Gemeinsamer Bundesausschuss

Kriterien zur Bestimmung der zweckmäßigen Vergleichstherapie

und

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

und

Schriftliche Beteiligung der wissenschaftlich-medizinischen Fachgesellschaften und der Arzneimittelkommission der deutschen Ärzteschaft (AkdÄ) zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: 2022-B-043 Dupilumab

Stand: April 2023

I. Zweckmäßige Vergleichstherapie: Kriterien gemäß 5. Kapitel § 6 VerfO G-BA

Dupilumab **[Prurigo nodularis bei Erwachsenen]** **Kriterien gemäß 5. Kapitel § 6 VerfO**	
Sofern als Vergleichstherapie eine Arzneimittelanwendung in Betracht kommt, muss das Arzneimittel grundsätzlich eine Zulassung für das Anwendungsgebiet haben.	siehe unter II.
Sofern als Vergleichstherapie eine nicht-medikamentöse Behandlung in Betracht kommt, muss diese im Rahmen der GKV erbringbar sein.	Phototherapie: NB-UV-B-Bestrahlungen
Beschlüsse/Bewertungen/Empfehlungen des Gemeinsamen Bundesausschusses zu im Anwendungsgebiet zugelassenen Arzneimitteln/nicht-medikamentösen Behandlungen	Es liegen keine Beschlüsse vor
Die Vergleichstherapie soll nach dem allgemein anerkannten Stand der medizinischen Erkenntnisse zur zweckmäßigen Therapie im Anwendungsgebiet gehören.	*Siehe systematische Literaturrecherche*

II. Zugelassene Arzneimittel im Anwendungsgebiet

Wirkstoff **ATC-Code** **Handelsname**	**Anwendungsgebiet** (Text aus Fachinformation)
Zu bewertendes Arzneimittel:	
Dupilumab D11AH05 Dupixent®	Zugelassenes Anwendungsgebiet: “Dupixent ist angezeigt zur Behandlung von mittelschwerer bis schwerer Prurigo nodularis (PN) bei Erwachsenen, die für eine systemische Therapie in Betracht kommen.”
topische Kortikosteroide (nur beispielhafte Auflistung)	
Betamethason **z.B. Cordes® Beta Creme**	Zur Behandlung von entzündlichen Hauterkrankungen, bei denen die Anwendung von stark wirksamen Glucocorticoiden angezeigt ist.
Hydrocortison **z.B. Hydrocutan® Creme 1 %**	Zur Behandlung von entzündlichen Hauterkrankungen, bei denen schwach wirksame, topisch anzuwendende Glukokortikosteroide angezeigt sind.
Triamcinolon-acetonid **z.B. Volon® A Creme**	Dermatosen, allergische bzw. unspezifische Entzündungen, die auf eine lokale Kortikoid-Behandlung ansprechen und bei denen die Anwendung eines mittelstark wirksamen Kortikoids angezeigt ist, wie z.B. akute und chronische Ekzemformen, Psoriasis vulgaris.
Zur Behandlung der Prurigo nodularis bei Erwachsenen sind keine Arzneimittel zugelassen.	

Quellen: AMIce-Datenbank, Fachinformationen (Stand April 2023)

Gemeinsamer Bundesausschuss

Abteilung Fachberatung Medizin

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie nach § 35a SGB V

Vorgang: 2022-B-043 (Dupilumab)

Auftrag von:	Abt. AM
Bearbeitet von:	Abt. FB Med
Datum:	17. März 2022

Inhaltsverzeichnis

Abkürzungsverzeichnis 3
1 Indikation 4
2 Systematische Recherche 4
3 Ergebnisse 5
3.1 Cochrane Reviews 5
3.2 Systematische Reviews 9
3.3 Leitlinien 11
4 Detaillierte Darstellung der Recherchestrategie 16
Referenzen 18

Abkürzungsverzeichnis

AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
CP	chronic pruritus
CPG	chronic prurigo
CPUO	chronic pruritus of unknown origin
ECRI	ECRI Guidelines Trust
G-BA	Gemeinsamer Bundesausschuss
GIN	Guidelines International Network
GoR	Grade of Recommendations
HR	Hazard Ratio
IQWiG	Institut für Qualität und Wirtschaftlichkeit im Gesundheitswesen
KI	Konfidenzintervall
LoE	Level of Evidence
NICE	National Institute for Health and Care Excellence
NK1R	neurokinin 1 receptor
OR	Odds Ratio
PN	prurigo nodularis
RR	Relatives Risiko
SIGN	Scottish Intercollegiate Guidelines Network
TRIP	Turn Research into Practice Database
WHO	World Health Organization

1 Indikation

Behandlung von mittelschwerer bis schwerer Prurigo nodularis bei erwachsenen Patienten, die für eine systemische Therapie in Betracht kommen.

Hinweis zur Synopse: Informationen hinsichtlich nicht zugelassener Therapieoptionen sind über die vollumfängliche Darstellung der Leitlinienempfehlungen dargestellt.

2 Systematische Recherche

Es wurde eine systematische Literaturrecherche nach systematischen Reviews, Meta-Analysen und evidenzbasierten systematischen Leitlinien zur Indikation *Prurigo* durchgeführt und nach PRISMA-S dokumentiert [A]. Die Recherchestrategie wurde vor der Ausführung anhand der PRESS-Checkliste begutachtet [B]. Es erfolgte eine Datenbankrecherche ohne Sprachrestriktion in: The Cochrane Library (Cochrane Database of Systematic Reviews), PubMed. Die Recherche nach grauer Literatur umfasste eine gezielte, iterative Handsuche auf den Internetseiten von Leitlinienorganisationen. Ergänzend wurde eine freie Internetsuche (*https://www.startpage.com*) unter Verwendung des privaten Modus, nach aktuellen deutsch- und englischsprachigen Leitlinien durchgeführt.

Der Suchzeitraum wurde auf die letzten fünf Jahre eingeschränkt und die Recherche am 22.02.2022 abgeschlossen. Die detaillierte Darstellung der Recherchestrategie inkl. verwendeter Suchfilter sowie eine Angabe durchsuchter Leitlinienorganisationen ist am Ende der Synopse aufgeführt. Mit Hilfe von EndNote wurden Dubletten identifiziert und entfernt. Die Recherche ergab 44 Referenzen.

In einem zweistufigen Screening wurden die Ergebnisse der Literaturrecherche bewertet. Im ersten Screening wurden auf Basis von Titel und Abstract nach Population, Intervention, Komparator und Publikationstyp nicht relevante Publikationen ausgeschlossen. Zudem wurde eine Sprachrestriktion auf deutsche und englische Referenzen vorgenommen. Im zweiten Screening wurden die im ersten Screening eingeschlossenen Publikationen als Volltexte gesichtet und auf ihre Relevanz und methodische Qualität geprüft. Dafür wurden dieselben Kriterien wie im ersten Screening sowie Kriterien zur methodischen Qualität der Evidenzquellen verwendet. Basierend darauf, wurden insgesamt 4 Referenzen eingeschlossen. Es erfolgte eine synoptische Darstellung wesentlicher Inhalte der identifizierten Referenzen.

