4 [2010 [accessed2011 Feb 24]
** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*

Sizto S, Bansback N, Feldman SR et al. Economic evaluation of systemic therapies for moderate to severe psoriasis. Br J Dermatol. 2009; 160(6):1264-1272. Ref ID: SIZTO2009

Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
Economic analysis: Cost utility analysis **Study design:** Decision analytic model **Approach to analysis:** The model separately examines a trial period and a treatment period. Only	**Population:** Patients with moderate to severe psoriasis **Cohort settings:** Start age = not stated M = not stated **Intervention 1:** Methotrexate (15-25 mg/wk,	**Total costs (mean per patient):** Intvn 1: Not reported Intvn 2: Not reported Incremental(2-1): £1,857 (CI £1,736, £2,125 ; p=NR) **Currency & cost year:** 2005/06 UK pounds	**Primary outcome measure:** QALYs (mean per patient) Intvn 1: 0.129 Intvn 2: 0.079 Incremental (2-1): - 0.05 (CI -0.034, -0.069; p=NR)	**Primary ICER (Intvn 2 vs Intvn 1):** Methotrexate dominates ciclosporin Probability cost-saving: approximately 80% (pa) **Analysis of uncertainty:** One way sensitivity analyses around assumed weight of patient (60 kg), increased response rates and higher dosage of ciclosporin do not change results.

Sizto S, Bansback N, Feldman SR et al. Economic evaluation of systemic therapies for moderate to severe psoriasis. Br J Dermatol. 2009; 160(6):1264-1272. Ref ID: SIZTO2009				
responders during the trial period continue treatment and at a later point they may withdraw due to loss of efficacy or toxicity **Perspective:** UK NHS **Time horizon:** not stated **Treatment effect duration:** Assumed to maintain response achieved at the end of trial **Discounting:** Not stated	16 weeks treatment) **Intervention 2:** Cyclospoine (3 mg/kg/day for 80 kg patient, 12 weeks treatment)	**Cost components incorporated:** Medications, monitoring and inpatient visits; cost of dermatology outpatient visits and GP visits excluded		
Data sources				
Health outcomes: Short term efficacy of treatments was determined through a systematic review and network meta-analysis, described in full by Bansback and colleagues[10]. No estimates, sources or assumptions reported for the longer term treatment parameters. **Quality-of-life weights:** EQ-5D weights were attached to responder (moderate (≥PASI50 to <PASI90) and good (≥PASI90)) and non-responder (<PASI50) health states. Weights based on data from the CHAMPION[12] and REVEAL (Menter 2008) trials. **Cost sources:** Unit costs of drugs were taken from the British National Formulary 2007. Unit costs for laboratory tests and outpatient visits for the administration of drugs were taken from Woolacott and colleagues[3] and the NHS Reference Costs and National Tariff (2004). Out of date costs were inflated using the PSSRU inflation index.				
Comments				
Source of funding: Abbott Laboratories **Limitations:** Time horizon not stated; estimates of long-term effectiveness/withdrawal of treatments not stated; excludes important costs of outpatient dermatology and GP visits; funded by Abbott laboratories (makers of Adalimumab – biologic therapy included in the analysis); no discounting rates reported for costs or effects **Other:**				
Overall applicability*: Directly applicable **Overall quality**:** Potentially serious limitations				

Abbreviations: CI = confidence interval; ICER = incremental cost-effectiveness ratio; NR = not reported; pa = probabilistic analysis
** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*

