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: 2025-B-269-z Dupilumab

Stand: November 2025

I. Zweckmäßige Vergleichstherapie: Kriterien gemäß 5. Kapitel § 6 VerfO G-BA	
Dupiluma zur Behandlung chronisch spontaner Urtikaria **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 Übersicht „II. Zugelassene Arzneimittel im Anwendungsgebiet“.
Sofern als Vergleichstherapie eine nicht-medikamentöse Behandlung in Betracht kommt, muss diese im Rahmen der GKV erbringbar sein.	nicht angezeigt
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	Dupixent is indicated for the treatment of moderate to severe chronic spontaneous urticaria in adult and adolescent (12 years and above) patients with inadequate response to H1 antihistamines and who are naive to anti-IgE therapy for CSU.
Biologika	
Omalizumab R03DX05 Xolair®	Chronische spontane Urtikaria (csU) Xolair wird als Zusatztherapie für die Behandlung der chronischen spontanen Urtikaria bei Erwachsenen und Jugendlichen (ab 12 Jahren) mit unzureichendem Ansprechen auf eine Behandlung mit H1-Antihistaminika angewendet.
Antihistaminika	
sedierende H_1-Antihistaminika (1. Generation)	
z.Bsp. Hydroxyzin N05BB01 Atarax®	Symptomatische Behandlung von Juckreiz bei Nesselsucht (Urtikaria) und Ekzem (Neurodermitis).
nicht sedierende H_1-Antihistaminika (ab 2. Generation)	
Cetirizin R06AE07 Cetirizinhydro-chlorid elac®	bei Erwachsenen und Kindern ab 6 Jahren: - […] - zur Linderung von Symptomen bei chronischer idiopathischer Urtikaria
Desloratadin R06AX27 Aerius®	Bei Erwachsenen und Jugendlichen ab 12 Jahren zur Besserung der Symptomatik bei: - allergischer Rhinitis - Urtikaria.

II. Zugelassene Arzneimittel im Anwendungsgebiet	
Ebastin R06AX22 Ebastel®	Zur symptomatischen Behandlung der - saisonalen und perennialen allergischen Rhinitis mit oder ohne allergischer Bindehautentzündung. - Urtikaria
Fexofenadin R06AX26 Fexofenaderm®	Bei Erwachsenen und Kindern ab 12 Jahren zur symptomatischen Behandlung der chronischen idiopathischen Urtikaria.
Levocetirizin R06AE09 Levocetirizin AbZ®	Zur Linderung von Symptomen bei chronischer idiopathischer Urtikaria.
Loratadin R06AX13 Loratadin-ratiopharm®	Zur symptomatischen Therapie der allergischen Rhinitis und der chronischen idiopathischen Urtikaria.
Mizolastin R06AX25 Mizollen®	Mizolastin ist ein langwirksames H1-Antihistaminikum, das zur symptomatischen Behandlung der saisonalen allergischen Rhinokonjunktivitis (Heuschnupfen), der perennialen allergischen Rhinokonjunktivitis und Urtikaria indiziert ist.
Rupatadin R06AX28 Urtimed®	Symptomatische Behandlung einer allergischen Rhinitis und Urtikaria bei Erwachsenen und Jugendlichen (ab 12 Jahren).
Bilastin R06AX29 Bitosen®	Symptomatische Behandlung der allergischen Rhinokonjunktivitis (saisonal und perennial) und Urtikaria.
Glukokortikoide (systemisch, oral) zur Akutbehandlung	

II. Zugelassene Arzneimittel im Anwendungsgebiet	
z.Bsp. Prednisolon H02AB06 Prednisolon acis®	[…] <u>Dermatologie</u> Erkrankungen der Haut und Schleimhäute, die aufgrund ihres Schweregrades und/oder Ausdehnung bzw. Systembeteiligung nicht oder nicht ausreichend mit topischen Glucocorticoiden behandelt werden können. Dazu gehören: - allergische, pseudoallergische und infekt-allergische Erkrankungen: z.B. akute Urtikaria, anaphylaktoide Reaktionen, Arzneimittelexantheme, Erythema exsudativum multiforme […]

Quellen: AMIce-Datenbank, Fachinformationen

Gemeinsamer Bundesausschuss

Abteilung Fachberatung Medizin

Recherche und Synopse der Evidenz zur Bestimmung der zweckmäßigen Vergleichstherapie

Vorgang: 2025-B-269-z (Beratung nach § 35a SGB V) Dupilumab

Auftrag von:	Abt. AM
Bearbeitet von:	Abt. FB Med
Datum:	23. Oktober 2025

Inhaltsverzeichnis

Abkürzungsverzeichnis

AAAAI	American Academy of Allergy, Asthma & Immunology
ACAAI	American Academy of Allergy, Asthma & Immunology (AAAAI)/American College of Allergy Asthma and Immunology
AGREE II	Appraisal of Guidelines for Research & Evaluation II
AMSTAR2	A MeaSurement Tool to Assess systematic Reviews 2
APAAACI	Asia Pacific Association of Allergy, Asthma and Clinical Immunology
AWMF	Arbeitsgemeinschaft der wissenschaftlichen medizinischen Fachgesellschaften
BAD	British Association of Dermatologists
BHRA	Basophil histamine release assay
BSACI	British Society of Allergy and Clinical Immunology
CI	Confidence interval
CNKI	China National Knowledge Infrastructure
CSU	Chronic Spontaneous Urticaria
DLQI	Dermatology Life Quality Index
EAACI	European Academy of Allergology and Clinical Immunology
ECRI	Emergency Care Research Institute
EFA	European Federation of Allergy and Airways Diseases Patients‘ Associations
GA²LEN	Global Allergy and Asthma European Network
GDG	Guideline Development Group
GI	Gastrointestinal
GIN	Guidelines International Network
GoR	Grade of recommendations
GPP	Good practice point
GRADE	Grading of Recommendations Assessment, Development and Evaluation
IgE	Immunoglobulin E
LoE	Level of evidence
MNW	Mean number of wheals
MPS	Mean pruritus score
MTSS	Mean total symptom score
NNT	Number needed to treat
NSAID	Non-steroidal anti-inflammatory drug
OR	Odds ratio
R	Recommendation
RCT	Randomized Controlled Trial
RR	Risk ratio
sgAH	Second-generation H1-antihistamines
SIGN	Scottish Intercollegiate Guidelines Network
TD	Treatment duration
TRIP	Turn Research into Practice Database
WHO	World Health Organization

1 Indikation

Erwachsene und Jugendliche ab 12 Jahren mit mittelschwerer bis schwerer chronischer spontaner Urtikaria, die trotz einer H1-Antihistamin-Behandlung symptomatisch bleiben und therapienaiv gegenüber einer Anti-IgE-Behandlung sind.

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 Urtikaria 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.google.com/*) unter Verwendung des privaten Modus, nach aktuellen deutsch- und englischsprachigen Leitlinien durchgeführt.

Der Suchzeitraum der systematischen Literaturrecherche wurde auf die letzten fünf Jahre eingeschränkt. Die Datenbankrecherche erfolgte am 25.03.2025 und die Recherche nach grauer Literatur am 07.10.2025.

Die detaillierte Darstellung der Recherchestrategie inkl. verwendeter Suchfilter sowie eine Auflistung durchsuchter Leitlinienorganisationen ist am Ende der Synopse aufgeführt. Mit Hilfe von EndNote wurden Dubletten identifiziert und entfernt. Die Recherchen ergaben insgesamt 410 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. Dabei wurde für systematische Reviews, inkl. Meta-Analysen, ein Publikationszeitraum von 2 Jahren und für Leitlinien von 5 Jahren betrachtet. 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 6 Referenzen eingeschlossen. Es erfolgt eine synoptische Darstellung wesentlicher Inhalte der identifizierten Referenzen.

3 Ergebnisse

3.1 Cochrane Reviews

Es wurden keine Cochrane Reviews identifiziert.

3.2 Systematische Reviews

Chu X et al., 2024 [1].