3 Ergebnisse

3.1 Cochrane Reviews

Andrade A et al., 2020 [1].

Interventions for chronic pruritus of unknown origin.

Fragestellung

To assess the effects of interventions for chronic pruritus of unknown origin (CPUO) in adults and children.

Methodik

Population:

- We included participants of any age (adults and children), of either sex, with a diagnosis of chronic pruritus of unknown origin (CPUO), as defined in category VI of the IFSI classification. This includes individuals receiving a diagnosis of pruritus for whom no dermatological, systemic, neurological, or psychiatric disorder has been identified as a cause (Stander 2007). We included participants who underwent some degree of diagnostic workup to exclude dermatological disorders, systemic disease, neurological disorders, or psychiatric disorders. A diagnostic workup for CPUO could include a wide range of evaluations, from minimal to very thorough, depending on the settings in which the study has been performed. The diagnostic workup may have included a full medical history; a full physical examination; a complete blood count; ferritin levels; a chest radiograph; measurements of hepatic, renal, and thyroid function; serology for sexually transmitted infection; and, when appropriate, tests that identify endemic parasitic infection. The review did not include participants with drug-induced pruritus.
- When we found studies with a subset of patients with a diagnosis of CPUO, we included them if data were presented separately for these patients, or if a majority (> 50%) of included participants met the inclusion criteria. If data were not available for this subset of participants, we tried to retrieve this information from the investigators before excluding the study.

Intervention:

- Non-pharmacological interventions
  - Emollient creams
  - Neutral or mild pH soaps
  - Natural products
  - Alternative therapies
- Topical pharmacological interventions
  - Corticosteroids
  - Cooling lotions
  - Calcineurin inhibitors
  - Anaesthetics
  - Antihistamines
  - Phosphodiesterase-4 inhibitors

  - Capsaicin
  - Salicylic acid
  - Ketamine
  - Amitriptyline and other topical antidepressants
  - Cannabinoids
  - Botulinum toxins
- Systemic pharmacological interventions
  - Antihistamines
  - Opioid receptor antagonists
  - Antidepressants
  - Anticonvulsants
  - Substance P and neurokinin 1 receptor (NK1R) antagonists
  - Cannabinoids
  - Thalidomide
  - Monoclonal antibodies and other biological agents
  - Phototherapy
  - Ondansetron

Komparator:

- Active treatment versus placebo, sham procedure, or no treatment or equivalent (e.g. waiting list)
- Active treatment versus another active treatment

Endpunkte:

- Patient- or parent-reported pruritus intensity, Adverse events, Health-related quality of life (HRQoL), Sleep disturbances, Depression, Patient satisfaction

Recherche/Suchzeitraum:

- Up to July 2019: Cochrane Skin Group Specialised Register, CENTRAL, MEDLINE, EMBASE, and trials registries.

Qualitätsbewertung der Studien:

- Cochrane approach / GRADE

Ergebnisse

Anzahl eingeschlossener Studien / Charakteristika der Population:

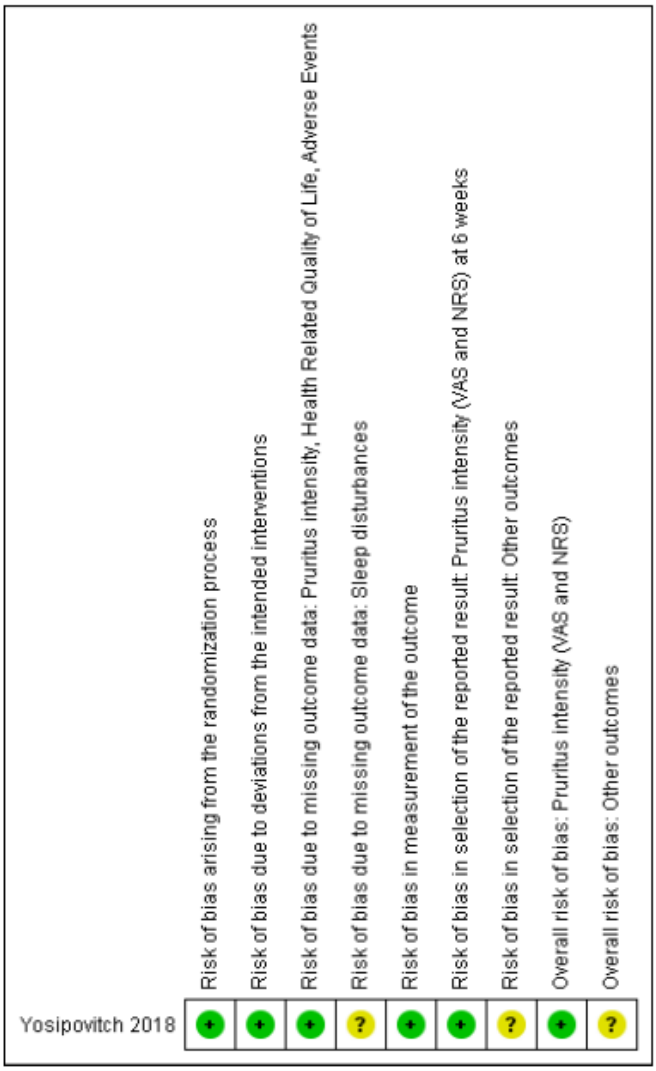
- One study with 257 randomised (253 analysed) participants, aged 18 to 65 years; 60.6% were female. This study investigated the safety and efficacy of three different doses of oral serlopitant (5 mg, 1 mg, and 0.25 mg, once daily for six weeks) compared to placebo for severe chronic pruritus; 25 US centres participated (clinical research centres and universities). All outcomes were measured at the end of treatment (six weeks from baseline), except adverse events, which were monitored throughout. A pharmaceutical company funded this study.
- Fifty-five per cent of participants suffered from CPUO, and approximately 45% presented a dermatological diagnosis (atopic dermatitis/ eczema 37.3%, psoriasis 6.7%, acne 3.6%, among other diagnoses). We unsuccessfully attempted to retrieve outcome data from

study authors for the subgroup of participants with CPUO. Participants had pruritus for six weeks or longer. Total study duration was 10 weeks.

- There was an absence of evidence for the main interventions of interest: emollient creams, cooling lotions, topical corticosteroids, topical antidepressants, systemic antihistamines, systemic antidepressants, systemic anticonvulsants, and phototherapy

Qualität der Studien:

- We downgraded the certainty of evidence for all outcomes due to indirectness (only 55% of study participants had CPUO) and imprecision. We downgraded outcomes other than patient-reported pruritus intensity a further level due to concerns regarding risk of bias in selection of the reported result and some concerns with risk of bias due to missing outcome data (sleep disturbances only). We deemed risk of bias to be generally low.



