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: 2026-B-037-z Remibrutinib

Stand: Mai 2026

I. Zweckmäßige Vergleichstherapie: Kriterien gemäß 5. Kapitel § 6 VerfO G-BA	
Remibrutinib **zur Behandlung chronischer 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:	
Remibrutinib	„Zur Behandlung der chronischen spontanen Urtikaria (CSU) bei Erwachsenen, die unzureichend auf eine Behandlung mit H1-Antihistaminika ansprechen.“
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.
Dupilumab D11AH05 Dupixent®	Chronische spontane Urtikaria (CSU) Dupixent ist angezeigt zur Behandlung von mittelschwerer bis schwerer chronischer spontaner Urtikaria bei Erwachsenen und Jugendlichen (ab 12 Jahren), die auf eine Behandlung mit H1-Antihistaminika unzureichend ansprechen und im Rahmen ihrer CSU-Therapie bisher keine Anti-IgE-Antikörper erhalten haben.
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	bei Erwachsenen und Kindern ab 6 Jahren: - […] - zur Linderung von Symptomen bei chronischer idiopathischer Urtikaria

II. Zugelassene Arzneimittel im Anwendungsgebiet	
Cetirizinhydro-chlorid elac®	
Desloratadin R06AX27 Aerius®	Bei Erwachsenen und Jugendlichen ab 12 Jahren zur Besserung der Symptomatik bei: - allergischer Rhinitis - Urtikaria.
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).

II. Zugelassene Arzneimittel im Anwendungsgebiet	
Bilastin R06AX29 Bitosen®	Symptomatische Behandlung der allergischen Rhinokonjunktivitis (saisonal und perennial) und Urtikaria.
Glukokortikoide (systemisch, oral) zur Akutbehandlung	
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: 2026-B-037-z (Beratung nach § 35a SGB V)

Remibrutinib

Auftrag von:	Abt. AM
Bearbeitet von:	Abt. FB Med
Datum:	2. April 2026

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

Behandlung von Erwachsenen mit chronischer spontaner Urtikaria, die unzureichend auf eine Behandlung mit H1-Antihistaminika ansprechen.

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 und die Recherchen am 22.01.2026 abgeschlossen. Nachträglich wurde am 17.02.2026 eine neue Leitlinie identifiziert. Am 05.03.2026 erfolgte eine Überprüfung der iterativen Handsuche. 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 453 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 4 Referenzen eingeschlossen. Es erfolgt eine synoptische Darstellung wesentlicher Inhalte der identifizierten Referenzen.

3 Ergebnisse

3.1 Cochrane Reviews

Es wurden keine relevanten Cochrane Reviews identifiziert.

3.2 Systematische Reviews

Es wurden keine relevanten systematischen Reviews identifiziert.

3.3 Leitlinien

Information zur deutschen S3-Leitlinie

Die deutsche AWMF S3-LL „Klassifikation, Diagnostik und Therapie der Urtikaria“ befindet sich aktuell in Überarbeitung. Die Fertigstellung ist für den 30.06.2026 geplant.

Zuberbier T et al., 2026 [1, 2, 4].

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 with regard to underlying causes, eliciting factors, comorbidities, the burden on patients and society, and the 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, with consideration given to the global diversity of patients, physicians, medical systems, and access to diagnosis and treatment.

Methodik

Grundlage der Leitlinie

- Repräsentatives Gremium: **Trifft teilweise zu** – Eine Patientenbeteiligung war nicht gegeben.
- 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**

Recherche/Suchzeitraum:

- Systematic searches for randomized controlled trials and clinical, controlled trials were undertaken using the following databases on February 9, 2024 limiting the time to 2021 – February 9, 2024:
  - Ovid MEDLINE(R) ALL
  - Embase Classic + Embase

  - Cochrane Central Register of Controlled Trials (CENTRAL)
- Because the update of the International Guideline for Urticaria is an update of an existing guideline, we did not search for other guidelines or systematic reviews.

