Cost-effectiveness of an 8% Capsaicin Patch in the Treatment of Brachioradial Pruritus and Notalgia Paraesthetica, Two Forms of Neuropathic Pruritus

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In brachioradial pruritus and notalgia paraesthetica, the 8% capsaicin patch is a novel and effective, but cost-intense, therapy. Routine data for 44 patients were collected 6 months retrospectively and prospectively to first patch application. The cost to health insurance and the patient, and patient-reported outcomes were analysed (visual analogue scale, numerical rating scale, verbal rating scale for pruritus symptoms, Dermatological Life Quality Index, and Patient Benefit Index). Mean inpatient treatment costs were reduced by €212.31, and mean outpatient treatment and medication costs by €100.74 per patient (p.p.). However, these reductions did not offset the high cost of the patch itself (€767.02 p.p.); thus the total cost to health insurance increased by €453.97 p.p. ($p \leq 0.01$). The additional costs of therapy to the patient decreased by €441.06, thus the overall cost p.p. remained approximately the same (€3,306.03 vs. €3,318.94). Capsaicin patch therapy resulted in reduced pruritus, improved quality of life and greater patient benefit, thus long-term cost-efficiency analyses are necessary.

Key words: pruritus; cost; capsaicin; cost-benefit analysis.

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Notalgia paraesthetica (NP) and brachioradial pruritus (BRP) are 2 forms of neuropathic pruritus (1). The sensation may be composed of pain, pruritus or pricking, either on the upper back (NP) or on the lateral arm (BRP) (2, 3). The aetiology is attributed mostly to the damage of peripheral nerves, with a reduction in intraepidermal nerve fibre density (4, 5).

In a range of diseases with a similar pathogenesis, such as post-herpetic neuralgia, peripheral neuropathic pain and atopic dermatitis, the cutaneous application of capsaicin is one of the therapeutic mainstays (6–9). Eradication of morphologically and functionally abnormal epidermal nerve fibres by capsaicin, followed by re-growth of normal epidermal nerve fibres, evens out the sensory symptoms. Within this therapeutic setting, the capsaicin 8% dermal patch (Qutenza™, Astellas Pharma GmbH, Munich, Germany) is a new option, providing a higher concentration of capsaicin than capsaicin-containing creams, and therefore resulting in a longer period of symptom relief, of up to 12 weeks after a single 30–60-min application (7, 8). A single application is recommended, with repetition every 3 months, if necessary.

The similar pathogenesis of neuropathic pruritus also suggests a high relevance of capsaicin patch therapy for these patients. Topical application of capsaicin-containing creams (0.025–0.1%) has already been described to be effective in NP and BRP, but to relieve symptoms only transiently (3, 10, 11). Further treatment options, such as antihistaminic drugs, neuroleptics or antidepressants, are often ineffective, or are associated with systemic side-effects. The application of high-dose capsaicin might thus provide a therapeutic breakthrough for NP and BRP patients, as the 8% capsaicin patch has the potential to reduce itch and pain rapidly with almost no side-effects and a long-lasting effect (12).

Since a single capsaicin patch application costs €341.22, cost-effectiveness studies are required by medical decision-makers in order to obtain insight into the therapeutic relevance of the capsaicin patch. The current study analysed the cost and benefit of the novel treatment for NP and BRP patients within routine care. To our knowledge, this is the first cost-effectiveness study in pruritus research.

MATERIALS AND METHODS

Study design

Routine data were analysed for 44 BRP and NP patients 6 months retrospectively to the first application of the capsaicin patch (T1) and 6 months prospectively (T2) at the Center for Chronic Pruritus, Münster, Germany. A paper-based standardized interview on sociodemographic criteria, different patient-reported outcomes and cost variables was complemented by data from the medical records.

Inclusion criteria were: written informed consent, a confirmed diagnosis of BRP and NP; compulsory health insurance; and age ≥18 years. The treatment decision was made according to clinical routine. Ethical approval was gained from the ethics commission of the State Medical Association Westfalen-Lippe, Münster, Germany (2015-262-fS). The patients completed an informed consent form.