Studienergebnisse:

- Participants who received serlopitant 5 mg may have a greater rate of relief of patient-reported pruritus intensity as measured by the visual analogue scale (VAS; a reduction in VAS score indicates improvement) compared to placebo (126 participants, risk ratio (RR) 2.06, 95% confidence interval (CI) 1.27 to 3.35; low-certainty evidence).
- We are uncertain of the effects of serlopitant 5 mg compared to placebo on the following outcomes due to very low-certainty evidence: adverse events (127

participants; RR 1.48, 95% CI 0.87 to 2.50); health-related quality of life (as measured by the Dermatology Life Quality Index (DLQI); a higher score indicates greater impairment; 127 participants; mean difference (MD) -4.20, 95% CI -11.68 to 3.28); and sleep disturbances (people with insomnia measured by the Pittsburgh Sleep Symptom Questionnaire-Insomnia (PSSQ-I), a dichotomous measure; 128 participants; RR 0.49, 95% CI 0.24 to 1.01).

- Participants who received serlopitant 1 mg may have a greater rate of relief of patient-reported pruritus intensity as measured by VAS compared to placebo; however, the 95% CI indicates that there may also be little to no difference between groups (126 participants; RR 1.50, 95% CI 0.89 to 2.54; low-certainty evidence).

  We are uncertain of the effects of serlopitant 1 mg compared to placebo on the following outcomes due to very low-certainty evidence: adverse events (128 participants; RR 1.45, 95% CI 0.86 to 2.47); health-related quality of life (DLQI; 128 participants; MD -6.90, 95% CI -14.38 to 0.58); and sleep disturbances (PSSQ-I; 128 participants; RR 0.38, 95% CI 0.17 to 0.84).
- Participants who received serlopitant 0.25 mg may have a greater rate of relief of patient-reported pruritus intensity as measured by VAS compared to placebo; however, the 95% CI indicates that there may also be little to no difference between groups (127 participants; RR 1.66, 95% CI 1.00 to 2.77; low-certainty evidence).

  We are uncertain of the effects of serlopitant 0.25 mg compared to placebo on the following outcomes due to very low-certainty evidence: adverse events (127 participants; RR 1.29, 95% CI 0.75 to 2.24); health-related quality of life (DLQI; 127 participants; MD -5.70, 95% CI -13.18 to 1.78); and sleep disturbances (PSSQ-I; 127 participants; RR 0.60, 95% CI 0.31 to 1.17).
- The most commonly reported adverse events were somnolence, diarrhoea, headache, and nasopharyngitis, among others. Our included study did not measure depression or patient satisfaction.

Anmerkung/Fazit der Autoren

Little research has been conducted to investigate our review question. We found no eligible studies assessing the main comparisons of interest in this review.

We found evidence for only a certain subset of our interventions and participants of interest. The one included study assessed serlopitant in adults, and provided insufficient evidence to enable us to formulate conclusions.

Low-certainty evidence suggests that compared to placebo, serlopitant 5 mg may reduce pruritus intensity. Lower doses of 1 mg and 0.25 mg may also cause a greater rate of relief of itching intensity; however, at these doses, trial results are more uncertain.

We cannot make conclusions about effects of serlopitant on our other measured outcomes of interest - adverse effects, health related quality of life, and sleep disturbances - due to very low certainty evidence. (…)

Kommentare zum Review

- Gemischte Population. Keine Angaben zu Patienten mit Prurigo Nodularis.

3.2 Systematische Reviews

Qureshi AA et al., 2019 [3].
A systematic review of evidence-based treatments for prurigo nodularis.

Fragestellung
to provide a summary of evidence-based PN treatments.

Methodik

Population:

- PN patients

Intervention/Komparator:

- Siehe Ergebnisteil

Endpunkte:

- Siehe Ergebnisteil

Recherche/Suchzeitraum:

- PubMed and Scopus databases between January 1, 1990 and March 22, 2018

Qualitätsbewertung der Studien:

- Oxford Center for Evidence-based Medicine

Ergebnisse

Anzahl eingeschlossener Studien:

- A total of 35 original reports, including 15 prospective cohort studies, 11 retrospective reviews, 8 RCTs, and a single case series. Only 3 of the 8 RCTs included samples of > 22 patients with PN

Charakteristika der Population:

Table I. Randomized controlled trials for prurigo nodularis treatment with published results[18,21,22,27,28,56,57,72]

Studied intervention	Control group intervention	N	Key findings	Side effects
Betamethasone valerate 0.1% tape once daily[21]	Moisturizing itch-relief cream twice daily	11/12 subjects completed treatment course	Betamethasone-treated side with better clinical response at week 4 compared with Aveeno-treated side (mean VAS reductions from baseline of 4.85 and 3.15 points, respectively)	None reported
Calcipotriol 50 μg/g ointment twice daily[18]	Betamethasone valerate 0.1% ointment twice daily	10	Number and size of nodules decreased 49% and 56%, respectively, in calcipotriol group and 18% and 25%, respectively, in betamethasone group after 8 weeks	Self-resolving mild perilesional skin irritation with calcipotriol
Pimecrolimus 1% cream twice daily[22]	Hydrocortisone 1% cream twice daily	30	Significant mean VAS reduction from baseline with both pimecrolimus (2.7 points) and hydrocortisone (2.8 points) treatments at day 10, along with significantly improved prurigo lesions for both treatments at 10 days, 4 weeks, and 8 weeks	Progression, suspected contact allergy to wound dressing
308-nm excimer weekly[28]	Clobetasol 0.05% ointment once daily	13	PAIS with ≥40% improvement in 8 excimer-treated sites at week 34 compared with 3 clobetasol-treated sites, VAS with 63% improvement with excimer treatment at week 34 compared with 49% improvement with clobetasol treatment, and PGA with 6 excimer-treated sites were mild-almost clear at week 34 compared with 2 clobetasol-treated sites	Hyperpigmentation, erythema, burning, vesicles, and blistering
PUVA plus 308-nm excimer twice weekly[27]	PUVA alone 4 times weekly	21	6/11 patients receiving PUVA alone with complete remission, 7/10 patients receiving combination therapy with complete remission	PUVA alone; moderate erythema Combination therapy; erythema, vesicles and edema
Aprepitant 10 mg/g gel twice daily[56]	Vehicle gel twice daily	6 subjects with PN (19 total)	Presented for all patients combined and not PN patients alone; no significant difference in pruritus or lesion appearance improvement between groups (however, both groups with >50% reduction in VAS)	Pain at administration site, cutaneous reactions
Oral serlopitant 5 mg daily[57]	Placebo daily	127	Significantly improved VAS reduction in serlopitant group (-3.6 cm) compared with the placebo group (-1.9 cm) at 8 weeks from baseline, 54.4% of serlopitant patients with ≥4 cm VAS response by week 8 compared with only 25.0% of placebo patients	Well-tolerated, only mild-moderate adverse events
Oral ketotifen 1 mg daily plus topical antibiotic 3 times daily (with halobetasol ointment daily plus oral hydroxyzine 25 mg as needed)[72]	Halobetasol ointment daily plus oral hydroxyzine 25 mg as needed alone	27	9/14 patients in the ketotifen group had complete resolution of pruritus by the end of week 1, which was maintained until the end of week 4 (overall, 10/14 patients with complete resolution by the end of week 4 compared with 0/13 patients in the control group)	Many subjects with sedation and drowsiness at varying points throughout treatment

PAIS, Physician Assessment of Individual Signs; *PGA*, Physician Global Assessment; *PN*, prurigo nodularis; *PUVA*, psoralen plus ultraviolet A light phototherapy; *VAS*, visual analog score.