Efficacy and Safety of Systemic Corticosteroids for Urticaria: A Systematic Review and Meta-Analysis of Randomized Clinical Trials

Fragestellung

As part of the American Academy of Allergy, Asthma & Immunology (AAAAI)/American College of Allergy Asthma and Immunology (ACAAI) Joint Task Force on Practice Parameters Chronic Urticaria guideline update, we systematically reviewed the benefits and harms of systemic corticosteroids, compared with treatment without systemic corticosteroids, for acute urticaria and chronic urticaria flares.

Methodik

Population:

- Acute urticaria or chronic urticaria
- We did not limit the type of urticaria, including spontaneous urticaria, inducible urticaria, or both

Intervention:

- Systemic corticosteroids

Komparator:

- Placebo
- Standard of care

Endpunkte:

- Urticaria activity, itch severity, quality of life, angioedema activity, emergency department visits, hospital admission, and adverse effects.

Recherche/Suchzeitraum:

- MEDLINE, EMBASE, Cochrane Central Register of Controlled, CNKI, VIP, Wanfang, and CBM databases from inception to July 8, 2023

Qualitätsbewertung der Studien:

- Three reviewers (JW, XJC, LO) independently assessed the risk of bias per outcome for each study using a modified version of the Cochrane risk of bias tool, version 2.0, for randomized trials.21
- We subclassified “some concerns” judgments as “some concerns, probably high” and “some concerns, probably low.” If at least one domain was at a “high” or “probably high” risk of bias, we considered the study to be at a high risk of bias.

Ergebnisse

Anzahl eingeschlossener Studien:

- 12 RCTs enrolling 944 patients

Charakteristika der Population/Studien:

TABLE I. Characteristics of included studies addressing systemic corticosteroids for urticaria

Study (first author, year)	Country	No. randomized	Urticaria type	Age group (adults/children)*	Female, n (%)	Background therapy	Name of corticosteroid (dosage)	Corticosteroid treatment duration	Follow-up time
Barniol, 2018[39]	France	100	Acute	Adults	53 (53.0)	Levocetirizine	Oral prednisone (40 mg)	4 days	2 days
Bukhari, 2014[28]	Pakistan	140	Acute	Adults	62 (44.3)	Pheniramine/ranitidine	Oral dexamethasone (4 mg)	Single dose	3 hours
Godse, 2014[36]	India	49	Acute	Adults	28 (57.1)	Levocetirizine	Oral prednisolone (10-20 mg)	5 days	5 days
Jin, 2021[29]	China	56	Acute	Adults/children	31 (55.4)	Loratadine and cetirizine	Oral corticosteroids (0.5-1 mg/kg)	3 days	3 days
Jyothi, 2011[35]	India	100	Chronic	Adults/children	57 (57.0)	Loratadine	Oral prednisolone (5-20 mg)	12 days	12/15 days
Liu, 2013[37]	China	50	Acute	Children	21 (42.0)	Chlorpheniramine maleate	IV dexamethasone (1-4 mg/kg)/IV methylprednisolone (0.25-0.75 mg/kg)	4 days	4 days
Lou, 2014[38]	China	80	Acute	Adults/children	36 (45.0)	Levocetirizine + hydrochloride + cimetidine	IV dexamethasone (10 mg)	3 days	3 days
Palungwachira, 2021[30]	Thailand	75	Acute	Adults	58 (77.3)	Chlorpheniramine maleate + cetirizine	IV dexamethasone (5 mg)/ oral prednisolone (20 mg)	Single dose/7 days	15-60 minutes
Paradis, 1996[34]	Canada	19	Chronic	Adults	14 (73.7)	None	Oral methylprednisolone (32 mg)	7 days	7 days
Pollack, 1995[33]	United States	43	Acute	Adults	19 (44.3)	Hydroxyzine	Oral prednisone (20 mg)	4 days	5 days
Rasool, 2015[32]	India	192	Chronic	NR	130 (67.7)	Hydroxyzine/cholecalciferol	Oral deflazacort (6 mg)	6 weeks	4/6 weeks
Vena, 1998[31]	Italy	40	Chronic	Adults	18 (45.0)	None	Oral prednisone (40 mg)	7 weeks	3 weeks

IV, Intravenous; *NA*, not applicable; *NR*, not reported.
*Adults were defined as age ≥18 years. Children were defined as age <18 years.

Qualität der Studien:

Domains:
D1 Bias arising from the randomization process
D2 Bias due to deviations from the intended intervention
D3 Bias due to missing outcome data
D4 Bias in measurement of the outcome
D5 Bias in selection of the reported results
D6 Other biases (e.g., early termination, competing risks)

Low risk of bias.
Probably Low risk of bias.
Probably High risk of bias.
High risk of bias.

[1] Low risk of bias for Itch severity.
[2] Low risk of bias for Adverse effects.
[3] Probably high risk of bias for Itch severity.

FIGURE 2. Risk of bias assessment per outcome among randomized trials addressing systemic corticosteroids for urticaria.

Studienergebnisse:

- Nine RCTs (N = 669) informed the effect of systemic corticosteroids on **urticaria activity**. 28-30,34-39 Compared with patients treated with antihistamines alone, add-on systemic corticosteroids improved urticaria (moderate certainty; OR, 2.17 [95% CI: 1.43-3.31]. The absolute effects of adding systemic corticosteroids depended on the baseline probability for urticaria to improve.
  - For patients with low or moderate probability (17.5%-64%) for urticaria to improve with antihistamines alone, add-on systemic corticosteroids improved urticaria activity by 14% to 15% (number needed to treat [NNT], 7).
  - Among patients with a high chance (95.8%) for urticaria to improve with antihistamines alone, addon systemic corticosteroids improved urticaria activity by a 2.2% absolute difference (NNT, 45)
- Four RCTs (N = 353) informed the effect of systemic corticosteroid intervention on **itch severity**.30,32-34 Compared with patients treated with antihistamines alone, add-on systemic corticosteroids may improve itch severity in 93% versus 84% (low certainty; OR, 2.44 [95% CI: 0.87-6.83]; NNT, 11).
- The most common reported **adverse effects** being gastrointestinal (GI) upset (eg, gastric irritation, dyspepsia, and vomiting) (N = 23), headache or anxiety (N = 7), fatigue (N = 7), or sedation (N = 7). Four studies were included in the meta-analysis.30,35,36,39 Compared with non-corticosteroids, given the control group risk of approximately 11.4%, corticosteroids may increase the risk of adverse effects (moderate certainty; OR, 2.76 [95% CI: 1.00-7.62]; risk difference: 14.8%; number needed to harm, 7).

Anmerkung/Fazit der Autoren

Among children and adults with acute urticaria or chronic urticaria exacerbations, systemic corticosteroids, often added to antihistamines, likely improve urticaria activity and may improve itch, but also likely increase adverse effects. Considering the lack of evidence-based guidance addressing systemic corticosteroids for urticaria,46 this systematic review may inform the optimal management of urticaria.

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Xiao X. et al., 2023 [5].

The efficacy and safety of high-dose non-sedating antihistamines in chronic spontaneous urticaria: a systematic review and meta-analysis of randomized clinical trials

Fragestellung

To evaluate the efficacy and side effects of high-dose second-generation H1-antihistamines (sgAHs) in the treatment of chronic spontaneous urticaria (CSU), in order to provide new evidence for its clinical application.