Patient-reported outcomes

Pruritus intensity was measured using the following validated scales: a 0–10 visual analogue scale (VAS); a 0–3 verbal rating scale (VRS); and a 0–10 numerical rating scale (NRS) (13–17). Considerations of the minimum clinically important difference (MCID) suggest that a reduction of at least 2.0 points (VAS and NRS) is required for a change in pruritus symptoms to be perceived by the patient (18). As NP and BRP can induce pain sensations a pain VAS (0–10) was also examined.

Anxiety and depression are common symptoms in patients with chronic pruritus (CP) and were measured using the Hospital Anxiety and Depression Scale questionnaire (HADS; 0–21) (13).

Patients' quality of life (QoL) was analysed with the Dermatological Life Quality Index (DLQI). A score of 0–30 can be calculated, indicating "no", "little", "moderate", "strong" or "very strong" impairment (19, 20). An improvement of at least 4 points has been shown to be the MCID (21).

The Patient Benefit Index (PBI) provides a validated method for the assessment of patient-relevant treatment benefit, related to the individual importance of 27 treatment needs in the form of a global score of 0–4. The patient is thought to have a relevant benefit from the respective therapy in case of a PBI ≥ 1 ("cut-off-value"). The higher the value of the PBI, the higher the therapeutic benefit is thought to be (22).

Cost definition and calculation

Costs were classified into direct cost, first to the German compulsory health insurance and secondly to the patient, and indirect cost through loss of productivity.

Direct costs to the compulsory health insurance were the cost for inpatient treatment, outpatient medication, consultation and diagnostics. These costs were assessed according to the Diagnosis Related Groups (DRG) and Einheitlicher Bewertungsmaßstab, Uniform Value Scale (EBM) catalogues valuable in 2014, according to information on "standard service volumes" by the appropriate Association of Statutory Health Insurance Physicians, and according to valid medication prices in Germany, as referenced in the Lauer-Taxe (German medical information system) or in pharmacies.

Direct costs to the patient included travel expenses or the time taken for skin care. The time taken for skin care, as well as the loss of productivity due to loss of working time (indirect cost), were estimated from the mean gross income according to the human capital approach (23, 24).

Almost all cost questionnaires were completed. One patient had missing values for the calculation of outpatient treatment cost and travel expenses at T2. Due to the fact that this patient did not differ from the other study patients according to clinical and economic outcomes, missing values were replaced by a group mean at T2.

The cost-effectiveness analysis was performed with a pre-post comparison of the cost-effectiveness relation at T1 and T2, which is calculated by the division of the change in benefit by the change in cost in order to determine the incremental cost-effectiveness ratio (23, 25, 26).

Statistical analysis

Data input was executed by means of double entries by experienced data managers. All data were described using standard statistical parameters (frequencies for categorical data, mean value, standard deviation for continuous data) using IBM SPSS Statistics Version 22.0. The paired Wilcoxon signed-rank test was applied for significance testing. A result of $p \leq 0.05$ was seen as statistically significant.

RESULTS

Three-quarters of patients were female ($n = 33$) and one-quarter male ($n = 11$), with a mean age of 61.3 ± 10.0 years. A high proportion, 57.5% ($n = 23$), were retired and only 24.5% ($n = 10$) of patients were economically active.

BRP was diagnosed in 24 patients, NP in 19 patients, and one patient had both diagnoses. The mean disease duration at baseline was 16.9 ± 23.9 months, with a maximal duration of 92.0 months.

Cost of illness

At T1, 15.9% ($n = 7$) of patients had needed an inpatient pruritus treatment within the past 6 months, at T2 only one patient had needed such treatment. Outpatient visits to the doctor accounted for 6.3 ± 5.2 (T1) and 4.7 ± 2.5 visits (T2) ($p > 0.05$). Taking into account the entire study population, mean inpatient and outpatient treatment cost for diagnostics and consultations were reduced by €227.23 per patient (p.p.) (**Table I**).