LoE

- Cochrane Risk of Bias Tool für RCTs und ROBINS I für nicht-randomisierte kontrollierte Studien

GoR

- GRADE, AGREE II

TABLE 6: WORDING OF RECOMMENDATIONS[19-22]

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.

TABLE 7: STRENGTH OF CONSENSUS ACCORDING TO EUROGUIDERM GUIDELINE MANUAL[4]

Strong consensus	Agreement of >95% participants
Consensus	Agreement of >75-95% participants
Agreement of the majority	Agreement of >50-75% participants

Sonstige methodische Hinweise

BOX 1 | The format for individual guideline recommendations, including strength of consensus and evidence.

Should we ... in chronic urticaria?		
We **recommend** that ...	↑↑	Strong consensus[1] Expert consensus
[1] > 95% agreement		

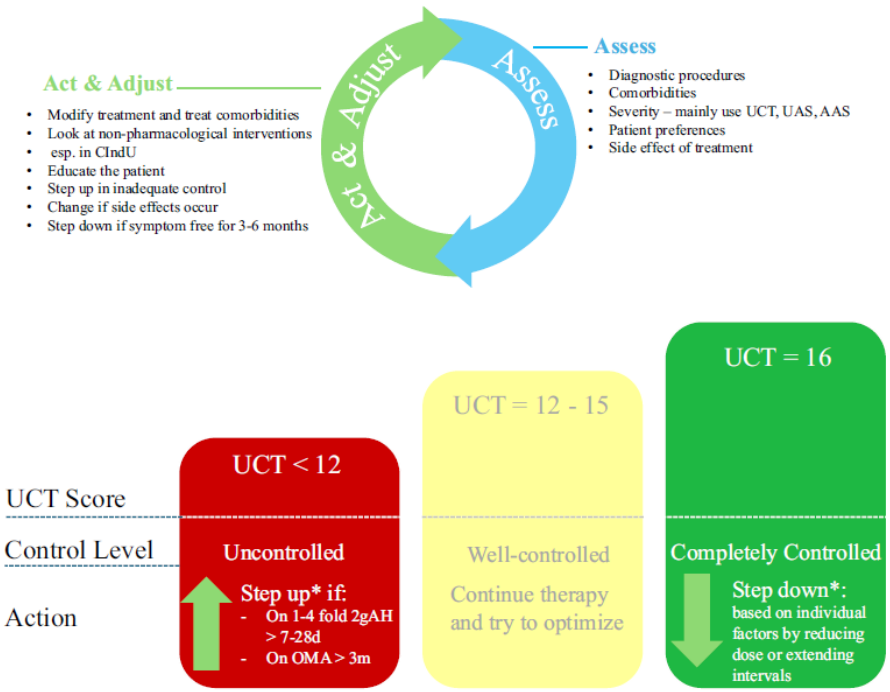
BOX 2 | The format for multiple guideline recommendations voted upon separately, including strength of consensus and evidence for each.

Should we ... in chronic urticaria?		
We **recommend** that ...	↑↑	Strong consensus[1] Expert consensus
[1] > 95% agreement		
We **suggest** that ...	↑	Strong consensus[1] Expert consensus
[1] > 95% agreement		

BOX 3 | The Format for Multiple Guideline Recommendations Voted on Jointly, Including Strength of Consensus and Evidence.

