Le prurigo chronique

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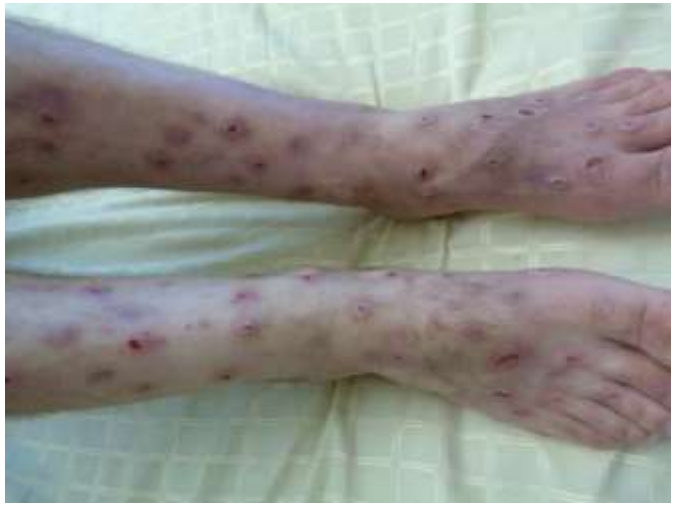
Introduction

- Maladie méconnue
- Prévalence?



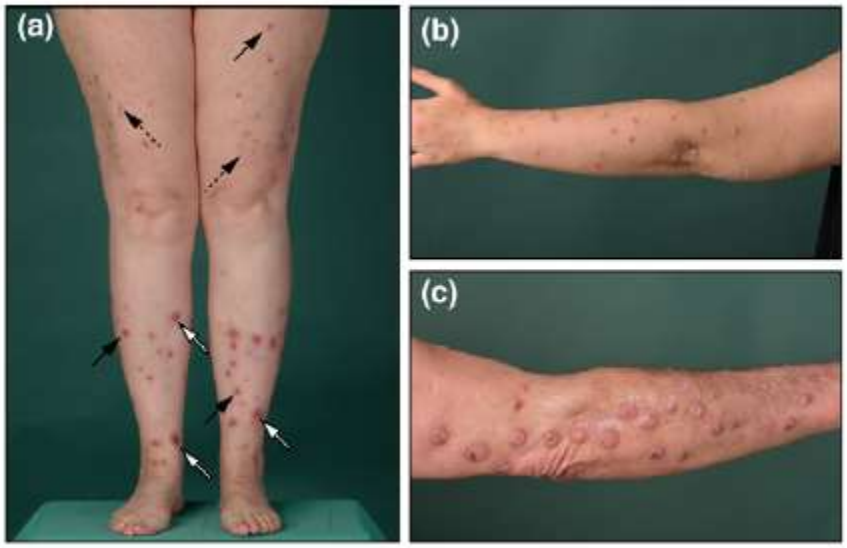
Définition

Parameter	Term	Comment
Definition	Chronic prurigo (CPG) is a distinct disease defined by the presence of chronic pruritus and multiple localized or generalized pruriginous lesions. CPG occurs due to a neuronal sensitization to itch and the development of an itch-scratch cycle. CPG can be of dermatological, systemic, neurologic, psychiatric/psychosomatic, multifactorial or undetermined origin.	
Diagnosis	Chronic prurigo (CPG)	• Umbrella term for all stages and manifestations of CPG. • `Chronic` points to chronicity as an important part of the pathophysiology (peripheral and central neuronal sensitization)
State	Disease	Indicates an own state and distinction from the underlying aetiology
Core symptoms (Major criteria)	(1) Chronic pruritus (≥6 weeks) (2) History and/or signs of repeated scratching (e.g. excoriations and scars) (3) Localized or generalized presence of multiple pruriginous* lesions	• All core symptoms must be present to make a diagnosis of chronic prurigo. • Pruritus must be present and should be the initial sign. • Localized: an area such as the lower leg or lower arm. Initial presence of singular lesions does not fulfill the diagnostic criteria.