Qualität der Studien:

- 6 of 8 reports investigating photo- and photochemotherapy = levels of evidence 2b or greater.
- Thalidomide was studied by 6 reports only 2 of which were rated level 2b or greater.
- Cyclosporine and methotrexate with level 4 evidence. Pregabalin, amitriptyline, paroxetine, fluvoxamine, and neurokinin-1 receptor antagonists have evidence in 5 level 2b studies.

Studienergebnisse:

- Keine Metaanalyse → Siehe Tabelle 1 unter ,,Key findings‘‘

Anmerkung/Fazit der Autoren

This summary provides evidence-based guidance for practitioners while helping researchers to identify gaps in PN treatment development and study. In addition to direct treatment of comorbidities, patients with PN would benefit from safer and more effective systemic therapies. Neurokinin-1 receptor antagonists, k-opioid receptor modulators, and IL-31 receptor antibodies under recent investigation all show promise in achieving this goal. In addition, the genetic underpinning of disease warrants further investigation for possible development of targeted and personalized therapies. As new reports emerge, the variety of options in the practitioner’s toolbox will grow to meet the needs of an equally diverse population of patients with PN.

3.3 Leitlinien

Weisshaar E et al., 2019 [4].

European Dermatology Forum (EDF)

European S2k Guideline on Chronic Pruritus.

Siehe auch: European Centre for Guidelines Development, European Dermatology Forum (EDF), 2020 [2]

Zielsetzung/Fragestellung

Consensus based (S2k) European guideline on chronic pruritus.

Methodik

Die Leitlinie erfüllt nicht ausreichend die methodischen Anforderungen. Aufgrund limitierter höherwertiger Evidenz, wird die LL jedoch ergänzend dargestellt.

Grundlage der Leitlinie

- Repräsentatives Gremium;
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt;
- Systematische Suche, Auswahl und Bewertung der Evidenz;
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt;
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt;
- Regelmäßige Überprüfung der Aktualität gesichert.

Recherche/Suchzeitraum:

- This version is an updated version of the guideline that was published in 2012 and updated in 2014
- *"Systematic search for, and appraisal of evidence only applies to EuroGuiDerm Guidelines. For EuroGuiDerm Consensus Statements - these are done at the discretion of the Development Group – no systematic review process has to be completed."*

EuroGuiDerm Consensus Statement	S2k	Consensus	Representative subcommittee Systematic evidence search and evaluation Reaching consensus in a structured way	YES NO YES

LoE/GoR

- GRADE

Quality of evidence	Definition
High ++++	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate +++0	We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low ++00	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
Very Low +000	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

Table 5: Wording of recommendations (15, 16, 19, 20)

Strength	Wording	Symbols	Implications
Strong recommendation for the use of an intervention	'We recommend . . .'	↑↑	We believe that all or almost all informed people would make that choice. Clinicians will have to spend less time on the process of decision-making, and may devote that time to overcome barriers to implementation and adherence. In most clinical situations, the recommendation may be adopted as a policy.
Weak recommendation for the use of an intervention	'We suggest . . .'	↑	We believe that most informed people would make that choice, but a substantial number would not. Clinicians and health care providers will need to devote more time on the process of shared decision-making. Policy makers will have to involve many stakeholders and policy making requires substantial debate.
No recommendation with respect to an intervention	'We cannot make a recommendation with respect to . . .'	0	At the moment, a recommendation in favour or against an intervention cannot be made due to certain reasons (e.g. no reliable evidence data available, conflicting outcomes, etc.)
Weak recommendation against the use of an intervention	'We suggest against . . .'	↓	We believe that most informed people would make a choice against that intervention, but a substantial number would not.
Strong recommendation against the use of an intervention	'We recommend against . . .'	↓↓	We believe that all or almost all informed people would make a choice against that intervention. This recommendation can be adopted as a policy in most clinical situations.

Recommendations

THE CLINICAL PICTURE OF CHRONIC PRURITUS

- 4.1.1.Chronic pruritus in lesional and non-lesional skin. CP may occur as a common symptom in patients with dermatoses with primary skin lesions and systemic, neurologic

and psychiatric/psychosomatic diseases without primary skin lesions (9). In the 3 latter instances, the skin may appear normal or have skin lesions induced by scratching. In chronic and severe cases, patients can develop chronic prurigo (CPG), which may present as chronic nodular prurigo (CNPG) or other subtypes (30). In these cases, a clinical diagnosis is difficult to establish and diagnostics should be performed.