Woolacott N, Hawkins N, Mason A et al. Etanercept and efalizumab for the treatment of psoriasis: a systematic review. Health Technol Assess. 2006; 10(46):1-iv. Ref ID: WOOLACOTT2006				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: Cost utility analysis **Study design:** Decision analytic model **Approach to analysis:** The model separately examines a trial period and a treatment period. Only responders during the trial period continue treatment and at a later point they may withdraw due to loss of efficacy or toxicity **Perspective:** UK NHS **Time horizon:** up to 10 years **Treatment effect duration:** Assumed to maintain response achieved at the end of trial **Discounting:** Costs: 6%; Outcomes: 1.5%	**Population:** Patients with moderate to severe chronic plaque psoriasis **Intervention 1:** Methotrexate (10-25 mg/wk, 16 weeks treatment) **Intervention 2:** Ciclosporin (2.5-5 mg/day, 12 weeks treatment)	**Total costs (mean per patient):** Intvn 1:Not reported Intvn 2: Not reported Incremental(2-1): £3,771 (CI £3265,£3,809; p=NR) **Currency & cost year:** 2004/05 UK Pounds **Cost components incorporated:** Direct NHS costs only: drugs and their administration, monitoring, outpatient visits and inpatient stays	**Primary outcome measure:** QALYs (mean per patient) Intvn 1: 0.126 Intvn 2: 0.122 Incremental (2-1): -0.004 (CI 0, -0.007; p=NR)	**Primary ICER (Intvn 2 vs Intvn 1):** Methotrexate dominates ciclosporin Probability most cost-effective: 100% **Analysis of uncertainty:** Evaluation of methotrexate and ciclosporin was part of a sensitivity analysis to an analysis focused on the evaluation of two biologics, etanercept and efalizumab. In this sensitivity analysis, both methotrexate and ciclosporin were cost-saving compared to 'best supportive care and all biologics except for infliximab, which was not cost-effective.
Data sources				
Health outcomes: Short term efficacy of treatments was determined through a systematic review and network meta-analysis, described in full within the same report. Estimates of longer term treatment duration were based on an assumed annual drop-out rate for responding patients receiving treatment and a maximum assumed				

Woolacott N, Hawkins N, Mason A et al. Etanercept and efalizumab for the treatment of psoriasis: a systematic review. Health Technol Assess. 2006; 10(46):1-iv. Ref ID: WOOLACOTT2006
treatment period based on published guidelines (Griffiths 2004; Sterry 2004) if appropriate. Mean length of treatment response was then estimated from a 10-year Markov model with annual cycles. **Quality-of-life weights:** Health state utilities were estimated from an analysis of data from three etanercept regulatory trials and the HODaR Database (http://www.hodar.co.uk/). The estimates process consisted of 2 stages. First, the mean change in DLQI score between basely and week 12 was estimated for patients from etanercept trials with different levels of PASI response and different baseline DLQI scores. This analysis was facilitated by access to patient-level data by Wyeth but is commercial in confidence. Data within the HODaR database included patients who had completed both the DLQI and EQ-5D. These data were used to 'map' the change in DLQI associated with PASI responses to changes in EQ-5D utility. An ordinary least-squares linear regression analysis of the DLQI-EQ-5D data from HODaR allowed for the calculation of an algorithm (commercial in confidence). Based on these data, the mean gain in utility was estimated for the various PASI response categories (<PASI50, ≥PASI50 to <PASI75, ≥PASI75 to <PASI90, and ≥PASI90). **Cost sources:** Drug dosage and titration rates were based on the British National Formulary. Several sources were used to inform the estimates of types and frequency of laboratory tests. No published data were available to inform an estimate of the rate of hospitalisation, so estimates were based on a range of scenarios informed by expert opinion. Length of stay for an inpatient admission was based on Department of Health Hospital Episode Statistics for psoriasis and supported by evidence from recently conducted audits. Frequency of liver biopsy was based on estimates from a recent economic evaluation[13]. Expert opinion was used to generate the frequency of outpatient visits, drug tablet sizes, monitoring requirements and titration rates not available in the literature. Prices were taken from the BNF where available. Prices of monitoring tests were obtained from the Biochemistry Department at York NHS Trust. Outpatient visits were based on the NHS Reference Cost category 'Other attendance with other investigation or procedure.' The cost of an inpatient day was based on an average of 'Elective inpatient HRG data, major dermatological conditions J39' and 'Elective inpatient HRG data, major dermatological conditions J40.' Where necessary, costs were updated to 2003-04 using the PSSRU inflation index.
Comments
Source of funding: NHS R&D HTA Programme **Limitations:** Analysis was mainly focused on evaluation of etanercept and efalizumab – ciclosporin and methotrexate were evaluated as part of one probabilistic scenario analysis; discounting rates were 6% for costs and 1.5% for benefits instead of 3.5% for both **Other:** This was the economic analysis underpinning NICE Technology Appraisal 103, guidance on the use of etanercept and efalizumab.
Overall applicability*: Directly applicable **Overall quality**:** Minor limitations

Abbreviations: CI = confidence interval; ICER = incremental cost-effectiveness ratio; NR = not reported; pa = probabilistic analysis
** Directly applicable / Partially applicable / Not applicable; ** Minor limitations /Potentially serious Limitations / Very serious limitations*

I.11 Methotrexate and risk of hepatotoxicity

None.