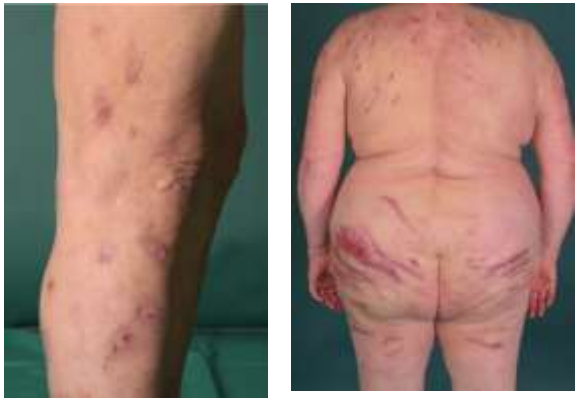
EADV European Prurigo Project: expert consensus on the definition, classification and terminology of chronic prurigo
Pereira et al., JEADV 2017

5 types

Range of Manifestations	(1) Papular type (2) Nodular type (3) Plaque type (4) Umbilicated type	Patients may present with one or more than one clinical manifestation of chronic prurigo. It is sufficient to diagnose the patients as chronic prurigo without mentioning the subtype.



a, c: forme nodulaire
b: forme papuleuse



Forme linéaire

EADV European Prurigo Project: expert consensus on the definition, classification and terminology of chronic prurigo
Pereira et al., JEADV 2017

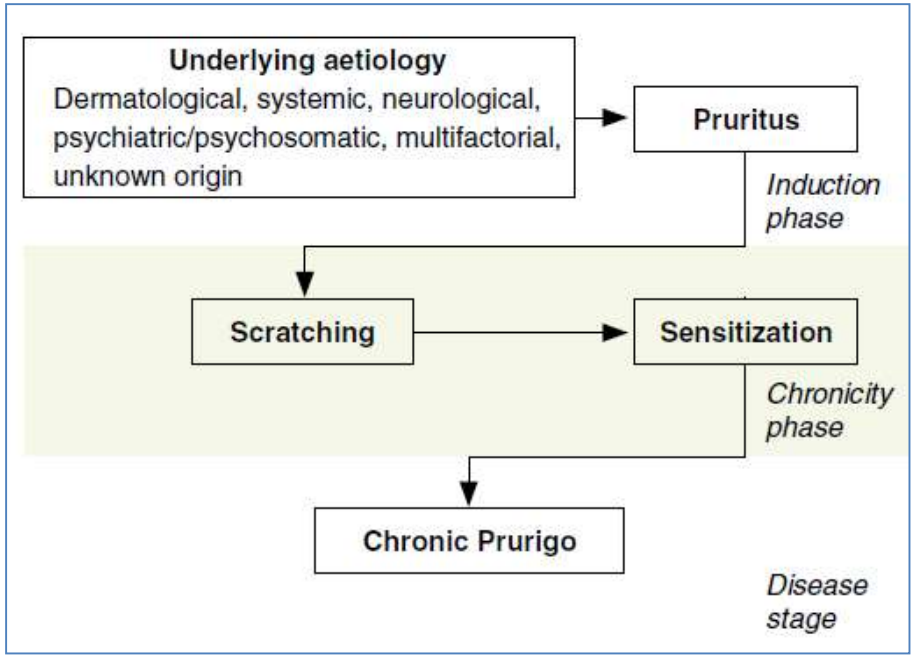
Position Statement – Linear Prurigo is a Subtype of Chronic Prurigo
M. P. Pereira et al., JEADV 2018

Critères associés

Associated criteria (Frame the disease in more detail)	(1) **Signs** • Pruriginous lesions are distributed on areas of the skin accessible to scratching • Pruriginous lesions are usually symmetrically distributed • Normal or lichenified skin between pruriginous lesions • Other scratch-induced lesions may be associated: e.g. excoriations and scars • Face and palms are rarely affected • Pruriginous lesions are persistent (2) **Symptoms** • Pruritus precedes development of skin lesions • Pruritus might be accompanied by burning, stinging, pain and other sensations • Signs of chronicity: continuous pruritus of high intensity, alloknesis, hyperknesis, spreading of pruriginous skin lesions (3) **Function** • Impaired quality of life • Sleep loss due to disease • Days of absence from work • Obsessive-compulsive behaviour (4) **Emotions** • Depression • Anxiety • Anger • Disgust • Shame • Helplessness (5) **Pathophysiology** • Neuronal sensitization towards itch induced by chronic pruritus and development of a chronic itch-scratch cycle • Aetiology of chronic pruritus might be of dermatological, systemic, neurological, psychiatric/psychosomatic, multifactorial aetiology or idiopathic • Presence of other specific skin lesions may point to a concomitant skin disease