Methodik

Population:

- Patients with CSU

Intervention/Komparator:

- compared two or more fixed-doses sgAHs in their treatment groups (i.e. an active drug with placebo, or two or more doses of an active drug with or without placebo)

Endpunkte:

- response rates (defined as pruritus symptoms reduction higher than 50%, or at least a moderate to very good global symptom improvement.)
- MPS (mean pruritus score, reflecting the overall situation of pruritus)
- MNW (mean number of wheals, reflecting the overall situation of wheals)
- MTSS (calculated as the sum of MPS and MNW, reflecting the overall situation of urticaria symptoms)
- DLQI (dermatology life quality index) and/or adverse events of the treatment

Recherche/Suchzeitraum:

- up to February 2023
- Medline, Embase, Cochrane library, PsycInfo, Web of Science

Qualitätsbewertung der Studien:

- Cochrane risk of bias tool

Ergebnisse

Anzahl eingeschlossener Studien:

- 13 RCTs, one triple-blind, one quadruple-blind and eleven double-blind, were finally included in the meta-analysis, enrolling 3079 patients

Charakteristika der Population:

Table 1 Characteristics of studies included in the systematic review

Study	Sample Size (female,%)	Age	Course of the disease (week)	Outcome measurement	Intervention	TD	Definition of response	Response rate[a], no. (%)	Adverse events, no. (%)	Somnolence (%)	Main outcome
Gimenez-Arnau et al. (2007) [23]	329 (68.39%)	12–65	≥ 6	5-point rating score [b] (MPS, MNW, MTSS); 5-point rating score [c] (Global efficacy); DLQI	Rupatadine 10 mg Rupatadine 20 mg Placebo	6 weeks	pruritus symptoms reduction higher than 50%	72 (65.5%) 79 (73.15%) 51 (45.9%)	13 (11.6%) 18 (16.5%) 13 (11.5%)	3 (2.7%) 9 (8.3%) 6 (5.3%)	Rupatadine 10 mg has an overall better AE profile than rupatadine 20 mg. Rupatadine 10 mg is the preferred dose of choice for patients with CIU
Finn et al. (1999) [24]	439 (74.26%)	12–65	≥ 6	5-point rating score [b] (MPS, MNW, MTSS), Sleep and daily activities[d]	Fexofenadine HCl 20 mg bid Fexofenadine HCl 60 mg bid Fexofenadine HCl 120 mg bid Fexofenadine HCl 240 mg bid Placebo	4 weeks	NA	NA	67 (71%) 51 (57%) 60 (65%) 50 (59%) 61 (66%)	NA	Fexofenadine 60 mg bid had a larger treatment effect than fexofenadine 20 mg bid. All doses were well tolerated, with safety profiles similar to that of placebo
Gibson et al. (1984) [25]	20 (60%)	19–74	≥ 4	5-point rating score[b] (pruritus, wheals, Discomfort VAS[e]	Acrivastine 4 mg tid Acrivastine 8 mg tid Placebo tid	5 days	NA	NA	4 (20%) 8 (40%) 6 (30%)	2 (10%) 7 (35%) 3 (15%)	Acrivastine 8 mg was significantly better than Acrivastine 4 mg in improving itching and whealing
Nelson et al. (2000) [29]	418 (70.10%)	12–65	≥ 6	5-point rating score [b] (MPS, MNW) sleep and daily activities[d]	fexofenadine HCl 20 mg bid fexofenadine HCl 60 mg bid fexofenadine HCl 120 mg bid fexofenadine HCl 240 mg bid Placebo	4 weeks	NA	NA	NA	NA	Fexofenadine HCl significantly reduced pruritus severity, number of wheals, and twice-daily doses of 60 mg or greater were most effective

Study	Sample Size (female,%)	Age	Course of the disease (week)	Outcome measurement	Intervention	TD	Definition of response	Response rate[a], no. (%)	Adverse events, no. (%)	Somnolence (%)	Main outcome
Paul et al. (1998) [22]	208 (57.69%)	≥ 18	≥ 6	4-point rating scoref(MPS); 5-point rating score[b] (MNW); TSS; Sleep and daily activities[d]; Medication effectiveness[i]	Fexofenadine HCl 60 mg Fexofenadine HCl 120 mg Fexofenadine HCl 180 mg Fexofenadine HCl 240 mg Placebo	6 weeks	rated the effectiveness of the medication as good, very good or excellent	25 (63%) 18 (50%) 30 (64%) 21 (55%) 19 (41%)	7 (18%) 9 (26%) 13 (28%) 10 (26%) 15 (33%)	0 (0%) 0 (0%) 0 (0%) 0 (0%) 0 (0%)	There was no significant difference between the 180 mg/day and the 240 mg/day doses. The authors recommend fexofenadine HCl 180 mg/day as the optimal dose for the treatment of CSU
Dubertret et al. (2007) [33]	277 (72.92%)	12–65	≥ 6	5-point rating score[b] (MPS, MNS, MTSS); sleep and daily activities[d]; Global efficacy[c]	Rupatadine 5 mg Rupatadine 10 mg Rupatadine 20 mg Placebo	4 weeks	0: worse 1: unchanged 2:slight improvement 3:good improvement	37 (54.24%) 42 (57.04%) 49 (72.80%) 17 (25.04%)	NA	3 (4.29%) 4 (5.41%) 14 (21.43%) 2 (2.90%)	Rupatadine 10 mg and 20 mg provides rapid and long-lasting relief from pruritus, in CSU
Weller et al. 2013 [26]	29 (55.17%)	21–65	NA	UAS7; Discomfort VAS[e]; Area size of wheals;	Desloratadine 5 mg (on demand) Desloratadine 20 mg (on demand)	21 days	NA	NA	0 (0%) 0 (0%)	0 (0%) 0 (0%)	The beneficial effects of desloratadine on existing wheals (on-demand treatment) seem to be low
Sánchez et al. (2016) [30]	180 (55.17%)	12–50	≥ 6	UAS, DLQI	First 4 weeks: cetirizine 10 mg Fexofenadine 180 mg bilastine 20 mg Desloratadine 5 mg Ebastine 20 mg Placebo Second 4 weeks: 2 ~ fourfold dose based on the original drug	8 weeks	Controlled: (DLQI ≤ 5) Moderate: (DLQI 6–9) Uncontrolled: (DLQI ≥ 10)	onefold: 88 (58.7%) 2 ~ fourfold: 115 (76.7%)	87 (58%)	onefold: 43 (28.6%) ~ 2–fourfold: 34 (22.6%)	The safety and efficacy of the 5 antihistamines were similar. After updosing, rates of disease control increased from 58.7% to 76.7%

Study	Sample Size (female,%)	Age	Course of the disease (week)	Outcome measurement	Intervention	TD	Definition of response	Response rate[a], no. (%)	Adverse events, no. (%)	Somnolence (%)	Main outcome
Hide et al. (2016) [27]	294 (73.81%)	18–74	≥4	4-point rating score[f] (wheals); 5-point rating score [b] (pruritus); TSS; DLQI; Overall improvement score[g]	Bilastine 10 mg Bilastine 20 mg Placebo	2 weeks	1.markedly improved; 2.moderately improved; 3.mildly improved; 4.no change; 5.exacerbated 6.not evaluable	84 (84.8%) 74 (74.7%) 30 (31.6%)	24 (24.0%) 14 (13.9%) 20 (19.4%)	2 (2.0%) 0 (0.0%) 3 (2.9%)	Bilastine 20 and 10 mg once a day was effective and tolerable in Japanese patients with CSU.
Hide et al. (2019) [28]	276 (65.94%)	12–64	≥4	5-point rating score [b] (TPS, NWS, RDS); PWS, DLQI; Overall improvement score [h]	Rupatadine 10 mg Rupatadine 20 mg Placebo	2 weeks	1.extremely improved 2.very improved 3.moderately improved 4.no change 5.worsened	68 (74.8%) 71 (78.1%) 29 (30.8%)	19 (20.9%) 16 (17.4%) 8 (8.5%)	10 (11.0%) 9 (9.8%) 0 (0%)	The optimal rupatadine dose was 10 mg once daily. The dose can be safely increased to 20 mg once daily,
Staevska et al.2010 [31]	80 (62.67%)	19–67	≥6	CU-Q2oL; Discomfort VAS[e]; ASST	Levocetirizine (5 mg/1st wk, 10 mg/2nd wk, 20 mg/3rd wk) Desloratadine (5 mg/1st wk, 10 mg/2nd wk, 20 mg/3rd wk) levocetirizine 20 mg switch desloratadine 20 mg (4th wk)	4 weeks	Patients who had no urticarial lesions and no pruritus for the last 3 days of treatment were considered to be symptom-free	Levocetirizine/ Desloratadine: 1st wk 9/4 2nd wk 8/7 3rd wk 5/1 4th wk 7/0	6 (15%) 11 (27.5%)	No detailed data	Levocetirizine and desloratadine, to up to 4 times the conventionally prescribed doses increases the control of urticaria symptoms in approximately 75% of patients without compromising somnolence or safety. Levocetirizine was more effective drug in the course of treatment with 5-mg to 20-mg daily doses
Kalivas et al. 1990 [32]	215 (NA)	≥12	≥6	Four-point rating score[f] (wheals, pruritus and number of episodes); Global efficacy[c]	Cetirizine 5 mg ~ 20 mg; Hydroxyzine 25 ~ 75 mg; Placebo	4 weeks	NA	NA	No detailed data	15 (21.7%) 26 (36. 1%) 10 (13.5%)	cetirizine has a greater safety margin over the older parent drug hydroxyzine