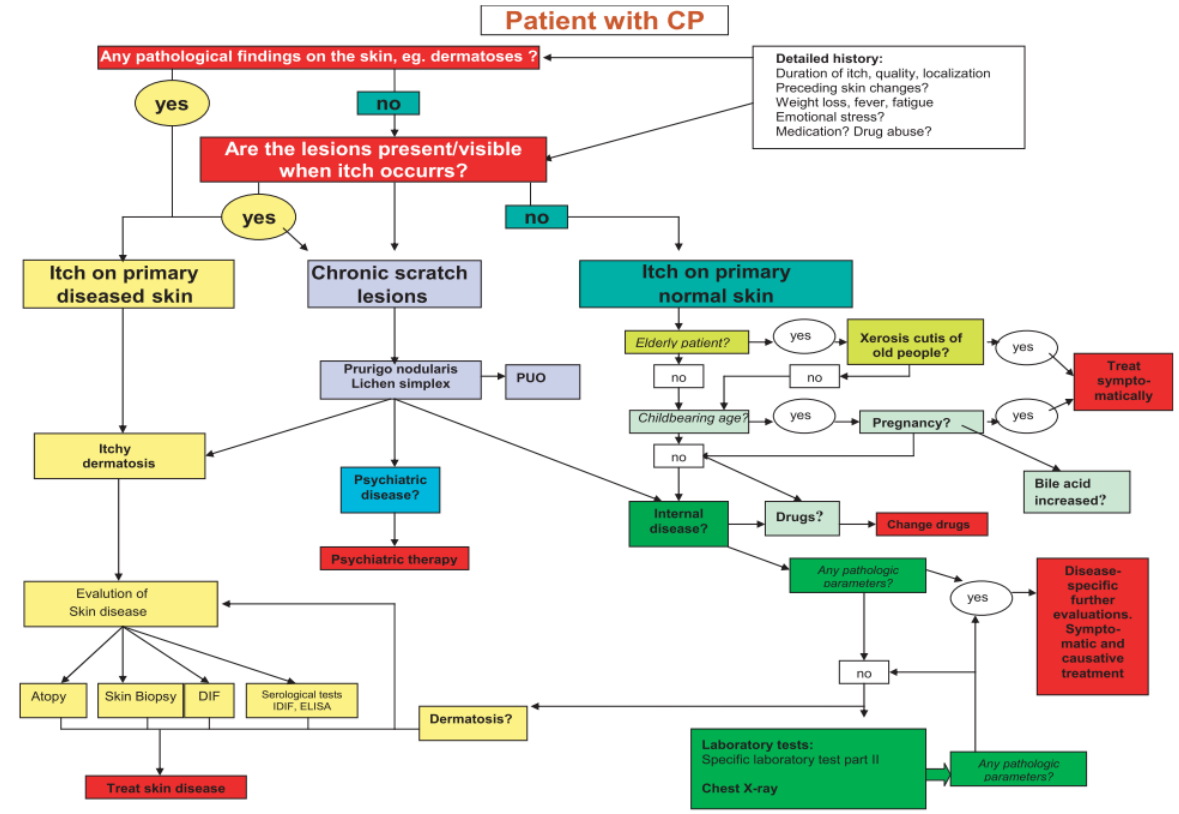


Fig. 1. Diagnostic algorithm.

- (…) Topical capsaicin's effects have been confirmed in controlled clinical trials for different pain syndromes and neuropathy, as well as notalgia paraesthetica (185), brachioradial pruritus (83), pruritic psoriasis (186, 187) and haemodialysis-related pruritus (188, 189). Case reports and case series described effects in hydroxyethyl starch-induced pruritus (190, 191), prurigo nodularis (191–194), lichen simplex (191, 193), nummular eczema (191), aquagenic pruritus (195) and psoralen and ultraviolet A (PUVA)-associated pruritus (196). Highconcentration topical capsaicin for the treatment of postherpetic neuralgia and HIV neuropathy have been evaluated in a Cochrane review (197).

  Expert recommendation: We suggest topical capsaicin for localized forms of CP.

- (…) Some studies suggest that topical corticosteroids such as betamethasone valerate are effective in CNPG (203, 204). Intralesional application in single nodules of CPG may be considered but there are no studies verifying the efficacy of this therapy.

  Expert recommendation: We recommend application of topical glucocorticosteroids in CP associated with inflammatory dermatoses and CPG. We recommend against topical glucocorticosteroids in CP on non-inflamed skin. We recommend against long-term treatment with topical glucocorticosteroids.

- (…) In an open study 30 patients with CNPG were treated with 75 mg pregabalin per day orally. Treatment improved itch in 76% of patients after a 3-month treatment course

(303). Pregabalin 50 mg every other day or 10 mg doxepin given daily for 4 weeks in patients with CKD-associated pruritus led to a significant improvement of pruritus in both groups, but was significantly more effective in patients receiving pregabalin (304). However, regarding the use of gabapentin or pregabalin an analysis by the US Renal Data System on a large cohort issued a caveat to the use of these drugs. Their use was associated with much higher hazards of altered mental status, falls and fractures (305).

Expert recommendation: We recommend gabapentin and pregabalin in neuropathic CP and in CKD-associated pruritus. We suggest gabapentin and pregabalin for refractory CP and PUO.

- (…) In a retrospective report on 13 patients with CNPG, 10 markedly improved on methotrexate at doses of 7.5–20 mg once weekly for a minimum of 6 months (370). In a recent multicenter study, a 90% overall response rate was reported in 39 patients with difficult-to-treat prurigo using methotrexate with a median weekly dose of 15 mg (371).

  Expert recommendation: We suggest cyclosporine, methotrexate and azathioprine for refractory CP associated with inflammatory dermatoses and CPG.

- (…) Several case series and case reports suggest a positive role of the NK1R antagonist aprepitant in CP, e.g. cutaneous T-cell lymphoma, solid tumours, drug-induced pruritus, CP with atopic predisposition and CNPG (377–382). However, recent controlled trials including a randomized double-blind, placebo-controlled phase-II study using topical or systemic aprepitant failed to show a benefit compared to placebo (383–385). Serlopitant is a novel NK1R antagonist that can be administered for long-term therapy. RCTs demonstrated a significant effect on pruritus of CPG and was well tolerated (386, 387).

  Expert recommendation: We suggest NKR1 antagonists such as serlopitant in refractory CP and CPG.

Referenzen:

9. 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(4):291-4.

30. Pereira MP, Steinke S, Zeidler C, Forner C, Riepe C, Augustin M, et al. European academy of dermatology and venereology European prurigo project: expert consensus on the definition, classification and terminology of chronic prurigo. J Eur Acad Dermatol Venereol. 2018;32(7):1059-65.

183. Lysy J, Sistiery-Ittah M, Israelit Y, Shmueli A, StraussLiviatan N, Mindrul V, et al. Topical capsaicin--a novel and effective treatment for idiopathic intractable pruritus ani: a randomised, placebo controlled, crossover study. Gut. 2003;52(9):1323-6

185. Wallengren J, Klinker M. Successful treatment of notalgia paresthetica with topical capsaicin: vehicle-controlled, double-blind, crossover study. J Am Acad Dermatol. 1995;32(2 Pt 1):287-9.

187. Ellis CN, Berberian B, Sulica VI, Dodd WA, Jarratt MT, Katz HI, et al. A double-blind evaluation of topical capsaicin in pruritic psoriasis. J Am Acad Dermatol. 1993;29(3):438-42.

188. Breneman DL, Cardone JS, Blumsack RF, Lather RM, Searle EA, Pollack VE. Topical capsaicin for treatment of hemodialysis-related pruritus. J Am Acad Dermatol. 1992;26(1):91-4.

189. Tarng DC, Cho YL, Liu HN, Huang TP. Hemodialysisrelated pruritus: a double-blind, placebo-controlled, crossover study of capsaicin 0.025% cream. Nephron. 1996;72(4):617-22.

190. Szeimies RM, Stolz W, Wlotzke U, Korting HC, Landthaler M. Successful treatment of hydroxyethyl starchinduced pruritus with topical capsaicin. Br J Dermatol. 1994;131(3):380-2.

191. Reimann S, Luger T, Metze D. [Topical administration of capsaicin in dermatology for treatment of itching and pain]. Hautarzt. 2000;51(3):164-72.

192. Hoogenberg K, Tupker RA, van Essen LH, Smit AJ, Kallenberg CG. Successful treatment of ulcerating livedo reticularis with infusions of prostacyclin. Br J Dermatol. 1992;127(1):64-6.

193. Tupker RA, Coenraads PJ, van der Meer JB. Treatment of prurigo nodularis, chronic prurigo and neurodermatitis circumscripta with topical capsaicin. Acta Derm Venereol. 1992;72(6):463.

194. Ständer S, Luger T, Metze D. Treatment of prurigo nodularis with topical capsaicin. J Am Acad Dermatol. 2001;44(3):471-8.

195. Lotti T, Teofoli P, Tsampau D. Treatment of aquagenic pruritus with topical capsaicin cream. J Am Acad Dermatol. 1994;30(2 Pt 1):232-5.