EADV European Prurigo Project: expert consensus on the definition, classification and terminology of chronic prurigo
Pereira et al., JEADV 2017

Mécanisme



EADV European Prurigo Project: expert consensus on the definition, classification and terminology of chronic prurigo
Pereira et al., JEADV 2017

Etiologie

Catégories	Maladies
I Dermatologiques	Résultant de "maladies de la peau" comme le psoriasis, la dermatite atopique, la xérose, la gale et l'urticaire
II Systémiques	Résultant de "maladies des organes" autres que la peau comme le foie (cirrhose biliaire primitive), le rein (insuffisance rénale chronique), le sang (maladie de Hodgkin) et médicaments
III Neurologiques	Résultant de "maladies ou troubles" du système nerveux central ou périphérique comme une compression nerveuse
IV Psychogènes/ psychosomatiques	Prurit avec comorbidité de "maladies psychiatriques ou psychosomatiques"
V Mixtes	Coexistence de plusieurs maladies
VI Autres	Origine indéterminée

Traduit de:
Clinical Classification of Itch: a Position Paper of the International Forum for the Study of Itch
Stander et al., Acta Derm Venereol 2011

- Etude sur 108 patients avec un prurigo
  - Maladie sous-jascente chez 87%
    - Dermatologique 19%
    - Systémique 7%
    - Neurologique 2%
    - Mixte 59%
    - Inconnue 13%
  - Prédisposition atopique chez 1/2

Prurigo as a symptom of atopic and non-atopic diseases: aetiological survey in a consecutive cohort of 108 patients
Iking et al., JEADV 2013

Bilan étiologique

Biopsie de peau avec IF (si sujet âgé)
Numération sanguine, CD4/CD8
VS, CRP
Urée, créatinine
Bilan hépatique
LDH
Glycémie à jeun
Calcémie
Fer sérique, ferritine
TSH
Électrophorèse et immunoélectrophorèse des protéines
Sérologie VIH
Sérologie VHA, VHB, VHC
Sérologie toxocara
Examen parasitologique des selles
Radiographie thoracique
Échographie abdominale

Score de sévérité

Prurigo Activity Score (PAS)

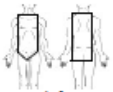
1. Type
a) Which lesions do you see?
- ◻ papules
- ◻ nodules
- ◻ plaques
- ◻ umbilicated ulcers
- ◻ ulcers
- ◻ hypo-/hyperpigmented maculae

b) Which type of prurigo is predominant?
- ◻ Prurigo papular type
- ◻ Prurigo nodular type
- ◻ Prurigo plaques type
- ◻ Prurigo ulcerated type
- ◻ Prurigo umbilicated
- ◻ completely healed

2. Number
a) How many Prurigo lesions do you see? (estimate; do not count; do not consider scars)
- ◻ 0
- ◻ 1 - 19
- ◻ 20 – 100
- ◻ > 100

3. Distribution:
- ◻ disseminated
- ◻ localized (only 1 or 2 areas affected)
- ◻ neither of them

4. Please mark the affected area(s) (for definition of trunk see image).



whole body except head	◻	
whole body head included	◻	
or		
forearm:	◻ left	◻ right
upper arm:	◻ left	◻ right
lower leg:	◻ left	◻ right
upper leg:	◻ left	◻ right
trunk	◻ ventral	◻ dorsal
head	◻ capillitium	◻ face

5. Please choose a representative area (must be the same at each visit*):

forearm:	◻ left	◻ right
upper arm:	◻ left	◻ right
lower leg:	◻ left	◻ right
upper leg:	◻ left	◻ right
trunk	◻ ventral	◻ dorsal

*select one at screening, photos, biospies act always in this area. Do not change during study.

Exact number of pruriginous lesions in representative area (do not count scars):_____

6. Monitor lesions. Please mark IN THE REPRESENTATIVE AREA the biggest (B) and the most representative (R) pruriginous lesion (remains the same in every visit, make photos with mark).