Study	Sample Size (female,%)	Age	Course of the disease (week)	Outcome measurement	Intervention	TD	Definition of response	Response rate[a], no. (%)	Adverse events, no. (%)	Somnolence (%)	Main outcome
NCT00536380 2013 [34]	314(66.56%)	≥ 18	≥ 6 weeks	UAS	desloratadine 5 mg desloratadine 10 mg desloratadine 20 mg	4 weeks	NA	NA	7(6.6%) 5(4.8%) 2(1.9%)	NA	There was no significant difference in UAS scores improvement between the 5 mg, 10 mg and 20 mg desloratadine groups

Abbreviations: TD Treatment duration, *DLQI* Dermatology life quality index, *VAS* Visual analogue scale, *MPS* Mean pruritus score, *MNW* Mean number of wheals, *MTSS* Calculated as the sum of MPS and MNW, *NA* data were not available in the study, *TSS* The sum of the wheal and pruritus scores, *TPS* Total pruritus score, *NWS* Number of wheals score, *RDS* Rash duration score, *PWS* The sum of pruritus and number of wheals score, *UAS* Urticaria activity score, *ASST* Autologous serum skin test, *CU-Q2oL* Chronic urticaria quality of life questionnaire

[a] Response, pruritus symptoms reduction higher than 50%, or overall improvement rated at least moderately/very improved

[b] Five-point rating score (0–4): 0 = no symptom to 4 = the worst symptom, the higher the score, the worse the symptoms

[c] Global efficacy (0–4): 0 = worse to 4 = excellent improvement, the higher the score, the better the symptoms

[d] sleep and daily activities: (0–3): 0 = none, 1 = mild, 2 = moderate, and 3 = severe

[e] Discomfort VAS: patients evaluated their drowsiness, itching and severity of symptoms by marking along a 0–100 mm long horizontal line (0 = min to 106 = max)

[f] Four-point rating score (0–3): 0 = no symptom to 3 = the worst symptom, the higher the score, the worse the symptoms;

[g] Five-point rating score (1–5): 1 = markedly improved to 5 = exacerbated, the higher the score, the worse the symptoms;

[h] Overall improvement score (1–6): 1 = extremely improved, 2 = very improved, 3 = moderately improved, 4 = no change, 5 = worsened, and 6 = not evaluable

[i] medication effectiveness (0–4, 0 = excellent to 4 = none)

Qualität der Studien:

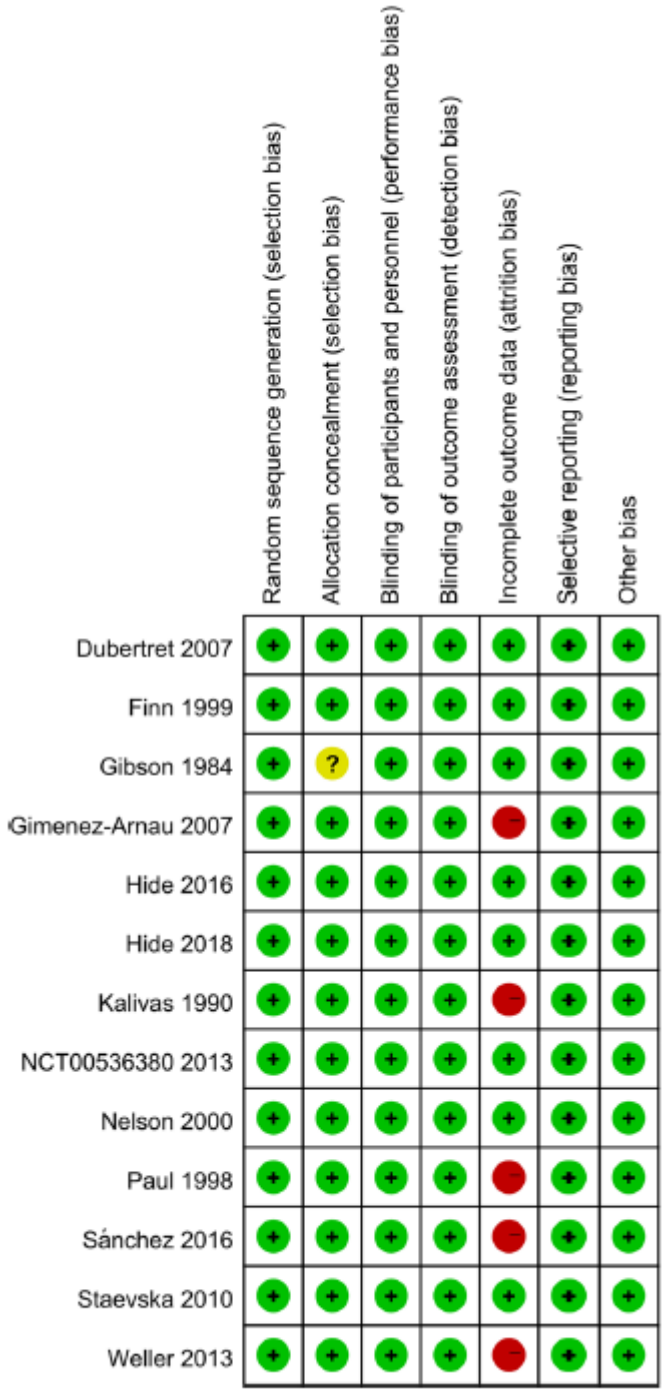

Fig. 2 Risk of bias of the included studies

Studienergebnisse:

- The response was reported in four studies [22,23, 28, 33] with a total of 352 patients treated with high-dose and 310 patients treated with standard-dose sgAHs. High-dose sgAHs was associated with a significantly higher response rate when compared with standard dose (RR 1.13, 95% CI 1.02 to 1.26; P = 0.02).

- Adverse events were reported in six studies [22–24, 28, 29, 34] with a total of 1367 patients evaluated (high dose n = 836; standard dose n = 531). There was no significant difference in patients with CSU who experienced at least one adverse event between high-dose and standard-dose treatments (RR 1.06, 95% CI 0.93 to 1.22; P = 0.36).
- Somnolence was reported in four studies [22, 23, 28, 33] including 666 patients (high dose n = 354; standard dose n = 312). A high-dose sgAHs was associated with significantly higher somnolence rates when compared with the standard dose (RD 0.05, 95% CI 0.01 to 0.09; P = 0.02).
  - Due to the noted significant heterogeneity between the included studies (I2 = 52%), the leave-one-out analysis was performed. When the study by Dubertret et al. [33]. was excluded from the analysis, the heterogeneity was significantly reduced (I2 = 0%), which suggested that it is a heterogeneous source. When other studies pooled, there was no significant difference in somnolence between high dose and standard dose (RD 0.02, 95% CI -0.02 to 0.06; P = 0.36). This indicated that the results were not robust enough and should be treated with caution.
- Withdrawal of patients due to adverse events was reported in four studies [24, 28, 29, 34] including 1039 patients (high dose n = 650; standard dose n = 389). There was no significant difference in the number of patients withdrawing from treatment due to adverse events between high-dose and standard-dose treatments (RR 0.60, 95% CI 0.31 to 1.17; P = 0.13).

Anmerkung/Fazit der Autoren

The findings of the meta-analyses showed that high-dose sgAHs (up to two times the standard dose) might be more effective than standard doses in the treatment of CSU. High-dose and standard-dose sgAHs showed similar safety profiles, with the exception of somnolence that might be dose-dependent. However, due to the limited number of studies in our meta-analysis, results should be interpreted with caution.