196. Kirby B, Rogers S. Treatment of PUVA itch with capsaicin. Br J Dermatol. 1997;137(1):152.

197. Derry S, Sven-Rice A, Cole P, Tan T, Moore R. Topical capsaicin (high concentration) for chronic neuropathic pain in adults. Cochrane Database Syst Rev. 2013;28(2):CD007393.

203. Saraceno R, Chiricozzi A, Nisticò SP, Tiberti S, Chimenti S. An occlusive dressing containing betamethasone valerate 0.1% for the treatment of prurigo nodularis. J Dermatolog Treat. 2010;21(6):363-6.

204. 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, doubleblind phase II trial. Dermatology. 2013;227(4):353-60.

303. Mazza M, Guerriero G, Marano G, Janiri L, Bria P, Mazza S. Treatment of prurigo nodularis with pregabalin. J Clin Pharm Ther. 2013;38(1):16–8.

304. Foroutan N, Etminan A, Nikvarz N, Shojai Shahrokh Abadi M. Comparison of pregabalin with doxepin in the management of uremic pruritus: a randomized single blind clinical trial. Hemodial Int. 2017;21(1):63-71.

305. Ishida JH, McCulloch CE, Steinman MA, Grimes BA, Johansen KL. Gabapentin and Pregabalin Use and Association with Adverse Outcomes among Hemodialysis Patients. J Am Soc Nephrol. 2018;29(7):1970-9.

370. Spring P, Gschwind I, Gilliet M. Prurigo nodularis: retrospective study of 13 cases managed with methotrexate. Clin Exp Dermatol. 2014;39(4):468-73.

371. Klejtman T, Beylot-Barry M, Joly P, Richard MA, Debarbieux S, Misery L, et al. Treatment of prurigo with methotrexate: a multicentre retrospective study of 39 cases. J Eur Acad Dermatol Venereol. 2018;32(3):437-40.

377. Vincenzi B, Fratto ME, Santini D, Tonini G. Aprepitant against pruritus in patients with solid tumours. Support Care Cancer. 2010;18(9):1229-30.

378. Torres T, Fernandes I, Selores M, Alves R, Lima M. Aprepitant: Evidence of its effectiveness in patients with refractory pruritus continues. J Am Acad Dermatol. 2012;66(1):e14-5.

379. Booken N, Heck M, Nicolay JP, Klemke CD, Goerdt S, Utikal J. Oral aprepitant in the therapy of refractory pruritus in erythrodermic cutaneous T-cell lymphoma. Br J Dermatol. 2011;164(3):665-7.

380. Vincenzi B, Tonini G, Santini D. Aprepitant for erlotinibinduced pruritus. N Engl J Med. 2010;363(4):397-8.

381. Ständer S, Luger TA. NK-1 antagonists and itch. Handb Exp Pharmacol. 2015;226:237-55.

382. Ständer S, Siepmann D, Herrgott I, Sunderkötter C, Luger TA. Targeting the neurokinin receptor 1 with aprepitant: a novel antipruritic strategy. PLoS One. 2010;5(6):e10968.

383. Lönndahl L, Holst M, Bradley M, Killasli H, Heilborn J, Hall MA, et al. Substance P antagonist aprepitant shows no additive effect compared with standardized topical treatment alone in patients with atopic dermatitis. Acta Derm Venereol. 2018;98(3):324-28.

384. Ohanyan T, Schoepke N, Eirefelt S, Hoey G, Koopmann W, Hawro T, et al. Role of substance P and its receptor neurokinin 1 in chronic prurigo: a randomized, proof-of-concept, controlled trial with topical aprepitant. Acta Derm Venereol. 2018;98(1):26-31.

385. Tsianakas A, Zeidler C, Riepe C, Borowski M, Forner C, Gerss J, et al. Aprepitant in histamine-refractory chronic nodular prurigo: a multicentre, randomized, double-blind, placebo-controlled, cross-over, phase- II trial (APREPRU). Acta Derm Venereol. 2019; 99:379–385.

386. Yosipovitch G, Ständer S, Kerby MB, Larrick JW, Perlman AJ, Schnipper EF, et al. Serlopitant for the treatment of chronic pruritus: Results of a randomized, multicenter, placebo-controlled phase 2 clinical trial. J Am Acad Dermatol. 2018;78(5):882-91.e10.

387. Ständer S, Kwon P, Hirman J, Perlman AJ, Weisshaar E, Metz M, et al. Serlopitant reduced pruritus in patients with Prurigo Nodularis in a phase 2, randomized, placebocontrolled trial. Am J Acad Dermatol. 2019 https://doi.org/10.1016/j.jaad.2019.01.052.

4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library - Cochrane Database of Systematic Reviews (Issue 02 of 12, February 2022) am 21.02.2022

#	Suchfrage
1	[mh Prurigo]
2	(Prurigo OR pruriginous):ti,ab,kw
3	"chronic pruritus":ti,ab,kw
4	{OR #1-#3}
5	#4 with Cochrane Library publication date from Feb 2017 to present

Systematic Reviews in PubMed am 21.02.2022

verwendete Suchfilter:
Konsentierter Standardfilter für Systematische Reviews (SR), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 02.01.2020.

#	Suchfrage
1	Prurigo[mh]
2	Prurigo[tiab] OR pruriginous[tiab]
3	"chronic pruritus"[tiab]
4	(#3) AND (((Meta-Analysis[ptyp] OR systematic[sb] OR ((systematic review [ti] OR meta-analysis[pt] OR meta-analysis[ti] OR systematic literature review[ti] OR this systematic review[tw] OR pooling project[tw] OR (systematic review[tiab] AND review[pt]) OR meta synthesis[ti] OR meta-analy*[ti] OR integrative review[tw] OR integrative research review[tw] OR rapid review[tw] OR umbrella review[tw] OR consensus development conference[pt] OR practice guideline[pt] OR drug class reviews[ti] OR cochrane database syst rev[ta] OR acp journal club[ta] OR health technol assess[ta] OR evid rep technol assess summ[ta] OR jbi database system rev implement rep[ta]) OR (clinical guideline[tw] AND management[tw]) OR ((evidence based[ti] OR evidence-based medicine[mh] OR best practice*[ti] OR evidence synthesis[tiab]) AND (review[pt] OR diseases category[mh] OR behavior and behavior mechanisms[mh] OR therapeutics[mh] OR evaluation study[pt] OR validation study[pt] OR guideline[pt] OR pmcbook)) OR ((systematic[tw] OR systematically[tw] OR critical[tiab] OR (study selection[tw]) OR (predetermined[tw] OR inclusion[tw] AND criteri* [tw]) OR exclusion criteri*[tw] OR main outcome measures[tw] OR standard of care[tw] OR standards of care[tw]) AND (survey[tiab] OR surveys[tiab] OR overview*[tw] OR review[tiab] OR reviews[tiab] OR search*[tw] OR handsearch[tw] OR analysis[ti] OR critique[tiab] OR appraisal[tw] OR (reduction[tw] AND (risk[mh] OR risk[tw]) AND (death OR recurrence))) AND (literature[tiab] OR articles[tiab] OR publications[tiab] OR publication [tiab] OR bibliography[tiab] OR bibliographies[tiab] OR published[tiab] OR pooled data[tw] OR unpublished[tw] OR citation[tw] OR citations[tw] OR database[tiab] OR internet[tiab] OR textbooks[tiab] OR references[tw] OR scales[tw] OR papers[tw] OR datasets[tw] OR trials[tiab] OR meta-analy*[tw] OR (clinical[tiab] AND studies[tiab]) OR treatment outcome[mh] OR treatment outcome[tw] OR pmcbook)) NOT (letter[pt] OR newspaper article[pt])) OR Technical Report[ptyp]) OR (((((trials[tiab] OR studies[tiab] OR database*[tiab] OR literature[tiab] OR