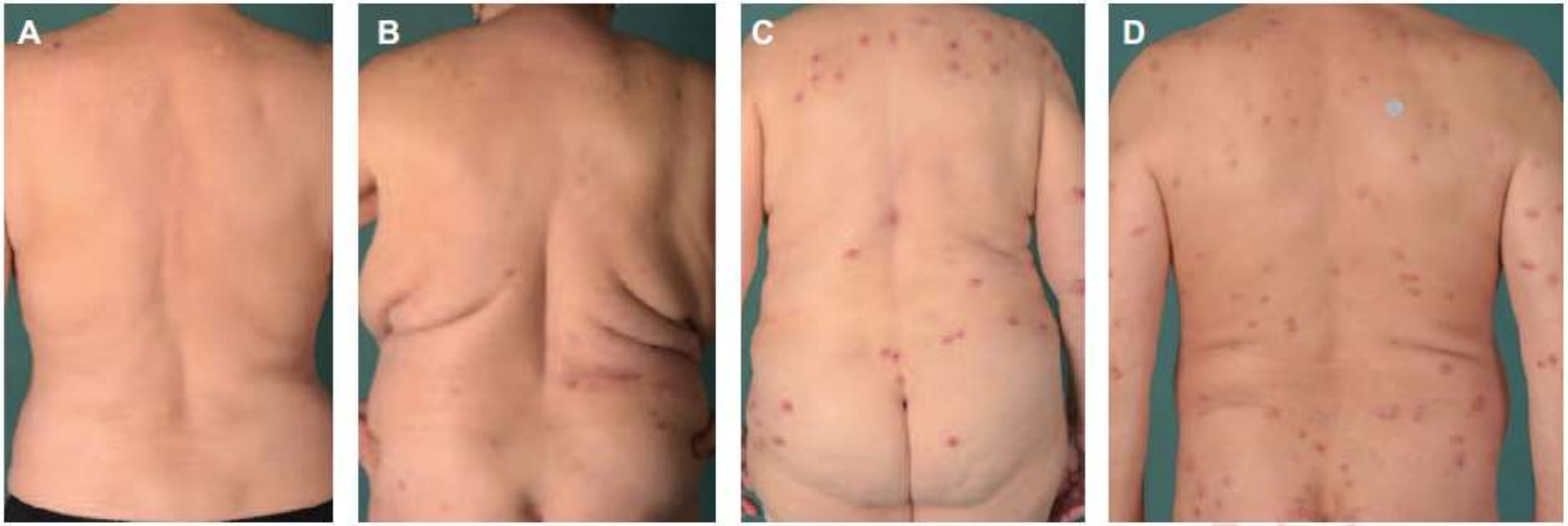
	Highest elevation [mm]	Biggest diameter [mm]	
		longitudinal	crosswise
biggest pruriginous lesion			
representative pruriginous lesion			

7. Activity. Please mark the stage for the whole body.

	stage 0	stage 1	stage 2	stage 3	stage 4
Pruriginous lesions with excoriations/crusts: estimated percent compared to all pruriginous lesions	0 %	1- 25 %	26 - 50 %	51 - 75 %	76 - 100 %
Healed pruriginous lesions: estimated percent compared to all pruriginous lesions	100 %	75-99 %	50 - 74 %	25 - 49 %	0 - 24 %

Prurigo Activity Score (PAS): validity and reliability of a new instrument to monitor chronic prurigo
Pölking J et al. J Eur Acad Dermatol Venereol. 2018

Score de sévérité



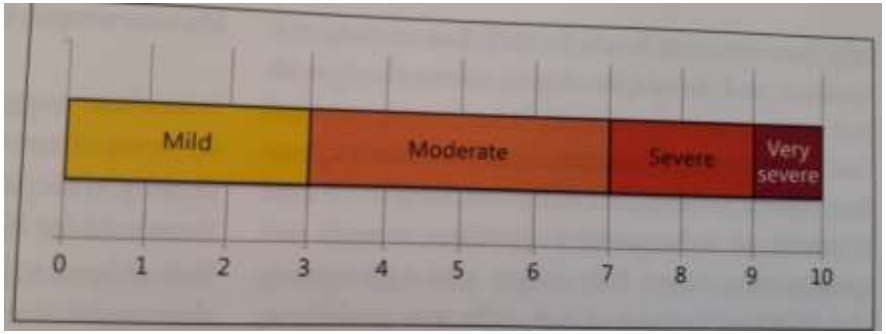
Score	Category	Description: Stage (IGA Prurigo Nodularis Severity)
0	Clear	No nodules (0 nodules)
1	Almost Clear	Rare, flattened lesions, with no more than 5 dome-shaped palpable nodules (approximately 1-5 nodules)
2	Mild	Few, mostly flattened lesions, with small number of dome-shaped palpable nodules (approximately 6-19 nodules)
3	Moderate	Many lesions, partially flattened, and dome-shaped palpable nodules (approximately 20-100 nodules)
4	Severe	Abundant lesions, majority are dome-shaped palpable nodules (over 100 nodules)