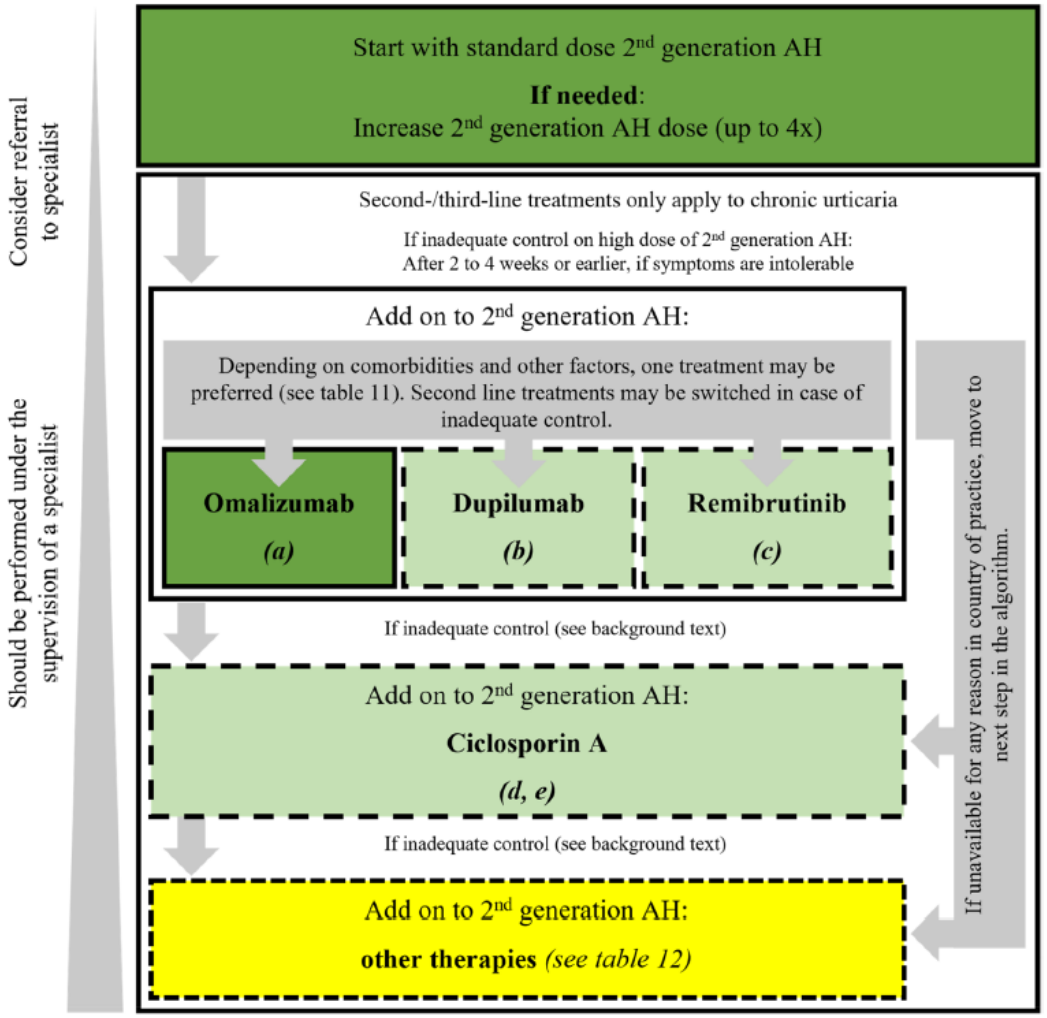
Should we ... in chronic urticaria?		
We **recommend** that ... We **recommend** using ...	↑↑	Strong consensus[1] Expert consensus
[1] > 95% agreement		

Empfehlungen



* For CIndU individual decisions are based on estimated trigger exposure (e.g. cold-urticaria in winter)

FIGURE 3 | Chronic urticaria: management decisions and treatment adjustments. Apart from UCT, in some patients a monthly diary using the UAS and AAS can render better advice as this can discover short-term exacerbations, especially although UCT states well controlled. In patients who are in the range of UCT 12–15, therefore a step up might also be required.



a) Currently licensed for chronic spontaneous urticaria in most countries (Dec. 2024); 300mg every 4 weeks; if needed: increase dose and/or shorten interval (up to 600mg every 2 weeks)
b) Patients with chronic spontaneous urticaria; might be off-label;
≥60 kg bodyweight: 600mg loading dose + 300mg every 2 weeks
≥30 kg and <60 kg bodyweight: 400mg loading dose + 200mg every 2 weeks
≥15 kg and <30 kg bodyweight: 400mg loading dose + 200mg every 4 weeks
c) Patients with chronic spontaneous urticaria; might be off-label / not yet licensed (market entry expected in 2025); 25mg twice per day
d) Monotherapy with up to 5mg/kg body weight
e) Consider combination with other treatments, e.g., omalizumab plus low-dose ciclosporin A (1-2mg/kg body weight) (consensus-based, no study data available)

This algorithm was voted on after achieving consensus on all separate evidence-based guideline questions. A detailed reasoning for the positioning of the treatment options in this algorithm can be found in the guideline text.