I.12 Methotrexate and monitoring for hepatotoxicity

Chalmers R, Kirby B, Smith A et al. Replacement of routine liver biopsy by procollagen III aminopeptide for monitoring patients with psoriasis receiving long-term methotrexate: a multicentre audit and health economic analysis. Br J Dermatol. 2005; 152(3):444-450. Ref ID: CHALMERS2005				
Study details	**Population & interventions**	**Costs**	**Health outcomes**	**Cost effectiveness**
Economic analysis: Cost consequence analysis **Study design:** Multicentre prospective audit in four centres in the UK and Ireland. Health care costs and outcomes of two intervention groups from centres where serial PIIINP measurement was employed were compared to those of two control groups from centres in which liver biopsy was used for monitoring patients at risk of methotrexate-induced hepatotoxicity. **Approach to analysis:** Within study analysis **Perspective:** UK NHS	**Population:** Patients established on methotrexate for psoriasis; similar duration of psoriasis between groups (24-27 years) **Group 1:** Serial PIIINP only (Manchester) n=138 Mean age = 38.3 years Mean duration of MTX therapy = 72 months **Group 2:** Serial PIIINP (London) + baseline liver biopsy (note that no patient actually underwent baseline liver biopsy) n=28 Mean age = 35.6 years Mean duration of MTX therapy = 66.3 months **Group 3:** Liver biopsy only (Essex) n=43	**Unit cost of monitoring tests:** PIIINP measurement: £22.50 Liver Biopsy: Group 1: £577.00 Group 2: £451.72 Group 3: NR Group 4: £270.00 **Total costs (mean per patient):** Group 1: £113 Group 2: £99 Group 3 & 4: £76 **Currency & cost year:** 2001 UK pounds **Cost components incorporated:** Direct medical costs related to different monitoring methods (e.g. hospitalisation, biopsy, histopathology, PIIINP analysis)	**Primary outcome measure:** **Mean biopsies per patient per year:** **Group 1: 0.04** (19 patient qualified for, but only 10 underwent liver biopsy; 8/10 had minor histology findings and did not change treatment, two had mild portal fibrosis for which change in treatment was considered) **Group 2: 0.02** (1 liver biopsy was performed and showed inflammation with portal fibrosis, thus the patient discontinued MTX) **Group 3: 0.26** (26 liver biopsies were peformed; 9/26 were normal and 16/26 had minor abnormalities and 1/26 had Roenigk grade 3a changes and discontinued MTX) **Group 4: 0.30**	The total costs of different strategies are highly dependent on the unit cost of performing a liver biopsy. When the unit cost of liver biopsy was low (e.g. £270 as quoted for group 3), then a strategy of only routine liver biopsy was less costly than routine PIIINP. However, when the unit cost of liver biopsy was higher (e.g. £641 as quoted in 2000 NHS reference costs), then serial PIIINP with occasional liver biopsy was cost-saving.

Chalmers R, Kirby B, Smith A et al. Replacement of routine liver biopsy by procollagen III aminopeptide for monitoring patients with psoriasis receiving long-term methotrexate: a multicentre audit and health economic analysis. Br J Dermatol. 2005; 152(3):444-450. Ref ID: CHALMERS2005				
Time horizon: **Treatment effect duration:** 2 yrs **Discounting:** NA	Mean age = 44.6 years Mean duration of MTX therapy = 73.2 months **Group 4:** Liver biopsy only (Dublin) n= 44 Mean age = 42.4 years Mean duration of MTX therapy = 87.9 months		(21 liver biopsies were performed; 5/21 were normal and 14/21 had minor abnormalities and 2/21 had Roenigk grade 3a changes and discontinued MTX) Mean liver biopsy rate from Essex and Dublin combined was 0.28 biopsies per patient per year. 54% of control patients (Essex and Dublin) underwent liver biopsy during 2 year study period, but in only 3 did the results change management. Thus, 15.7 biopsies were required to detect each abnormality of sufficient severity to influence management.	
Data sources				
Health outcomes: Within study analysis **Quality-of-life weights:** NA **Cost sources:** Local NHS costs; 2000 NHS reference costs				
Comments				
Source of funding: Northwest Regional Research and Development Fund **Limitations:** Given that treatment with methotrexate may continue for more than 2 years, time horizon may be insufficient. Does not report incidence of adverse events/ complications associated with liver biopsy and any effect on costs. Within trial analysis and so does not incorporate all available evidence on differences between monitoring methods but results appear consistent with results of clinical review. QALYs not used (cost consequence analysis).				