Table I. Cost to the compulsory health insurance and to the patient (direct cost) 6 months before (T1) and 6 months after (T2) start of treatment with the capsaicin patch ($n = 44$)

Cost/patient/6 months, €	T1 Mean (95% CI)	T2 Mean (95% CI)	Diff. T2–T1	*p*-value
Health insurance cost				
Inpatient treatment	316.90 (114.75–572.99)	104.59 (0.00–313.76)	–212.31	0.236
Outpatient treatment	81.25 (69.86–94.06)	66.33 (56.15–77.33)	–14.92	0.050
Systemic medication	352.34 (205.79–558.19)	277.74 (168.98–408.72)	–74.60	0.157
Topical medication	56.23 (34.18–85.53)	45.01 (25.30–70.75)	–11.22	0.232
Cost to the health insurance without capsaicin patch	806.72 (547.65–1,106.38)	493.67 (289.10–789.16)	–313.05	0.003
Cost for the capsaicin patch	0.00	767.02	+767.02	
Total cost to the health insurance	806.72 (563.34–1,091.78)	1,260.69 (992.21–1,613.82)	+453.97	0.005
Patient cost				
Travel expenses	208.22 (92.82–401.73)	168.89 (107.45–256.61)	–39.33	0.514
Other expenses	254.39 (163.19–361.47)	162.95 (108.00–224.58)	–91.44	0.034
Cost for loss of time for home skin care	2,036.70 (1,394.99–2,731.40)	1,726.41 (1,175.86–2,290.89)	–310.29	0.234
Total cost to the patient	2,499.31 (1,834.95–3,270.59)	2,058.25 (1,495.30–2,675.74)	–441.06	0.103
Total cost without capsaicin patch	3,306.03 (2,527.30–4,156.20)	2,551.92 (1,906.51–3,240.05)	–754.11	0.011
Total cost	3,306.03 (2,527.30–4,156.20)	3,318.94 (2,651.80–4,044.53)	+12.91	0.944

CI: confidence interval for mean (bootstrap results).

Table II. Systemic and topical treatments 6 months before (T1) and 6 months after (T2) the treatment start with the capsaicin patch (*n* = 44)[a]

	T1 *n* (%)	T2 *n* (%)
Systemic treatments		
Antihistamines	29 (65.9)	18 (40.9)
Anticonvulsants	26 (59.1)	23 (52.3)
Antidepressants	6 (13.6)	8 (18.2)
Other psychoanaleptics	1 (2.3)	0 (0.0)
Aprepitant	1 (2.3)	0 (0.0)
Naltrexone	1 (2.3)	2 (4.5)
Topical treatments		
Topical capsaicin	16 (36.4)	14 (31.8)
Topical corticosteroids	12 (27.3)	8 (18.2)
Topical immunomodulators	3 (6.8)	2 (4.5)
Topical antimycotics	2 (4.5)	0 (0.0)
Combination treatment	1 (2.3)	0 (0.0)
Topical anti-infectives	0 (0.0)	1 (2.3)
Over-the-counter	4 (9.1)	8 (18.2)

[a]Multiple selections possible.

Nearly all patients (98%, $n=43$) received a systemic pruritus medication, 61.4% a topical medication ($n=27$) prior to T1. After the first patch application, only 77.3% of patients ($n=34$) still needed systemic medication and 50.0% ($n=22$) needed topical treatments (**Table II**). The total cost of medication decreased by €85.82 p.p. (Table I).

A single capsaicin patch costs €341.22. As the number of individual patch applications differed (**Table III**), the mean cost of the capsaicin patch was €767.02 p.p. within 6 months (Table I).

To summarize, total costs to the compulsory health insurance were €806.72 at T1 and €1,260.69 at T2 ($p \leq 0.01$). Neglecting the cost of the capsaicin patch, costs were reduced by €313.05 (Table I).

Cost to the patients for travel expenses and skin care or special food decreased after introduction of the patch treatment. Time lost in skin care was reduced from T1 (2.5 ± 2.9 h per week) to T2 (2.1 ± 2.3 h per week), resulting in a total cost to the patient reduced by €441.06 (Table I).

Summarizing the costs to the compulsory health insurance and to the patient, these were nearly equal before and after the introduction of the capsaicin patch treatment. Without the cost of the capsaicin patch, costs were significantly lower at T2 (€2,551.92) than at T1 (€3,306.03).