In addition: A short course of glucocorticosteroids should be considered in case of an acute exacerbation.

Strong recommendation (↑↑)
Conditional recommendation (↑)
Recommendation cannot be made (0)

FIGURE 4 | Recommended treatment algorithm for urticaria. This algorithm outlines the stepwise management approach for urticaria, developed in accordance with clinical evidence evaluated using the GRADE methodology. Each treatment recommendation in the management section (Section 5) was formally endorsed through expert voting, as indicated in the corresponding boxes. AH, antihistamine.

H1-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, pp. 5–20)
[1]100% agreement		
Is an increase in the dose to up to four-fold 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 4-fold 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, pp. 24-27, 31-39)
[1]>95% 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 spontaneous urticaria. For the treatment of patients with chronic inducible urticaria, we **suggest** to decide based on the presence of triggers (e.g., time of the year in cold urticaria) whether 2nd generation H1-antihistamines should be taken regularly or as needed.	↑	Strong consensus[1] Evidence- and consensus-based (see Evidence Report, pp. 21–23)
[1]>95% 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 (against an updosing of a single H_1-antihistamine if not legally restricted in country)	↓	Consensus[1] Evidence- and consensus-based (see Evidence Report, pp. 28–30, 40–42)
[1]>95% 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 4-fold standard dosed H_1-antihistamines in chronic urticaria	↓↓	Strong consensus[1] Evidence- and consensus-based (see Evidence Report, p. 49)
[1] > 95% 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 doses of 2nd generation H_1-antihistamines. *Currently licensed for chronic spontaneous urticaria	↑↑	Strong consensus[1] Evidence- and consensus-based (see Evidence Report, pp. 49–60)
[1] > 95% agreement		

Dupilumab treatment

Is dupilumab useful as add-on treatment in patients unresponsive to high doses of H_1-antihistamines?		
We **suggest** using dupilumab* as add-on treatment for patients with CSU unresponsive to high doses of 2nd generation H1-antihistamines. *might be off-label	↑	Consensus[1] Evidence- and consensus-based (see Evidence Report, pp. 61–63)
[1] > 75% agreement		

Remibrutinib treatment

Is remibrutinib useful as add-on treatment in patients unresponsive to high doses of H_1-antihistamines?		
We **suggest** using remibrutinib* as add-on treatment for patients with CSU unresponsive to high doses of 2nd generation H1-antihistamines.	↑	Consensus[1] Evidence- and consensus-based (see Evidence Report, pp. 64–85)
[1]> 75% 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 licensed treatments or if these are not available. *currently not licensed for CU	↑	Consensus[1] Evidence- and consensus-based (see Evidence Report, pp. 94–96)
[1]> 75% 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 or depot preparations in CU.	↓↓	Strong consensus[1] Evidence- and consensus-based (see Evidence Report, p. 103)
We **suggest** considering a short course of rescue systemic glucocorticosteroids in patients with an acute exacerbation of CU.	↑	
[1]> 95% 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**	Consensus[1] Evidence- and consensus-based (see Evidence Report, pp. 43–48)
[1]> 75% 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 with comorbidities or where financial, legal, or other limitations for the recommended algorithm treatment exist.	**0**	Consensus[1] Expert consensus
[1] > 75% agreement		

TABLE 12 | Alternative treatment options.