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3.3 Leitlinien

Information zur deutschen S3-Leitlinie:

Die deutsche AWMF S3-LL „Klassifikation, Diagnostik und Therapie der Urtikaria“ befindet sich aktuell in Überarbeitung und wurde seit ≥ 5 Jahren nicht aktualisiert. Die Fertigstellung ist für den 31.12.2025 geplant. Es handelt sich dabei um eine Adaptation der International EAACI/GA²LEN/EuroGuiDerm/ APAAACI guideline for the definition, classification, diagnosis, and management of urticaria von Zuberbier et al. (2022) [6]. Diese LL ist in der Synopse dargestellt.

Zuberbier T et al., 2022 [2,3,6].

The international EAACI/GA²LEN/EuroGuiDerm/APAAACI guideline for the definition, classification, diagnosis, and management of urticaria

Zielsetzung/Fragestellung

The aim of the guideline is to provide a definition and classification of urticaria, thereby facilitating the interpretation of data from different centers and areas of the world regarding underlying causes, eliciting factors, comorbidities, burden to patients and society, and therapeutic responsiveness of subtypes of urticaria. Furthermore, the guideline provides recommendations for diagnostic and therapeutic approaches in common subtypes of urticaria. This is an international guideline and takes into consideration the global diversity of patients, physicians, medical systems and access to diagnosis and treatment.

Methodik

Grundlage der Leitlinie

- Repräsentatives Gremium: **Trifft teilweise zu** – es gab keine Patientenbeteiligung: „During the guideline development process, no patient representative or patient organization was involved, although we did attempt to invite patient representative from the European Federation of Allergy and Airways Diseases Patients‘ Associations (EFA).”
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt: **Trifft zu**
- Systematische Suche, Auswahl und Bewertung der Evidenz: **Trifft zu**
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt: **Trifft zu**
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt: **Trifft zu**
- Regelmäßige Überprüfung der Aktualität gesichert: **Trifft zu** – The expert panel will decide if and when an update is necessary, at the latest five years from the date of publication of the 2020/21 guideline.

Recherche/Suchzeitraum:

- Systematic searches for randomized controlled trials and clinical, controlled trials were undertaken using the following databases on 15 May 2020 limiting the time to 2016 – 15 May 2020:
  - Ovid MEDLINE(R) ALL 1946 to May 14, 2020
  - Embase Classic+Embase 1947 to 2020 May 14

LoE/GoR

- Cochrane Risk of Bias Assessment Tool
- Grading of Recommendations Assessment, Development and Evaluation (GRADE)

TABLE 5: SUMMARY OF THE GRADE APPROACH TO ASSESSING THE QUALITY OF EVIDENCE BY OUTCOME IN RANDOMISED CONTROLLED TRIALS[14]

Initial quality of the body of evidence	Criteria that may decrease the quality rating	Criteria that may increase the quality rating	Quality of the body of evidence	
High	– Risk of bias – Inconsistency – Indirectness – Imprecision – Publication bias	– Large effect – Dose response – Residual confounding	High (++++)	We are very confident that the true effect lies close to that of the estimate of effect.
			Moderate (+++)	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 (++)	Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.
			Very low (+)	We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

TABLE 6: WORDING OF RECOMMENDATIONS[20-23]

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 a choice in favor of using this intervention. Clinicians will not have to spend as much time on the process of decision-making with the patient and may devote that time instead to overcoming barriers to implementation and adherence. In most clinical situations, the recommendation can be adopted as a policy.
Weak recommendation **for** the use of an intervention	'We **suggest** . . .'	↑	We believe that most informed people would make a choice in favor of using this intervention, but a substantial number would not. Clinicians and other health care providers will need to devote more time to the process of shared decision-making. Policy makers will have to involve many stakeholders and policy making will require substantial debate.
No recommendation with respect to an intervention	'We **cannot make a recommendation** with respect to . . .'	0	Currently, a recommendation in favor of or against using this intervention cannot be made due to certain circumstances (for example, unclear or balanced benefit-risk ratio, no data available).
Weak recommendation **against** the use of an intervention	'We **suggest against** . . .'	↓	We believe that most informed people would make a choice against using this 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 using this intervention. This recommendation can be adopted as a policy in most clinical situations.

Empfehlungen

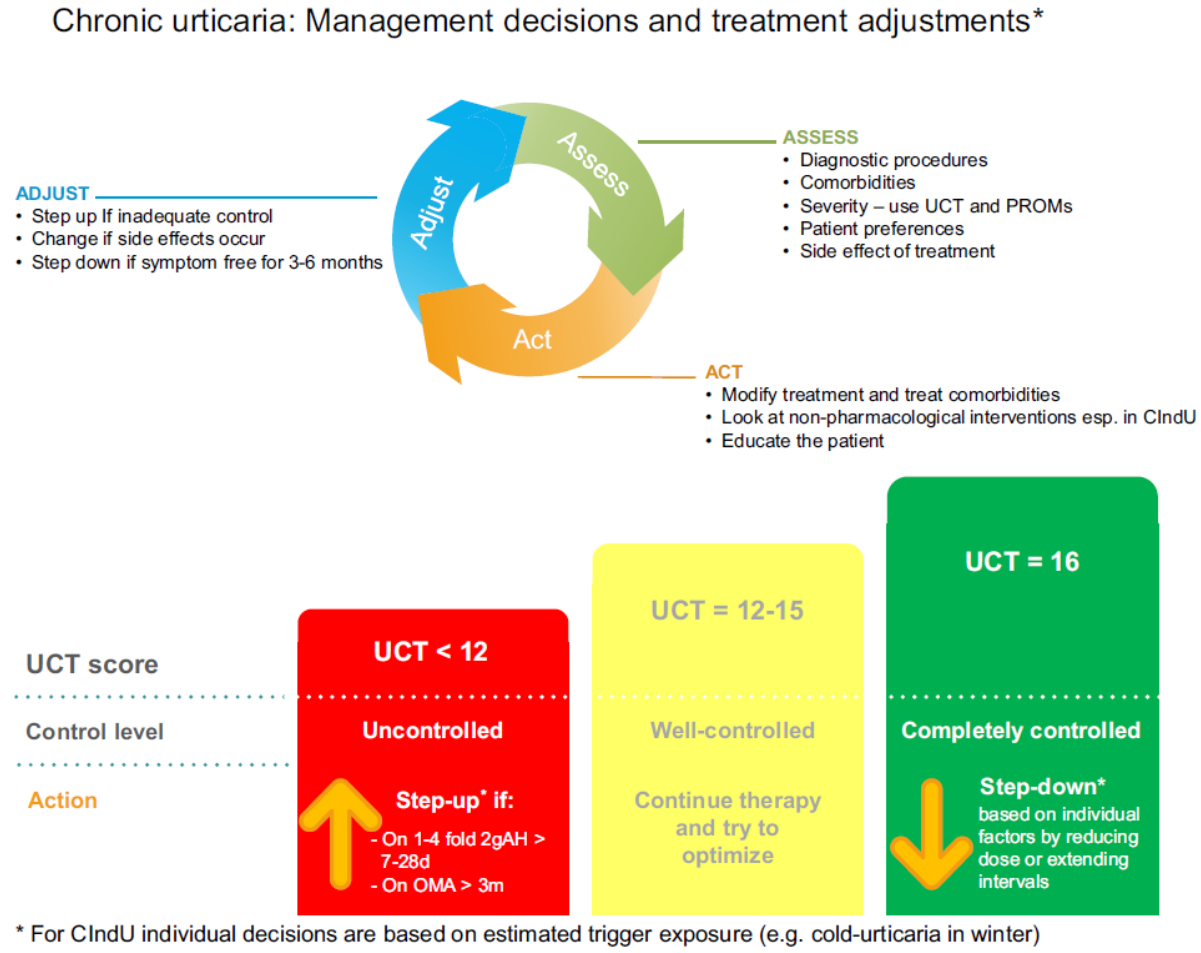

FIGURE 3 Chronic urticaria: Management decisions and treatment adjustments. CIndU: chronic inducible urticaria; d: days; m: months; PROMs: patient-reported outcome measures; OMA: omalizumab ; 2gAH: 2nd generation H_1-antihistamine; UCT: Urticaria Control Test