Score de prurit

- Echelle visuelle analogique (EVA)

Pas de démangeaisons — Pire démangeaisons imaginables

- Echelle numérique (EN)



Retentissement

Table 2 Anxiety, depression and suicidal ideation in patients with prurigo and controls

	Patients with prurigo *n* = 27	Controls *n* = 1359	*P*-value
HADS anxiety			
Range	0–17	0–18	
Mean ± SD	8.3 ± 4.8	4.7 ± 3.5	
≥ 11 (anxiety clinical case)	10 (37.1%)	150 (11.1%)	<0.001
HADS depression			
Range	1–16	0–16	
Mean ± SD	7.6 ± 4.1	4.3 ± 3.2	
≥ 11 (depression clinical case)	8 (29.6%)	58 (4.3%)	<0.001
Suicidal ideation (MD=1)			
Suicidal ideation	5 (19.2%)	88 (8.3%)	0.03
Suicidal ideation concerning the skin disease (among those with suicidal ideation)	4 (80.0%)	N.A	
Suicidal ideation concerning the skin disease (in the whole sample)	4 (15.4%)	N.A	

Anxiety in other skin diseases:
22.7% of patients with psoriasis
21.0% of patients with hand eczema
17.6% of patients with atopic eczema,
17.5% of patients with leg ulcers

Depression in other skin diseases
24.3% of patients with leg ulcers,
15.1% of patients with hand eczema
13.8% of patients with psoriasis
10.1% of patients with atopic eczema

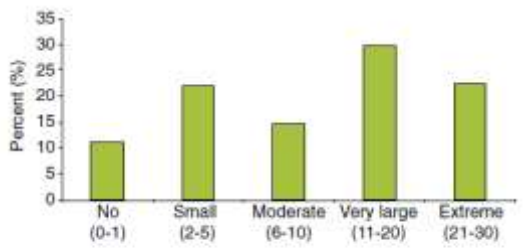
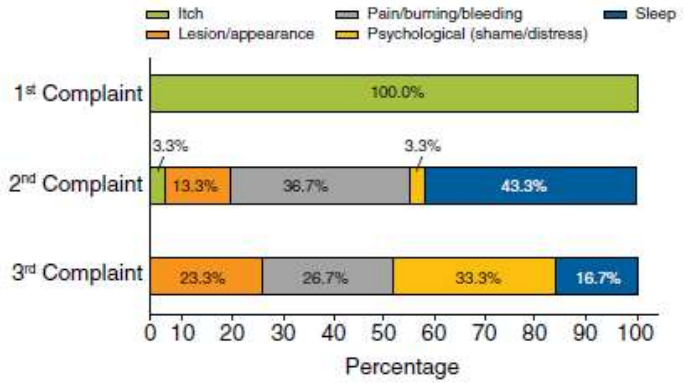