Although evidence from publications is low, clinical experience indicates that they may be useful in certain contexts. Interventions are listed in alphabetical order by frequency of use rather than efficacy

Intervention	Substance (class)	Possible indication
Widely used		
Tricyclic antidepressant with potent H1- and H2-antagonist activity	Doxepin[a]	CSU, Idiopathic cold-induced urticaria
Diet	Pseudoallergen-low diet[b]	CSU
H_2-antihistamine	Ranitidine[c], famotidine, Lafutidine (available in Japan, South Korea, and India)	CSU
Immunosuppressive	Methotrexate Mycophenolate mofetil	CSU ± DPU[d] Autoimmune CSU
Leukotriene receptor antagonist	Montelukast	CSU, DPU
Sulphones	Dapsone, Sulphasalazine	CSU ± DPU CSU ± DPU
Infrequently used		
Anabolic steroid	Danazol	Cholinergic urticaria
Anticoagulant	Warfarin	CSU
Antifibrinolytic	Tranexamic acid	CSU with angioedema
Immunomodulator	IVIG Plasmapheresis	Autoimmune CSU Autoimmune CSU
Miscellaneous	Autologous blood/serum Hydroxychloroquine	CSU CSU
Phototherapy	Narrow-band UVB	Symptomatic dermographism
Psychotherapy	Psychotherapy	CSU
Rarely used		
Anticoagulant	Heparin	CSU (elevated D-Dimer)
Immunosuppressive	Cyclophosphamide Rituximab	Autoimmune CSU Autoimmune CSU
Miscellaneous	Anakinra Anti-TNF-alpha Camostat mesilate Colchicine Miltefosine Mirtazapine PUVA Benralizumab[e]	DPU CSU ± DPU CSU CSU CSU CSU CSU CSU ± eosinophilic asthma
Very rarely used		
Immunosuppressive	Systemic Tacrolimus	CSU
Miscellaneous	Vitamin D Interferon alpha	CSU CSU

Abbreviations: CSU, Chronic Spontaneous Urticaria; DPU, Delayed Pressure Uriticaria; IVIG, Intravenous Immunoglobulin.
[a]Has also H_1 and H_2-antihistaminergic properties usually effective at a dose of 50–75 mg daily [26].
[b]Does include low histamine diet as pseudoallergen-free diet is also low in histamine. The evidence is controversial and different interpretations about what a pseudoallergen is or what foods contain them exist.
[c]No longer available in most countries; alternative H2-antihistamines are available including famotidine and nizatidine but evidence for their use in chronic urticaria varies.
[d]Treatment can be considered especially if CSU and DPU are co-existent in a patient.
[e]Treatment can be considered especially if CSU and eosinophilic asthma are co-existent in a patient.

Referenzen aus Leitlinien

19. Guyatt GH, Oxman AD, Schunemann HJ, et al. GRADE guidelines: a new series of articles in the Journal of Clinical Epidemiology. Journal of clinical epidemiology 2011;64(4):380–2. doi: 10.1016/j.jclinepi.2010.09.011 [published Online First: 2010/12/28]

20. The GRADE Working Group. 2018 [Available from: http://www.gradeworkinggroup.org/ accessed July 10 2018.

21. Werner RN, Nikkels AF, Marinovic B, et al. European consensus-based (S2k) Guideline on the Management of Herpes Zoster - guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV), Part 1: Diagnosis. Journal of the European Academy of Dermatology and Venereology : JEADV 2017;31(1):9–19. doi: 10.1111/jdv.13995 [published Online First: 2016/11/03]

22. Werner RN, Nikkels AF, Marinovic B, et al. European consensus-based (S2k) Guideline on the Management of Herpes Zoster - guided by the European Dermatology Forum (EDF) in cooperation with the European Academy of Dermatology and Venereology (EADV), Part 2: Treatment. Journal of the European Academy of Dermatology and Venereology : JEADV 2017;31(1):20–29. doi: 10.1111/jdv.13957 [published Online First: 2016/11/03].

Sabroe RA et al., 2022 [3].