Symptomatic pharmacological treatment

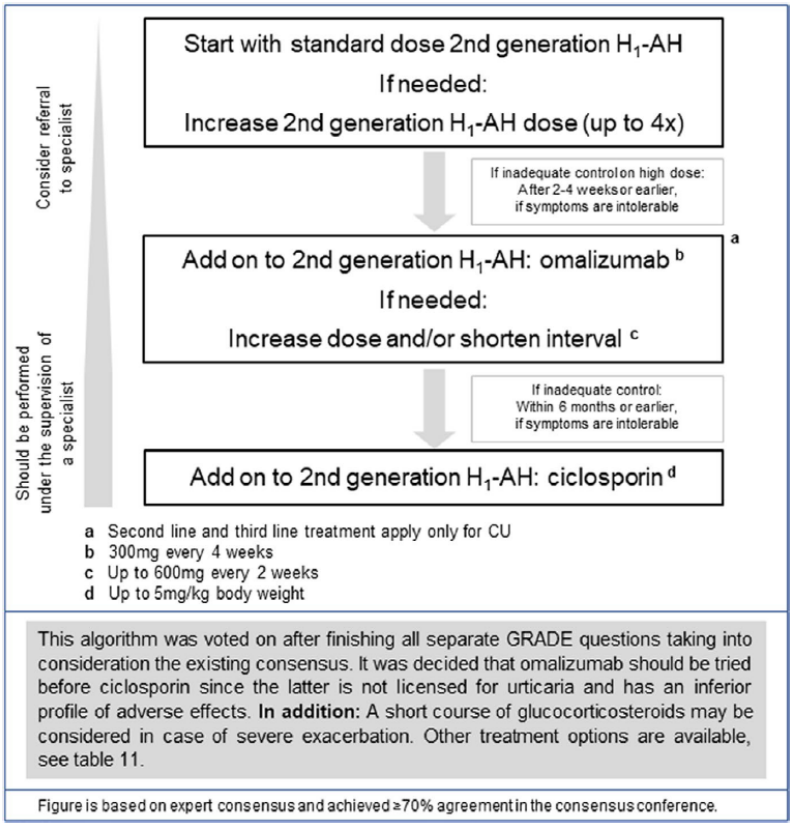

FIGURE 4 Recommended treatment algorithm for urticaria. AH: antihistamine; CU: chronic urticaria; GRADE: Grading of Recommendations Assessment, Development and Evaluation (working group). First line = High quality evidence: Low cost and worldwide availability (e.g. modern 2nd generation H1-antihistamines exist also in developing countries mostly cheaper than old sedating antihistamines), per daily dose as the half life time is much longer, very good safety profile, good efficacy. Second line (omalizumab as add on to 2nd generation H1-antihistamine) = High quality evidence: High cost, very good safety profile, very good efficacy. Third line (ciclosporin as add on) = High quality evidence: Medium to high cost, moderate safety profile, good efficacy. Short course of corticosteroids = Low quality evidence: Low cost, worldwide availability, good safety profile (for short course only), good efficacy during intake, but not suitable for long term therapy

H_1-antihistamine treatment

Should modern 2nd generation H_1-antihistamines be used as first-line treatment of urticaria?		
We **recommend** a 2nd generation H_1-antihistamine as first-line treatment for all types of urticaria.	↑↑	Strong consensus[1] Evidence- and consensus-based (see Evidence Report)

[1] 100% agreement

Is an increase in the dose to up to fourfold of modern 2nd generation H_1-antihistamines useful and to be preferred over other treatments in urticaria?		
We **recommend** updosing of a 2nd generation H_1-antihistamine up to fourfold in patients with chronic urticaria unresponsive to a standard-dosed 2nd generation H_1-antihistamines as second-line treatment before other treatments are considered.	↑↑	Strong consensus[1] Evidence- and consensus-based (see Evidence Report)

[1] ≥90% agreement

Should modern 2nd generation H_1-antihistamines be taken regularly or as needed?		
We **suggest** 2nd generation H_1-antihistamines to be taken regularly for the treatment of patients with chronic urticaria.	↑	Strong consensus[1] Evidence- and consensus-based (see Evidence Report)
[1]≥90% agreement		

Should different 2nd generation H_1-antihistamines be used at the same time?		
We **suggest against** using different H_1-antihistamines at the same time.	↓	Consensus[1] Evidence- and consensus-based (see Evidence Report)
[1] ≥70% agreement		

If there is no improvement, should higher than fourfold doses of 2nd generation H_1-antihistamines be used?		
We **recommend against** using higher than fourfold standard-dosed H_1-antihistamines in chronic urticaria	↓↓	Strong consensus[1] Evidence- and consensus-based (see Evidence Report)
[1]≥90% agreement		

Omalizumab treatment

Is omalizumab useful as add-on treatment in patients unresponsive to high doses of H_1-antihistamines?		
We **recommend** adding on omalizumab* for the treatment of patients with CU unresponsive to high dose 2nd generation H_1-antihistamines. *currently licensed for chronic spontaneous urticaria	↑↑	Strong consensus[1] Evidence- and consensus-based (see Evidence Report)

[1]≥90% agreement

Ciclosporin treatment

Is ciclosporin useful as add-on treatment in patients unresponsive to high doses of H_1-antihistamine?		
We **suggest** using ciclosporin for the treatment of patients with CU unresponsive to high dose of 2nd generation H_1-antihistamine and omalizumab.	↑	Strong consensus[1] Evidence- and consensus-based (see Evidence Report)

[1]≥90% agreement

Other symptomatic treatments

Should oral corticosteroids be used as add-on treatment in the treatment of urticaria?		
We **recommend against** the long-term use of systemic glucocorticosteroids in CU.	↓↓	Strong consensus[1]
We **suggest** considering a short course of rescue systemic glucocorticosteroids in patients with an acute exacerbation of CU.	↑	Evidence- and consensus-based (see Evidence Report)

[1] ≥90% agreement

Are H_2-antihistamines useful as add-on treatment in patients unresponsive to low or high doses of H_1-antihistamines?		
We **cannot make a recommendation** for or against the combined use of H_1- and H_2-antihistamines in patients with chronic urticaria.	0	Strong consensus[1] Expert consensus

[1] ≥90% agreement

Could any other treatment options be recommended for the treatment of urticaria?		
We **cannot make a recommendation** with respect to further treatment options as standard therapies, but these may be considered in special cases, which also include those where financial or legal limitations for the recommended algorithm treatment exist.	0	Strong consensus[1] Expert consensus

[1] ≥90% agreement

Treatment of special populations

Children

Should the same treatment algorithm be used in children?		
We **suggest** using the same treatment algorithm with caution (eg, weight-adjusted dosage) in children with chronic urticaria	↑	Strong consensus[1] Expert consensus

[1]≥90% agreement

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Sabroe RA et al., 2022 [4].

British Association of Dermatologists (BAD)

British Association of Dermatologists guidelines for the management of people with chronic urticaria 2021

Zielsetzung/Fragestellung

The overall objective of the guideline is to provide up-to-date, evidence-based recommendations for the management of urticaria.

Methodik

Grundlage der Leitlinie

- Repräsentatives Gremium: **Trifft zu**
- Interessenkonflikte und finanzielle Unabhängigkeit dargelegt: **Trifft teilweise zu** – Interessenkonflikte werden dargelegt, jedoch wird nicht angegeben, wie mit den Interessenkonflikten umgegangen wurde und Angaben zur Finanzierung fehlen ebenfalls.
- Systematische Suche, Auswahl und Bewertung der Evidenz: **Trifft zu**
- Formale Konsensusprozesse und externes Begutachtungsverfahren dargelegt: **Trifft zu**
- Empfehlungen der Leitlinie sind eindeutig und die Verbindung zu der zugrundeliegenden Evidenz ist explizit dargestellt: **Trifft zu**
- Regelmäßige Überprüfung der Aktualität gesichert: **Trifft zu** – The proposed revision date for this set of recommendations is scheduled for 2026; where necessary, important interim changes will be updated on the BAD website.

Recherche/Suchzeitraum:

A systematic literature search of the PubMed, MEDLINE, Embase and Cochrane databases was conducted to identify key articles on urticaria from January 2007 to March 2020. An additional, targeted literature search for the antihistamines acrivastine and bilastine was also carried out (from January 1980 to March 2020). Subsequently published papers known to the GDG were included. The final literature searches were run ahead of journal submission in 2021 to ensure currency.