Indirect cost for loss of labour time could be calculated for 2 patients at T1 (10 days and 14 days of unemployability, respectively) and for 1 patient at T2. The last patient had 183 days of unemployability. Therefore, indirect costs were €137.45 ± €646.38 at T1 and €1,048.09 ± €6,952.25 at T2.

Treatment benefits

According to all scales, except the VRS, pruritus and pain were significantly reduced from T1 to T2. Patients also presented a significantly higher rating of QoL according to the DLQI (**Table IV**).

The anxiety and depression ratings on the HADS scales did not show significant differences.

The patient-relevant benefit increased after treatment with the capsaicin patch. At T1 65.5% (19 out of 29 patients) had a relevant therapeutic benefit (PBI ≥ 1), and at T2 83.3% (20 out of 24 patients).

Table III. Capsaicin patch treatment regimen (*n*=44)

Number of patches needed because of pruritus size	T1 (first patch application) *n* (%)	T1+3 months *n* (%)	T1+6 months (T2) *n* (%)
0	0 (0.0)	29 (65.9)	36 (81.8)
1	26 (59.1)	5 (11.4)	5 (11.4)
2	12 (27.3)	9 (20.5)	2 (4.5)
3	1 (2.3)	0 (0.0)	0 (0.0)
4	5 (11.4)	1 (2.3)	1 (2.3)

Cost-effectiveness

The introduction of the capsaicin patch treatment increased the cost to the compulsory health insurance by €453.97 per patient per 6 months. Cost-effectiveness was calculated using the formula (**Fig. 1**), taking the perspective of the compulsory health insurance.

The costs to reach a 1-unit improvement, as well as a patient-relevant improvement in the respective benefit outcomes, are shown in **Table V**.

DISCUSSION

This cost-effectiveness analysis is, to our knowledge, the first in pruritus research, and compares the cost and benefit of a new and highly effective, but cost-intense 8% capsaicin patch treatment for BRP and NP.

Taking into account all cost changes 6 months after the introduction of the capsaicin patch, total costs remained almost the same (€3,306.03 p.p. at T1, €3,318.94 p.p. at

Table IV. Patient-reported outcomes (PRO) and their change after the introduction of the capsaicin patch treatment (*n* = 44)

	T1 (first patch application) Mean (95% CI)	T2 (T1 + 6 months) Mean (95% CI)	*p*-value
VAS [0–10][a]			
Pruritus VAS past 24 h	4.5 (3.8–5.3)	3.3 (2.5–4.3)	0.017
Pruritus VAS past 12 h	5.3 (4.7–6.0)	2.9 (2.1–3.7)	0.000
Pruritus VAS maximum past 4 weeks	6.3 (5.6–7.2)	4.9 (3.7–5.8)	0.026
Pruritus VAS mean past 4 weeks	5.7 (4.9–6.4)	4.0 (3.1–4.9)	0.006
Pain VAS past 12 h	3.4 (2.5–4.4)	1.8 (1.1–2.7)	0.014
VRS [0–3][a]: Pruritus VRS	1.7 (1.5–1.9)	1.4 (1.1–1.7)	0.052
NRS [0–10][a]: Pruritus NRS	5.1 (4.4–5.8)	4.1 (3.1–5.0)	0.015
DLQI [0–10][a]	7.4 (5.7–9.3)	4.6 (3.1–6.4)	0.001
HADS–Anxiety [0–21][a]	7.6 (6.2–9.1)	7.1 (5.7–8.5)	0.401
HADS–Depression [0–21][a]	5.9 (4.6–6.8)	5.0 (3.8–6.1)	0.089
PBI [0–4][b]	1.5 (1.3–2.2)	2.1 (1.6–2.4)	0.153

[a]Best achievable value to worst value. [b]Worst value to best achievable value.
CI: confidence interval for mean (bootstrap results); VAS: visual analogue scale: VRS: verbal rating scale; NRS: numerical rating scale; DLQI: Dermatological Life Quality Index; HADS: Hospital Anxiety and Depression Scale; PBI: Patient Benefit Index.

$$PrePostComparison = \frac{Cost_{T2} - Cost_{T1}}{Benefit_{T2} - Benefit_{T1}} = \frac{1260.69\ € - 806.72\ €}{\text{Benefit difference}} = \frac{453{,}97\ €}{\text{Benefit difference}}$$

Fig. 1. Cost-effectiveness calculation from the perspective of the compulsory health insurance.