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

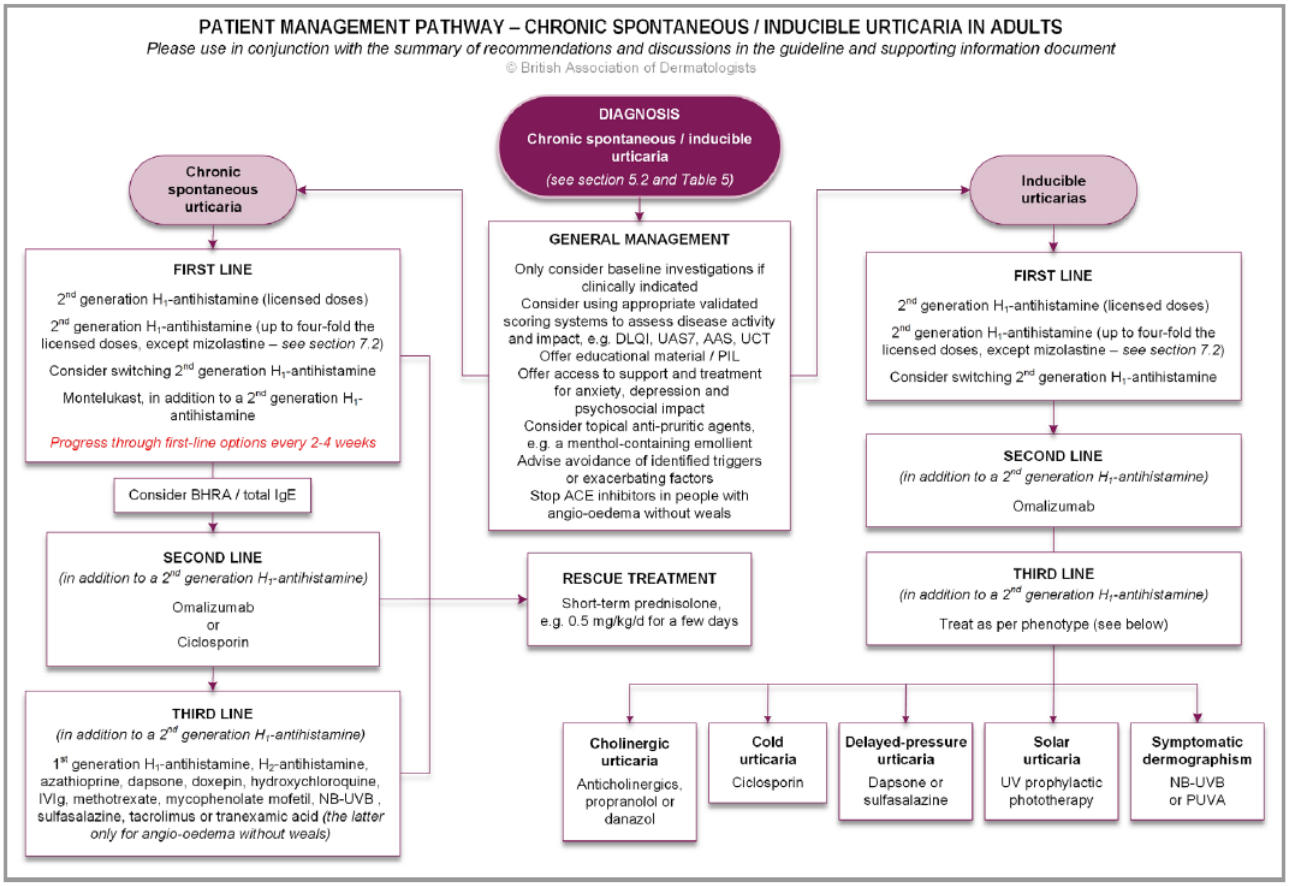


Figure 1 Patient management pathway for urticaria. For clarity we have divided management options into sections (general treatment, and first-, second- and third-line options). However, depending on disease severity, disease fluctuation, comorbidities and national criteria for use of drugs, the order 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

Referenzen aus Leitlinien

7 National Institute for Health and Care Excellence. NSAIDs – prescribing issues. Available at: https://cks.nice.org.uk/topics/nsaidsprescribing-issues (last accessed 15 November 2021).
8 British Society for Allergy & Clinical Immunology (BSACI). Nonsteroidal anti-inflammatory drugs (NSAIDS). Available at: https://www.bsaci.org/professional-resources/allergy-management/drugallergy/non-steroidal-anti-inflammatory-drugs-nsaids (last accessed 15 November 2021).
9 Kowalski ML, Asero R, Bavbek S et al. Classification and practical approach to the diagnosis and management of hypersensitivity to nonsteroidal anti-inflammatory drugs. Allergy 2013; 68:1219–32.
10 National Institute for Health and Care Excellence. Corticosteroids – oral. Available at: https://cks.nice.org.uk/topics/corticosteroidsoral (last accessed 15 November 2021).