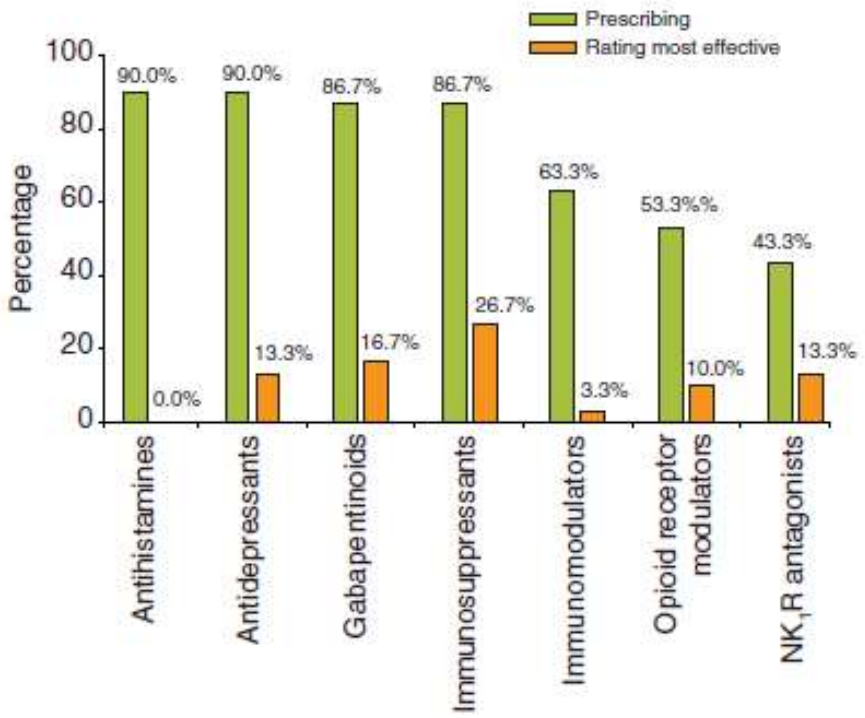
Figure 1 Dermatologic Life Quality Index (DLQI) score categories in patients with prurigo: impairment on the quality of life.

The self-assessed psychological comorbidities of prurigo in European patients: a multicentre study in 13 countries
E. Brenaut et al., JEADV 2019

Traitements utilisés

Enquête auprès de 30 spécialistes du prurigo





Prurigo nodularis: a physician survey to evaluate current perceptions
Pereira et al., JEADV 2018

Preuve d'efficacité

35 articles (15 prospectives, 11 rétrospectives, 8 RCT, 1 série de cas)

Studied intervention	Control group intervention	N	Key findings
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)
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
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
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
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
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)
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

Effets bénéfiques des DC, tacrolimus, calcipotriol, capsaïcine, UV, thalidomide, ciclo, MTX, prégabaline, amytriptyline, paroxetine, antagoniste NK1R

mais niveaux de preuve faibles

A systematic review of evidence-based treatments for prurigo nodularis
Qureshi et al., JAAD 2018

Traitements consensuels

	Traitement	Dose	Effets secondaires
Step 1	Dermocorticoïdes Tacrolimus topique Photothérapie		
Step 2	Capsaïcine topique Gabapentine Prégabaline	 300-900mg jusqu'à 3/j 150mg/j jusqu'à 600mg/j en 2-3 prises	 Somnolence, oedèmes périphériques, vertiges Somnolence, oedèmes périphériques, vertiges, bouche sèche
Step 3	Paroxetine Mirtazapine	20-50mg/j 15mg/j	Asthénie, constipation, perte d'appétit, bouche sèche, nausée, perte de libido, somnolence, sueurs Somnolence, augmentation appétit, prise de poids
Step 4	Ciclosporine Methotrexate		
Step 5	Naltrexone	50-150mg/j	Nausées, vomissements, diarrhée, vertiges, fatigue, céphalées CI si pathologie hépatique

Diagnostic and treatment algorithm for chronic nodular prurigo
Ständer et al., JAAD 2019

Association de patients

- Association France Prurigo Nodulaire (AFPN)
- Présidente: Docteur Christine Patras de Campaigno
- Contact: prurigonodulaire@gmail.com

Futur ?

- Nemolizumab
- Serlopitant
- Nalbuphine
- Dupilumab…

Conclusion

- Le prurigo chronique: maladie très prurigineuse avec fort impact sur la qualité de vie
- Thérapeutiques actuellement limitées mais les options se multiplient

Références

- EADV European Prurigo Project: expert consensus on the definition, classification and terminology of chronic prurigo
  Pereira et al., JEADV 2017

- Diagnostic and treatment algorithm for chronic nodular prurigo
  Ständer et al., JAAD 2019

- Un intérêt inédit pour le prurigo nodulaire
  Misery L, Ann Dermatol Venereol 2018

- A systematic review of evidence-based treatments for prurigo nodularis
  Qureshi AA, JAAD 2018

- Prurigo nodularis: a physician survey to evaluate current perception of its classification, clinical experience and unmet needs
  Pereira MP, JEADV 2018