T2). Where cost to the patient in the form of travel expenses or loss of time due to home skin-care diminished by €441.06, the total cost to the compulsory health insurance increased significantly, by €453.97 p.p. (Table I). This is mainly due to the high costs of the capsaicin patch itself (€341.22 per patch). In our collective 41% of patients needed more than one patch at T1, as the pruritus area had to be covered completely by the patch. In addition, repeated treatments had to be carried out because of a certain duration of the epidermal nerve fibre alteration, which is subject to actual research. A further application after 3 months was needed in 34.1% of patients, and in only 18.2% again after 6 months. Together with similar findings in pain research (27), it might be supposed, that the treatment repetitions, and therefore treatment cost, will further decline in a longer time horizon with the alteration of epidermal nerve fibres.

Similarly, further medical costs also declined continuously. Within 6 months, there was an almost 40% reduction in medical costs for concomitant treatments and diagnostics. Nevertheless, this cost reduction did not outweigh the additional costs for the patch, as Schweitzer et al. (28) also concluded in another study on pain patients. Many of the systemic treatments cannot be withdrawn abruptly, but need to be tapered off over a period of some weeks. In our study, 77.3% of all patients still had to continue their prior systemic medication for some time after the first patch application.

Therefore, if the study horizon was extended, continuous cost reductions for concomitant medication, as well as for the patch applications themselves, might outweigh the initial high product costs of the capsaicin patch. This aspect should be addressed in further studies.

On the benefit side, the capsaicin patch treatment led to an improvement in different patient-reported outcomes. The pruritus was significantly reduced on different scales (VAS, NRS). The reduction ranged from 1.0 points (NRS past 24 h) to 2.4 points (VAS past 12 h). Other studies report slightly greater reductions in pruritus in patients with CP, ranging from 2.8 to 3.7 points for gabapentin (NRS), paroxetine, fluvoxamine or pimecrolimus and hydrocortisone cream (VAS) (15, 29–31). As the reference period for the pruritus evaluation was not always indicated, these data cannot be directly compared.

The patch also helped to reduce pain sensations, which are frequent in NP and BRP. In pain research a 30% reduction is established as the minimum required effect. In our study the whole collective achieved a 47% pain reduction with patch treatment, which appears to be even higher than in pain patients (31). Our study has a comparably long time interval of 6 months due to the economic perspective. The reported studies had time intervals of up to 12 weeks maximum, due to which a comparison of the pain reduction is not fully reliable (32).

Before the start of treatment at T1, the mean DLQI was 7.4 points, which indicates a moderate effect on QoL and is comparable to other CP or dermatological patients (33–36). With patch therapy, QoL could be improved significantly, by 2.8 points, thus the score suggests only a small impairment in QoL. Other dermatological studies report similar reductions in the DLQI (31, 37, 38), which is why we assume that our patients also perceived the QoL improvement, even though the proposed MCID of 4 points (21) has not been reached. A 4-point DLQI improvement would therefore cost €644.52, which is low compared with US$2,250–27,136 for a 5-point DLQI improvement in psoriasis patients, as shown by cost-effectiveness studies for biologic treatments (26).

Regarding the increase in patient-relevant benefit by the patch treatment, approximately one-third of patients additionally presented a PBI ≥1 (T1 65.5%, T2 83.3%). Thus, the mean PBI increased from 1.5 to 2.1 points. This result was not significant, probably due to a reduced sample size as a result of missing values of up to 34% at T1 ($n = 15$ missing) and 45% at T2 ($n = 20$ missing).