#	Suchfrage
	publication*[tiab] OR Medline[tiab] OR Embase[tiab] OR Cochrane[tiab] OR Pubmed[tiab])) AND systematic*[tiab] AND (search*[tiab] OR research*[tiab]))) OR ((((((((((HTA[tiab]) OR technology assessment*[tiab]) OR technology report*[tiab]) OR (systematic*[tiab] AND review*[tiab])) OR (systematic*[tiab] AND overview*[tiab])) OR meta-analy*[tiab]) OR (meta[tiab] AND analyz*[tiab])) OR (meta[tiab] AND analys*[tiab])) OR (meta[tiab] AND analyt*[tiab]))) OR (((review*[tiab]) OR overview*[tiab]) AND ((evidence[tiab]) AND based[tiab]))))))
5	((#4) AND ("2017/02/01"[PDAT] : "3000"[PDAT]) NOT "The Cochrane database of systematic reviews"[Journal]) NOT (animals[MeSH:noexp] NOT (Humans[mh] AND animals[MeSH:noexp]))
6	(#5) NOT (retracted publication [pt] OR retraction of publication [pt])

Leitlinien in PubMed am 21.03.2022

verwendete Suchfilter:
Konsentierter Standardfilter für Leitlinien (LL), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 21.06.2017.

#	Suchfrage
1	Prurigo[mh] OR Pruritus[majr]
2	Prurigo[tiab] OR pruriginous[tiab]
3	chronic[tiab] AND prurit*[tiab]
4	#1 OR #2 OR #3
5	(#4) AND (Guideline[ptyp] OR Practice Guideline[ptyp] OR guideline*[Title] OR Consensus Development Conference[ptyp] OR Consensus Development Conference, NIH[ptyp] *OR recommendation*[ti])*
6	(((#5) AND ("2017/02/01"[PDAT] : "3000"[PDAT])) NOT (animals[MeSH:noexp] NOT (Humans[MesH] AND animals[MeSH:noexp])) NOT ("The Cochrane database of systematic reviews"[Journal]) NOT ((comment[ptyp]) OR letter[ptyp]))
7	(#6) NOT (retracted publication [pt] OR retraction of publication [pt])

Iterative Handsuche nach grauer Literatur, abgeschlossen am 21.02.2022

- Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)
- Leitlinienprogramm Onkologie (Deutsche Krebsgesellschaft, Deutsche Krebshilfe, AWMF)
- Nationale VersorgungsLeitlinien (NVL)

- National Institute for Health and Care Excellence (NICE)
- Scottish Intercollegiate Guideline Network (SIGN)
- World Health Organization (WHO)

- ECRI Guidelines Trust (ECRI)
- Dynamed / EBSCO
- Guidelines International Network (GIN)
- Trip Medical Database

Referenzen

1. **Andrade A, Kuah CY, Martin-Lopez JE, Chua S, Shpadaruk V, Sanclemente G, et al.** Interventions for chronic pruritus of unknown origin. Cochrane Database of Systematic Reviews [online]. 2020(1):Cd013128. URL: http://dx.doi.org/10.1002/14651858.CD013128.pub2.
2. **European Centre for Guidelines Development, European Dermatology Forum (EDF).** EuroGuiDerm guideline and consensus statement development manual: a pragmatic manual for the development of high-quality guidance in dermatology, version 1.3 [online]. Zürich (SUI): EDF; 2020. [Zugriff: 22.02.2022]. URL: https://www.edf.one/dam/jcr:c3d57052-678b-4901-9957-8711bac3aa20/EuroGuiDe_Manual_v1.3_20-03-03_for_website.pdf.
3. **Qureshi AA, Abate LE, Yosipovitch G, Friedman AJ.** A systematic review of evidence-based treatments for prurigo nodularis. J Am Acad Dermatol 2019;80(3):756-764.
4. **Weisshaar E, Szepietowski JC, Dalgard FJ, Garcovich S, Gieler U, Giménez-Arnau AM, et al.** European S2k Guideline on Chronic Pruritus. Acta Derm Venereol 2019;99(5):469-506.

[A] **Rethlefsen ML, Kirtley S, Waffenschmidt S, Ayala AP, Moher D, Page MJ, et al.** PRISMA-S: an extension to the PRISMA Statement for Reporting Literature Searches in Systematic Reviews. Syst Rev 2021;10(1):39. https://doi.org/10.1186/s13643-020-01542-z

[B] **McGowan J, Sampson M, Salzwedel DM, Cogo E, Foerster V, Lefebvre C.** PRESS Peer Review of Electronic Search Strategies: 2015 Guideline Statement. J Clin Epidemiol 2016;75:40-46. https://doi.org/10.1016/j.jclinepi.2016.01.021

Beteiligung von AkdÄ und Fachgesellschaften nach §35a Abs. 7 SGB V i.V.m. VerfO 5. Kapitel § 7 Abs. 6

2022-B-043

Kontaktdaten

Deutsche Dermatologische Gesellschaft

Indikation gemäß Beratungsantrag

„für die Behandlung von mittelschwerer bis schwerer Prurigo nodularis bei erwachsenen Patienten, die für eine systemische Therapie in Betracht kommen."

Was ist der Behandlungsstandard in o.g. Indikation unter Berücksichtigung der vorliegenden Evidenz? Wie sieht die Versorgungspraxis in Deutschland aus?

Eine Therapie ist derzeit nicht für die Behandlung der chronisch nodulären Prurigo (syn: Prurigo nodularis) zugelassen. Der Behandlungsstandard der Therapie einer chronisch nodulären Prurigo (CNPG) des Erwachsenen wurde u.a. in der AWMF S2k Leitlinie zur Therapie des chronischen Pruritus (zuletzt publiziert: Ständer S et al. 2017; Überarbeitung 2021 aktuell eingereicht) formuliert und basiert auf wenigen randomisierten kontrollierten Studien und zum überwiegenden Teil auf Fallberichten und Expertenerfahrung. Dementsprechend wird eine systemische Therapie nichtsedierende systemische H1-Antihistaminika, UV-Phototherapie, Gabapentinoide, Immunsuppressiva (insbesondere Cyclosporin, Methotrexat, Azathioprin), Opioidmodulatoren (Naltrexon, Naloxon) und Aprepitant (Tsianakas et al. 2019) empfohlen. Dupilumab wurde in die Empfehlungen mit aufgenommen, da umfangreiche internationale Fallberichte von einer Besserung der CNPG bei Indikationsgemäßem Einsatz bei der atopischen Dermatitis berichteten (Patruno et al. 2021).