LoE/GoR

- A MeaSurement Tool to Assess systematic Reviews (AMSTAR 2)
- Grading of Recommendations Assessment, Development and Evaluation (GRADE)
- Appraisal of Guidelines for Research & Evaluation II (AGREE II)

Table 1 Strength of recommendation ratings

Strength	Wording	Symbol	Definition
Strong recommendation for the use of an intervention	'Offer' (or similar, e.g. 'use', 'provide', 'take', 'investigate' etc.)	↑↑	Benefits of the intervention outweigh the risks; most patients would choose the intervention whilst only a small proportion would not; for clinicians, most of their patients would receive the intervention; for policymakers, it would be a useful performance indicator
Weak recommendation for the use of an intervention	'Consider'	↑	Risks and benefits of the intervention are finely balanced; most patients would choose the intervention but many would not; clinicians would need to consider the pros and cons for the patient in the context of the evidence; for policymakers it would be a poor performance indicator where variability in practice is expected
No recommendation		Θ	Insufficient evidence to support any recommendation
Strong recommendation against the use of an intervention	'Do not offer'	↓↓	Risks of the intervention outweigh the benefits; most patients would not choose the intervention whilst only a small proportion would; for clinicians, most of their patients would not receive the intervention

Empfehlungen

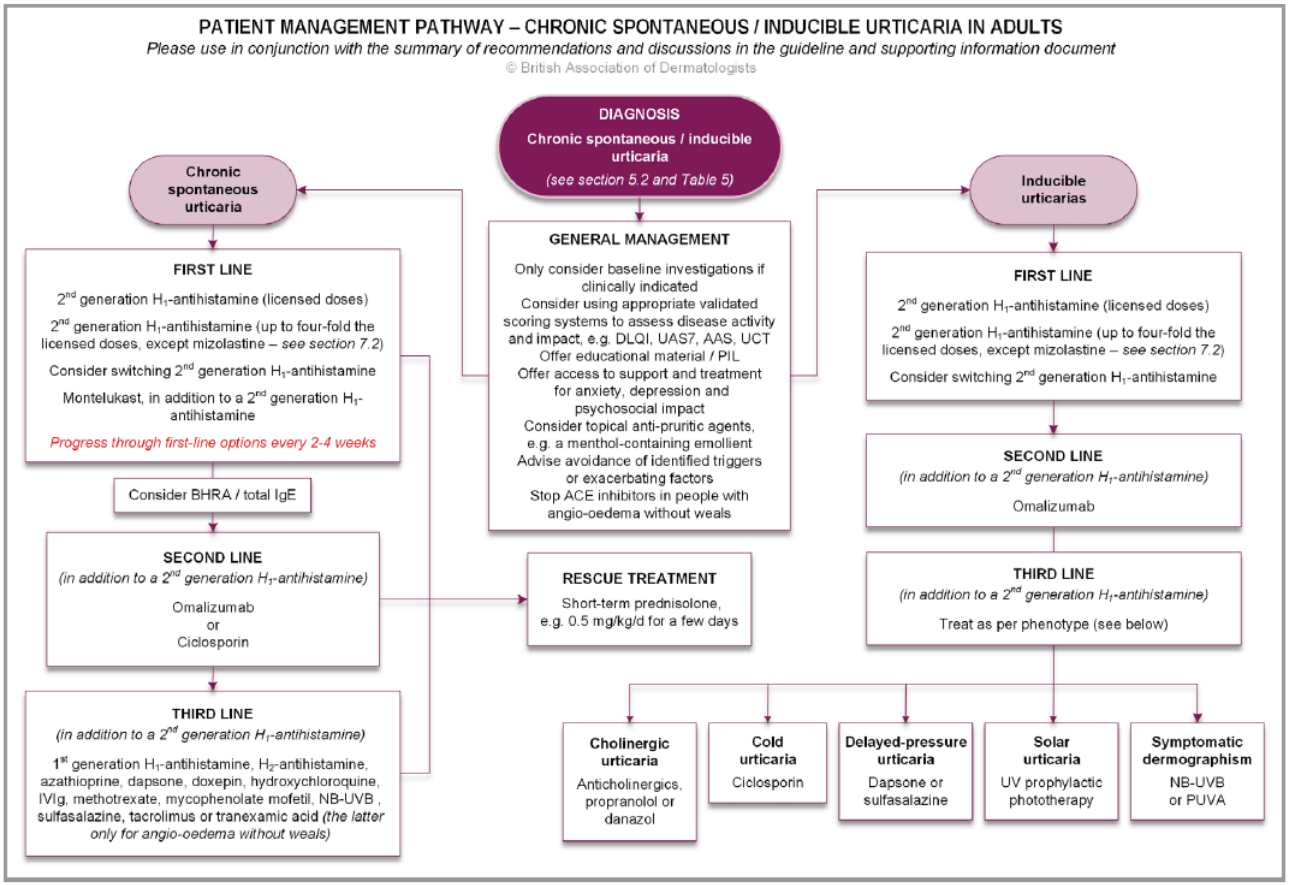

Figure 1 Patient management pathway for urticaria. For clarity we have divided management options into sections (general treatment, and first-, second- and third-line options). However, depending on disease severity, disease fluctuation, comorbidities and national criteria for use of drugs, the order and combinations of treatment may vary and change during each person's disease. AAS, Angioedema Activity Score; ACE, angiotensin-converting enzyme; BHRA, basophil histamine release assay; DLQI, Dermatology Life Quality Index; IVIg, intravenous immunoglobulin; NB-UVB, narrowband ultraviolet B; PIL, patient information leaflet; PUVA, psoralen plus ultraviolet A; UAS7, Urticaria Activity Score summed over 7 days; UCT, Urticaria Control Test.

General management for people with chronic spontaneous urticaria

R8 (↑ ↑) Avoid NSAIDs in people whose CSU appears to be exacerbated by this class of drugs.

R9 (↑) Consider switching NSAID treatment to a selective cyclooxygenase-2 inhibitor, if tolerated and not contraindicated, when there is a history of acute exacerbation of CSU after NSAID intake for inflammation. However, evidence of benefit from switching low-dose aspirin when taken as an antithrombotic to an alternative antiplatelet drug is lacking. Refer to the National Institute for Health and Care Excellence,7 British Society of Allergy and Clinical Immunology (BSACI)8 or European Academy of Allergy and Clinical Immunology (EAACI) guidance9 if reactivity to NSAIDs is suspected.

First-line treatment options for people with chronic spontaneous urticaria

R12 (↑ ↑) Offer a second-generation H1-antihistamine, using a regular daily licensed dose (Table 4).

R13 (↓ ↓) Do not offer first-generation H1-antihistamines routinely, unless there is no alternative, due to concerns about their short- and long-term effects on the central nervous system.

R14 (↑ ↑) Offer updosing (i.e. increasing the dose above the licensed dose) of a single second-generation H1-antihistamine, by up to fourfold the licensed dose, to people whose symptoms are inadequately controlled by the standard licensed dose, provided it is tolerated and there is no caution or contraindication (see section 7.2 and Appendix C – LETR narratives). Attempt stepwise dose reduction following complete symptom control. There is no evidence to guide the optimum duration of up-dosing or speed of dose reduction.

R15 (↓ ↓) Do not up-dose mizolastine.

R16 (GPP) Consider switching from one second-generation H1-antihistamine to another in people whose symptoms do not respond adequately to, or who do not tolerate, the first drug at standard or increased doses.

Θ3 There is insufficient evidence to make a recommendation on using two different second-generation H1-antihistamines at the same time.

R17 (↓ ↓) Do not up-dose first-generation H1-antihistamines (see R13).

R18 (↑) Consider montelukast, in addition to a second generation H1-antihistamine, in people whose symptoms are inadequately controlled by standard and increased doses of second-generation H1-antihistamines.

R19 (↑ ↑) Offer* progression of therapy, through first-line treatment options (see R12–R18) every 2–4 weeks (every 2 weeks in severe treatment-resistant disease).