It has to be kept in mind, that the capsaicin patch treatment was recently introduced as a therapeutic alternative to BP and NRP, resulting from scientific research

Table V. Benefit difference after the introduction of the capsaicin patch treatment from T1 (first patch application) to T2 (T1 + 6 months) and cost-effectiveness ($n = 44$)

	Benefit difference T2–T1 Mean	Cost per 1 unit incremental benefit per patient[c], € Base: Mean	Cost per patient for achieving the MCID[d], €
DLQI [0–30][a]	−2.8	161.13	644.52 (4 points)
HADS–Anxiety [0–21][a]	−0.5	907.94	n.a.
HADS–Depression [0–21][a]	−0.9	504.41	n.a.
Pruritus VAS past 24 h [0–10][a]	−1.2	378.31	756.62 (2 points)
Pruritus VAS past 12 h [0–10][a]	−2.4	189.15	378.30 (2 points)
Pruritus VAS maximum past 4 weeks [0–10][a]	−1.4	324.26	648.52 (2 points)
Pruritus VAS mean past 4 weeks [0–10][a]	−1.7	267.04	534.08 (2 points)
Pain VAS past 12 h [0–10][a]	−1.6	283.73	n.a.
Pruritus VRS [0–3][a]	−0.3	1,513.23	n.a.
Pruritus NRS [0–10][a]	−1.0	453.97	907.94 (2 points)
PBI–Score [0–4][b]	0.6	756.62	n.a.

[a]Best achievable value to worst value. [b]Worst value to best achievable value. [c]Cost to reach a 1-unit improvement of the respective outcome. [d]Cost to reach a patient-relevant improvement of the respective outcome.

DLQI: Dermatological Life Quality Index; HADS: Hospital Anxiety and Depression Scale; VAS: visual analogue scale: VRS: verbal rating scale; NRS: numerical rating scale.

on the origin of the disease. In addition, the 2 diseases are very rare and their treatment is mostly carried out in university centres specialized in the treatment of CP. The small patient number and the monocentric character of the study impair generalization of our results, especially as cost calculations are always country-specific.

In conclusion, according to the present data, the introduction of the 8% capsaicin patch treatment led to an overall improvement, not only of pruritus and pain, but also of QoL. Important therapeutic aims appeared to be fulfilled better through the novel treatment than through other standard therapies used within the previous 6 months. Although, at first glance, the patch treatment presented high costs to the health insurance companies, other medical and patient-related costs could be reduced, so that total costs did not increase within a short time of only 6 months. Moreover, all cost categories, especially to the health insurance companies, might be subject to further cost reductions in the long run, as the patch treatment regimen will change to longer patch application intervals, and co-medication will be further reduced. Therefore, the capsaicin patch treatment can be seen as a promising treatment for NP and BRP, 2 forms of neuropathic pruritus, which has the potential to be even more cost-effective in the long-term. Further studies including control groups with other treatment options should be promoted in the future. In addition, research concerning the MCID of different scales is of vital importance regarding future discussions on the cost-effectiveness of pruritus treatments.