Die topische Therapie hat einen wichtigen adjuvanten Stellenwert bei der mittelschweren bis schweren CNPG, da die Patienten neben der Pruritusreduktion eine Heilung der Kratz-verursachten Läsionen wünschen (d.h. Abheilung von Exkoriationen, Krusten, Ausgleich der Xerosis) (Pereira et al. 2018). Es werden topische Kortikosteroide, Calcineurininhibitoren (Pimecrolimus, Tacrolimus) und Capsaicin zur topischen Therapie empfohlen.

Publizierte randomisierte kontrollierte Studien sind für topische Kortikosteroide, Pimecrolimus und UV-Therapie verfügbar. Zu Serlopitant (Neurokinin 1 Antagonist) und Nemolizumab liegen publiziere Phase II Studien vor (Ständer et al. 2019, Ständer et al. 2020). Die Substanzen sind derzeit nicht verfügbar. Zu Dupilumab wurden kürzlich zwei positive Phase III Studien als Pressemitteilung des Sponsors veröffentlicht.

Die Versorgung der Patienten mit mittelschwerer bis schwerer CNPG erfolgt hauptsächlich in dermatologischen Praxen, Kliniken und Expertenzentren. Am häufigsten werden topische Therapien (hier hauptsächlich Kortikosteroide), Antihistaminika, eine UV-Therapie und systemische Immunsuppressiva eingesetzt. An Expertenzentren laufen Phase II/III Studien mit innovativen Substanzen (z.B. Nalbuphin, Vixarelizumab). Im Rahmen dieser Studien werden als rescue therapy ebenfalls z.B. topische Kortikosteroide und Antihistaminika eingesetzt.

Patruno C, Napolitano M, Argenziano G, Peris K, Ortoncelli M, Girolomoni G, Offidani A, Ferrucci SM, Amoruso GF, Rossi M, Stingeni L, Malara G, Grieco T, Foti C, Gattoni M, Loi C, Iannone M, Talamonti M, Stinco G, Rongioletti F, Pigatto PD, Cristaudo A, Nettis E, Corazza M, Guarneri F, Amerio P, Esposito M, Belloni Fortina A, Potenza C, Fabbrocini G; DADE - Dupilumab for Atopic Dermatitis of the Elderly study group. Dupilumab therapy of atopic dermatitis of the elderly: a multicentre, real-life study. J Eur Acad Dermatol Venereol. 2021 Apr;35(4):958-964.

Pereira MP, Zeidler C, Wallengren J, Halvorsen JA, Weisshaar E, Garcovich S, Misery L, Brenaut E, Savk E, Potekaev N, Lvov A, Bobko S, Szepietowski JC, Reich A, Bozek A, Legat FJ, Metz M, Streit M, Serra-Baldrich E, Goncalo M,

Kontaktdaten

Deutsche Dermatologische Gesellschaft

Indikation gemäß Beratungsantrag

„für die Behandlung von mittelschwerer bis schwerer Prurigo nodularis bei erwachsenen Patienten, die für eine systemische Therapie in Betracht kommen."

Storck M, Nau T, Hoffmann V, Steinke S, Greiwe I, Dugas M, Augustin M, Ständer S. Chronic Nodular Prurigo: A European Cross-sectional Study of Patient Perspectives on Therapeutic Goals and Satisfaction. Acta Derm Venereol 2021; 101: adv00403

Ständer S, Yosipovitch G, Legat FJ, Lacour JP, Paul C, Narbutt J, Bieber T, Misery L, Wollenberg A, Reich A, Ahmad F, Piketty C. Trial of Nemolizumab in Moderate-to-Severe Prurigo Nodularis. N Engl J Med. 2020; 382:706-716

Ständer S, Kwon P, Hirman J, Perlman AJ, Weisshaar E, Metz M, Luger TA, TCP-102 Study Group. Serlopitant Reduced Pruritus in Patients with Prurigo Nodularis in a Phase 2, Randomized, Placebo-Controlled Trial. J Am Acad Dermatol 2019; 80: 1395-1402

Ständer S, Zeidler C, Augustin M, Bayer G, Kremer AE, Legat FJ, Maisel P, Mettang T, Metz M, Nast A, Niemeier V, Raap U, Schneider G, Ständer H, Staubach P, Streit M, Weisshaar E. S2k-Leitlinie zur Diagnostik und Therapie des chronischen Pruritus. J Dtsch Dermatol Ges. 2017; 15: 860-873

Tsianakas A, Zeidler C, Riepe C, Borowski M, Forner C, Gerss J, Metz M, Staubach P, Raap U, Kaatz M, Urban M, Luger TA, Ständer S. Aprepitant in anti- histamine-refractory chronic nodular prurigo: a multicentre, randomized, double-blind, placebo-controlled, cross-over, phase- II trial (APREPRU). Acta Dermatol Venereol. 2019; 99:379-385

Gibt es Kriterien für unterschiedliche Behandlungsentscheidungen bei der Behandlung von „mittelschwerer bis schwerer Prurigo nodularis bei erwachsenen Patienten, die für eine systemische Therapie in Betracht kommen" die regelhaft berücksichtigt werden? Wenn ja, welche sind dies und was sind in dem Fall die Therapieoptionen?

Die Behandlung orientiert sich regelhaft an der Schwere der Erkrankung, Alter, Komorbidität und Komedikation der Patienten sowie bereits eingesetzte und nicht ausreichend effiziente Vortherapien. Für die Schwere der CNPG werden zum einen die klinische Ausprägung (d.h. Anzahl der Knoten), zum anderen von Patienten berichtete Beschwerden (am häufigsten: Pruritusintensität, Schlafstörung, Einschränkung der dermatologischen Lebensqualität) herangezogen (Zeidler et al. 2021, Pölking et al. 2018). Dabei ist die Schwere der Erkrankung unabhängig von Alter, Komorbidität und Komedikation und als unabhängiger Faktor zu berücksichtigen. Daher wird aus dem o.g. Therapien individuell ein Plan für die Patienten erstellt. Unterschiedliche Behandlungsentscheidungen bei mittelschwerer zu schwerer CNPG sind in der Leitlinie nicht vorgesehen und richten sich nach o.g. Kriterien.

Zeidler C, Pereira MP, Augustin M, Spellman M, Ständer S. Investigator's Global Assessment of Chronic Prurigo: A New Instrument for Use in Clinical Trials. Acta Derm Venereol 2021; 101: adv00401

Pölking J, Zeidler C, Schedel F, Osada N, Augustin M, Metze D, Pereira MP, Yosipovitch G, Bernhard JD, Ständer S. Prurigo Activity Score (PAS): Validity and Reliability of a New Instrument to Monitor Chronic Prurigo. J Eur Acad Dermatol Venereol. 2018; 32: 1754-1760