Θ4 There is insufficient evidence to recommend routine addition of H2-antihistamines to second-generation H1-antihistamines for people whose symptoms are inadequately controlled by the latter. However, they may be considered if urticaria is associated with dyspepsia, although dyspepsia should be investigated appropriately.

R20 (↑) Consider oral prednisolone (e.g. 0.5 mg kg^{-1}) for short, infrequent courses of a few days as rescue treatment to control severe exacerbations, in addition to continued use of a second-generation H1-antihistamine.

R21 (↓ ↓) Do not offer* long-term systemic corticosteroids unless there is no other option. Use the lowest effective dose for the shortest possible period.10

Second-line treatment options for people with chronic spontaneous urticaria

For people with CSU with an inadequate response to first-line treatment, the following additional investigations may be relevant when considering the next treatment options.

R22 (↓ ↓) Do not offer autologous serum skin tests (ASSTs) or autologous plasma skin tests (APSTs) routinely.

R23 (↑) Consider measuring total IgE levels: a high total IgE level may indicate a higher probability of early disease responsiveness to omalizumab, whereas a normal total IgE level may indicate disease responsiveness to ciclosporin (section 6 and Appendix C – LETR narratives).

R24 (↑) If available, consider a basophil histamine release assay (BHRA), although it is not yet subject to a national quality assurance scheme. A positive BHRA may indicate a higher probability of disease responsiveness to ciclosporin and slower or delayed response to omalizumab, whereas a negative BHRA may indicate a higher probability of disease responsiveness to omalizumab (section 6 and Appendix C – LETR narratives).

Note: total IgE levels (R23) and BHRAs (R24) are only indicative and may not reflect actual clinical responsiveness in all patients.

R25 (↑ ↑) Offer omalizumab, in addition to a second generation H1-antihistamine, to people whose symptoms are inadequately controlled by first-line options.

R26 (↑ ↑) Offer* ciclosporin for 3–6 months, in addition to a second-generation H1-antihistamine, to people whose symptoms are inadequately controlled by first-line options.

R27 (↑ ↑) Avoid long-term use of ciclosporin where possible; if not, use at the lowest effective dose, interrupt treatment periodically to confirm continued requirement, and consider alternative agents (see R25, R28 and Θ5).

Third-line treatment options for people with chronic spontaneous urticaria

R28 (↑) Consider the following options in people whose symptoms are inadequately controlled by first- and second-line treatment options, or where the latter are contraindicated or inappropriate (in alphabetical order):

- azathioprine
- dapsone
- doxepin (but there are concerns about central nervous system effects, as for first-generation antihistamines)
- hydroxychloroquine (particularly for urticaria occurring with systemic lupus erythematosus)
- IVIg
- methotrexate
- mycophenolate mofetil
- narrowband ultraviolet (UV)B (typically a course of around 30 treatments, repeated after 12 months if necessary, but not for continual treatment)
- oral tacrolimus
- sulfasalazine
- tranexamic acid (only if predominantly angio-oedema)

Θ5 There is insufficient evidence to recommend the following interventions (in alphabetical order):

- colchicine
- cyclophosphamide
- dipyridamole

- interleukin-1 antagonists (e.g. anakinra)
- plasmapheresis
- psychological interventions (although there is evidence that psychological interventions such as cognitive behavioural therapy, mindfulness and relaxation techniques are beneficial for general psychosocial wellbeing in patients with skin diseases)
- rituximab
- thyroxine
- tumour necrosis factor antagonists
- warfarin

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4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library - Cochrane Database of Systematic Reviews (Issue 03 of 12, March 2025) am 25.03.2025

#	Suchschritt
1	MeSH descriptor: [Urticaria] explode all trees
2	(urticaria* OR hives):ti,ab,kw
3	#1 OR #2
4	#3 with Cochrane Library publication date from Mar 2020 to present, in Cochrane Reviews
5	#3 with Cochrane Library publication date from Mar 2023 to present, in Cochrane Reviews
6	#4 NOT #5

Leitlinien und systematische Reviews in PubMed am 25.03.2025

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

verwendete Suchfilter für systematische Reviews:
Konsentierter Standardfilter für Systematische Reviews (SR), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 15.01.2025.

#	Suchschritt
	Leitlinien
1	urticaria[mh]
2	urticaria*[tiab] OR hives[tiab]
3	#1 OR #2
4	(#3) AND (Guideline[ptyp] OR Practice Guideline[ptyp] OR guideline*[ti] OR Consensus Development Conference[ptyp] OR Consensus Development Conference, NIH[ptyp] OR recommendation*[ti])
5	(#4) AND ("2020/03/01"[PDAT] : "3000"[PDAT])
6	(#5) NOT ("retracted publication"[pt] OR "retraction notice"[pt] OR "retraction of publication"[pt] OR "preprint"[pt])
	systematische Reviews
7	(#3) AND ("systematic review"[pt] OR "meta-analysis"[pt] OR "network meta-analysis"[mh] OR "network meta-analysis"[pt] OR (systematic*[tiab] AND (review*[tiab] OR overview*[tiab])) OR metareview*[tiab] OR umbrella review*[tiab] OR "overview of reviews"[tiab] OR meta-analy*[tiab] OR metaanaly*[tiab] OR metanaly*[tiab] OR meta-synthes*[tiab] OR metasynthes*[tiab] OR meta-study[tiab] OR metastudy[tiab] OR integrative review[tiab] OR integrative literature review[tiab] OR evidence review[tiab] OR (("evidence-based medicine"[mh] OR evidence synthes*[tiab]) AND "review"[pt]) OR ((("evidence based"[tiab:~3]) OR evidence base[tiab]) AND (review*[tiab] OR

#	Suchschritt
	overview*[tiab])) OR (review[ti] AND (comprehensive[ti] OR studies[ti] OR trials[ti])) OR ((critical appraisal*[tiab] OR critically appraise*[tiab] OR study selection[tiab] OR ((predetermined[tiab] OR inclusion[tiab] OR selection[tiab] OR eligibility[tiab]) AND criteri*[tiab]) OR exclusion criteri*[tiab] OR screening criteri*[tiab] OR systematic*[tiab] OR data extraction*[tiab] OR data synthes*[tiab] OR prisma*[tiab] OR moose[tiab] OR entreq[tiab] OR mecir[tiab] OR stard[tiab] OR strobe[tiab] OR "risk of bias"[tiab]) AND (survey*[tiab] OR overview*[tiab] OR review*[tiab] OR search*[tiab] OR analysis[ti] OR apprais*[tiab] OR research*[tiab] OR synthes*[tiab]) AND (literature[tiab] OR articles[tiab] OR publications[tiab] OR bibliographies[tiab] OR published[tiab] OR citations[tiab] OR database*[tiab] OR references[tiab] OR reference-list*[tiab] OR papers[tiab] OR trials[tiab] OR studies[tiab] OR medline[tiab] OR embase[tiab] OR cochrane[tiab] OR pubmed[tiab] OR "web of science" [tiab] OR cinahl[tiab] OR cinhal[tiab] OR scisearch[tiab] OR ovid[tiab] OR ebsco[tiab] OR scopus[tiab] OR epistemonikos[tiab] OR prospero[tiab] OR proquest[tiab] OR lilacs[tiab] OR biosis[tiab])) OR "technical report"[pt] OR HTA[tiab] OR technology assessment*[tiab] OR technology report*[tiab])
8	(#7) AND ("2020/03/01"[PDAT] : "3000"[PDAT])
9	(#8) NOT "The Cochrane database of systematic reviews"[Journal]
10	(#9) NOT ("retracted publication"[pt] OR "retraction notice"[pt] OR "retraction of publication"[pt] OR "preprint"[pt])
	systematische Reviews ohne Leitlinien
11	#10 NOT #6
12	(#11) AND ("2023/03/01"[PDAT] : "3000"[PDAT])
13	#11 NOT #12

Iterative Handsuche nach grauer Literatur, abgeschlossen am 07.10.2025

- Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften (AWMF)
- 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

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Gemeinsamer Bundesausschuss

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

- keine eingegangenen schriftlichen Rückmeldungen gem. § 7 Absatz 6 VerfO