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REFERENCES

1. Ständer S, Weisshaar E, Mettang T, Szepietowski JC, Carstens E, Ikoma A, et al. Clinical classification of itch: a position paper of the International Forum for the Study of Itch. Acta Derm Venereol 2007; 87: 291–294.
2. Fantini F, Zorzi F, Rizzitelli G, Benassi L, Pincelli C. Notalgia Paresthetica: clinical, pathological and immunohistochemical observations in 12 cases. Eur J Dermatol 1994; 4: 649–653.
3. Raison-Peyron N, Meunier L, Acevedo M, Meynadier J. Notalgia paresthetica: clinical, physiopathological and therapeutic aspects. A study of 12 cases. J Eur Acad Dermatol Venereol 1999; 12: 215–221.
4. Huesmann T, Cunha PR, Osada N, Huesmann M, Zanelato TP, Phan NQ, et al. Notalgia paresthetica: a descriptive two-cohort study of 65 patients from Brazil and Germany. Acta Derm Venereol 2012; 92: 535–540.
5. Schmelz M, Hilliges M, Schmidt R, Ørstavik K, Vahlquist C, Weidner C, et al. Active "itch fibers" in chronic pruritus. Neurology 2003; 6: 546–566.
6. Ständer S, Luger T, Metze D. Treatment of prurigo nodularis with topical capsaicin. J Am Acad Dermatol 2001; 44: 471–478.
7. Raber JM, Reichelt D, Grüneberg-Oelker U, Philipp K, Stubbe-Dräger B, Husstedt IW. Capsaicin 8% as a cutaneous patch (Qutenza™): analgesic effect on patients with peripheral neuropathic pain. Acta Neurol Belg 2015; 115: 335–343.
8. Backonja M, Wallace MS, Blonsky ER, Cutler BJ, Malan P Jr, Rauck R, et al. NGX-4010, a high-concentration capsaicin patch, for the treatment of postherpetic neuralgia: a randomised, double-blind study. Lancet Neurol 2008; 7: 1106–1112.
9. Armstrong EP, Malone DC, McCarberg B, Panarites CJ, Pham SV. Cost-effectiveness analysis of a new 8% capsaicin patch compared to existing therapies for postherpetic neuralgia. Curr Med Res Opin 2011; 27: 939–950.
10. Wallengren J, Klinker M. Successful treatment of notalgia paresthetica with topical capsaicin: vehicle-controlled, double-blind, crossover study. J Am Acad Dermatol 1995; 32: 287–289.
11. Leibsohn E. Treatment of notalgia paresthetica with capsaicin. Cutis 1992; 49: 335–336.
12. Zeidler C, Lüling H, Dieckhöfer A, Osada N, Schedel F, Steinke S, et al. Capsaicin 8% cutaneous patch: a promising treatment for brachioradial pruritus? Br J Dermatol 2015; 172: 1669–1671.
13. Ständer S, Blome C, Breil B, Bruland P, Darsow U, Dugas M, et al. Assessment of pruritus – current standards and implications for clinical practice: consensus paper of the Action Group Pruritus Parameter of the International Working Group on Pruritus Research (AGP). Hautarzt 2012; 63: 521–522.
14. Ständer S, Darsow U, Mettang T, Gieler U, Maurer M, Ständer H, et al. S2k Leitlinie – Chronischer Pruritus. J Dtsch Dermatol Ges 2012; 10: 1–27.
15. Ständer S, Augustin M, Reich A, Blome C, Ebata T, Phan NQ, et al. Pruritus assessment in clinical trials: consensus recommendations from the International Forum for the Study of Itch (IFSI) Special Interest Group Scoring Itch in Clinical Trials. Acta Derm Venereol 2013; 93: 509–514.
16. Phan NQ, Blome C, Fritz F, Gerss J, Reich A, Ebata T, et al. Assessment of pruritus intensity: prospective study on validity and reliability of the visual analogue scale, numerical rating scale and verbal rating scale in 471 patients with chronic pruritus. Acta Derm Venereol 2012; 92: 502–507.
17. Reich A, Heisig M, Phan NQ, Taneda K, Takamori K, Takeuchi S, et al. Visual analogue scale: evaluation of the instrument for the assessment of pruritus. Acta Derm Venereol 2012; 92: 497–501.
18. Reich A, Riepe C, Anastasiadou Z, Medrek K, Augustin M, Szepietwoski J, Ständer S. Itch assessment with visual analogue scale and numerical rating scale: determination of minimal clinically important difference in chronic itch. Acta Derm Venereol 2016; 96: 978–980.
19. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) – a simple practical measure for routine clinical use. Clin Exp Dermatol 1994; 19: 210–216.
20. Hongbo Y, Thomas CL, Harrison MA, Salek MS, Finlay AY. Translating the science of quality of life into practice: what do dermatology life quality index scores mean? J Invest Dermatol 2005; 125: 659–664.
21. Basra MK, Salek MS, Camilleri L, Sturkey R, Finlay AY. De-