Chalmers R, Kirby B, Smith A et al. Replacement of routine liver biopsy by procollagen III aminopeptide for monitoring patients with psoriasis receiving long-term methotrexate: a multicentre audit and health economic analysis. Br J Dermatol. 2005; 152(3):444-450. Ref ID: CHALMERS2005	
Other:	
Overall applicability*: Partially applicable	**Overall quality**:** Very serious limitations

I.13 Second line biologic therapy

None.

I.14 Cognitive behavioural therapy

None.

I.15 Self-management

Kernick D, Cox A, Powell R et al. A cost consequence study of the impact of a dermatology-trained practice nurse on the quality of life of primary care patients with eczema and psoriasis. Br J Gen Pract. 2000; 50:555-558. Ref ID: KERNICK2000

Study details	Population & interventions	Costs	Health outcomes	Cost effectiveness
Economic analysis: CCA **Study design:** Within RCT analysis **Approach to analysis:** DLQI and Euroqol QoL tool (0-100) were measured at baseline and 4 months later	**Population:** patients between 18 and 65 years who had a diagnosis of psoriasis (35%) or eczema (57%) or both (9%) **Intervention 1:** Routine GP care **Baseline characteristics:** Psoriasis: 35% Eczema: 57% Mixed: 9%	**Total costs (mean per patient):** Intvn 1: NR Intvn 2: NR **Currency & cost year:** 1997 UK pounds **Cost components incorporated:** Nurse and GP time for training and consultations	**Primary outcome measure:** QALYs (mean per patient) Intvn 1: 0.2127 Intvn 2: 0.2188 Incremental (2-1): 0.0062 (CI , ; p=NR)	**Primary ICER (Intvn 2 vs Intvn 1):** ICER: NR **Subgroup analyses:** NA **Analysis of uncertainty:** NR

Kernick D, Cox A, Powell R et al. A cost consequence study of the impact of a dermatology-trained practice nurse on the quality of life of primary care patients with eczema and psoriasis. Br J Gen Pract. 2000; 50:555-558. Ref ID: KERNICK2000				
Perspective: UK NHS **Time horizon:** 4 months **Treatment effect duration:** NA **Discounting:** Costs = NA; Outcomes = NA	Mean age = 47.4 (SD = ±18.4) Baseline DLQI: 6.1 (SD = ±4.9) Baseline Euroquol QoL: 62.9 (SD = ± 20.8) **Intervention 2:** Dermatology liaison nurse available in primary care **Baseline characteristics:** Psoriasis: 37% Eczema: 61% Mixed: 2% Mean age = 51.7 (SD = ±15.8) Baseline DLQI: 6.8 (SD = ±5.0) Baseline Euroquol QoL: 62.5 (SD = ± 23.1)			
Data sources				
Health outcomes: Health outcomes in terms of change in DLQI and change in Euroqol QoL as measured on a visual analogue scale were evaluated directly in the trial. Other qualitative outcomes were also reported and included in the clinical evidence review. **Quality-of-life weights:** Euroqol QoL was measured on a visual analogue scale directly from patients. **Cost sources:** Costs for nursing and GP time were taken from *Unit costs of health and social care* (Netten 1997).				
Comments				
Source of funding: Leo Pharmaceuticals **Limitations:** The population is a mixture of patients with psoriasis and eczema; costs are not aggregated and presented as mean/median cost per patient; costs of topicals and any other treatments administered not included; unit costs are out of date for current decision-making; no incremental analysis could be performed for costs; no sensitivity analyses were undertaken; funded by Leo Pharmaceuticals, makers of vitamin D analogues and combined vitamin D analogue and potent corticosteroid products. **Other:**				

Kernick D, Cox A, Powell R et al. A cost consequence study of the impact of a dermatology-trained practice nurse on the quality of life of primary care patients with eczema and psoriasis. Br J Gen Pract. 2000; 50:555-558. Ref ID: KERNICK2000	
Overall applicability*: Partially applicable	**Overall quality**:** Very serious limitations