termining the minimal clinically important difference and responsiveness of the Dermatology Life Quality Index (DLQI): further data. Dermatology 2015; 230: 27–33.
22. Blome C, Augustin M, Siepmann D, Phan NQ, Rustenbach SJ, Ständer S. Measuring patient-relevant benefits in pruritus treatment: development and validation of a specific outcomes tool. Br J Dermatol 2009; 161: 1143–1148.
23. Drummond MF, Sculpher MJ, Torrance GW, O'Brien BJ, Stoddart GL. Methods for the economic evaluation of health care programmes. 3rd edn. New York: Oxford University Press; 2005.
24. Bock JO, Brettschneider C, Seidl H, Bowles D, Holle R, Greiner W, et al. Ermittlung standardisierter Bewertungssätze aus gesellschaftlicher Perspektive für die gesundheitsökonomische Evaluation. Gesundheitswesen 2014; 77: 53–61.
25. Icks A, Chernyak N, Bestehorn K, Brüggenjürgen B, Bruns J, Damm O, et al. Methoden der gesundheitsökonomischen Evaluation in der Versorgungsforschung. Gesundheitswesen 2010; 72: 917–933.
26. Nelson AA, Pearce DJ, Fleischer AB Jr, Balkrishnan R, Feldman SR. Cost-effectiveness of biologic treatments for psoriasis based on subjective and objective efficacy measures assessed over a 12-week treatment period. J Am Acad Dermatol 2008; 58: 125–135.
27. Backonja MM, Malan TP, Vanhove GF, Tobias JK. NGX-4010, a high-concentration capsaicin patch, for the treatment of postherpetic neuralgia: a randomized, double-blind, controlled study with an open-label extension. Pain Med 2010; 11: 600–608.
28. Schweitzer M, Caillet JB, Paillet C, Baude C, Fagnoni P, Aulagner G, et al. Capsaicin cutaneous patch: a cost-consequences study in a French university hospital. Therapie 2015; 70: 359–368.
29. Maciel AA, Cunha PR, Laraia IO, Trevisan F. Efficacy of gabapentin in the improvement of pruritus and quality of life of patients with notalgia paresthetica. An Bras Dermatol 2014; 89: 570–575.
30. Ständer S, Böckenholt B, Schürmeyer-Horst F, Weishaupt C, Heuft G, Luger TA, et al. Treatment of chronic pruritus with the selective serotonin reuptake inhibitors paroxetine and fluvoxamine: results of an open-labeled, two-arm proof-of-concept study. Acta Derm Venereol 2009; 89: 45–51.
31. Siepmann D, Lotts T, Blome C, Braeutigam M, Phan NQ, Butterfass-Bahloul T, et al. Evaluation of the antipruritic effects of topical pimecrolimus in non-atopic prurigo nodularis: results of a randomized, hydrocortisone-controlled, double-blind phase II Trial. Dermatology 2013; 227: 353–360.
32. Uçeyler N, Sommer C. High-dose capsaicin for the treatment of neuropathic pain: what we know and what we need to know. Pain Ther 2014; 3: 73–84.
33. Steinke S, Langenbruch A, Ständer S, Franzke N, Augustin M. Therapeutic benefits in atopic dermatitis care from the patients' perspective: results of the German national health care study 'Atopic Health'. Dermatology 2014; 228: 350–359.
34. Lundberg L, Johannesson M, Silverdahl M, Hermansson C, Lindberg M. Quality of life, health-state utilities and willingness to pay in patients with psoriasis and atopic eczema. Br J Dermatol 1999; 141: 1067–1075.
35. Augustin M, Reich K, Reich C, Purwins S, Jeff Rustenbach S, Schäfer I, et al. Quality of psoriasis care in Germany – results of the national study PsoHealth 2007. J Dtsch Dermatol Ges 2008; 6: 640–645.
36. Warlich B, Fritz F, Osada N, Bruland P, Stumpf A, Schneider G, et al. Health-related quality of life in chronic pruritus: an analysis related to disease etiology, clinical skin conditions and itch intensity. Dermatology 2015; 231: 253–259.
37. Shikiar R, Willian MK, Okun MM, Thompson CS, Revicki DA. The validity and responsiveness of three quality of life measures in the assessment of psoriasis patients: results of a phase II study. Health Qual Life Outcomes 2006; 4: 71.
38. Shikiar R, Harding G, Leahy M, Lennox RD. Minimal important difference (MID) of the Dermatology Life Quality Index (DLQI): results from patients with chronic idiopathic urticaria. Health Qual Life Outcomes 2005; 3: 36.