4 Detaillierte Darstellung der Recherchestrategie

Cochrane Library - Cochrane Database of Systematic Reviews (Issue 01 of 12, January 2026) am 21.01.2026

#	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 Jan 2021 to present
5	#3 with Cochrane Library publication date from Jan 2024 to present
6	#4 NOT #5

Leitlinien und systematische Reviews in PubMed am 21.01.2026

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

verwendeter Suchfilter für systematische Reviews ohne Änderung:
Konsentierter Standardfilter für Systematische Reviews (SR), Team Informationsmanagement der Abteilung Fachberatung Medizin, Gemeinsamer Bundesausschuss, letzte Aktualisierung am 01.01.2026.

#	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 ("2021/01/01"[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"[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 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

#	Suchschritt
	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 ("2021/01/01"[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 ("2024/01/01"[PDAT] : "3000"[PDAT])
13	#11 NOT #12

Iterative Handsuche nach grauer Literatur, abgeschlossen am 22.01.2026, überprüft am 05.03.2026

- 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

Referenzen

1. **Heuer R, Pennitz A, Zeyen C, Nast A, Werner RN.** The international guideline for the definition, classification, diagnosis and management of urticaria; evidence report, version 2.0 [online]. Zürich (SUI): European Dermatology Forum; 2026. [Zugriff: 05.03.2026]. URL: https://www.guidelines.edf.one//uploads/attachments/cmljd7o9i1mhnrwjrff1pbari-urticaria-evidence-report.pdf.
2. **Heuer R, Zeyen C, Pennitz A, Stevanovic K, Ciupka K, Nast A, et al.** The international guideline for the definition, classification, diagnosis and management of urticaria; methods report, version 1.0 [online]. Zürich (SUI): European Dermatology Forum; 2026. [Zugriff: 05.03.2026]. URL: https://www.guidelines.edf.one//uploads/attachments/cmljd9w781mkwrwjrxwvpa9ar-urticaria-methods-report.pdf.
3. **Sabroe RA, Lawlor F, Grattan CEH, Ardern-Jones MR, Bewley A, Campbell L, et al.** British Association of Dermatologists guidelines for the management of people with chronic urticaria 2021. Br J Dermatol 2022;186(3):398-413. https://dx.doi.org/10.1111/bjd.20892.
4. **Zuberbier T, Abdul Hameed Ansari Z, Abdul Latiff AH, Abuzakouk MM, Agcaoili-De Jesus MS, Agondi RC, et al.** The international guideline for the definition, classification, diagnosis and management of urticaria. Allergy 2026 [online ahead of print]. https://dx.doi.org/10.1111/all.70210.

[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 Fachgesellschaften und der AkdÄ zu Fragen der Vergleichstherapie nach §35a Abs. 7 SGB V i.V.m. VerfO 5. Kapitel § 7 Abs. 6

Verfahrens-Nr.: 2026-B-037-z

Verfasser	
Name der Institution	Deutsche Dermatologische Gesellschaft, DGf Allergologie und klinische Immunologie (DGAKI)
Datum der Erstellung	14. April 2026

Indikation
is indicated for the treatment of chronic spontaneous urticaria (CSU) in adult patients with inadequate response to H1 antihistamine treatment.
Fragen zur Vergleichstherapie
Was ist der Behandlungsstandard in o.g. Indikation unter Berücksichtigung der vorliegenden Evidenz? Wie sieht die Versorgungspraxis in Deutschland aus? *(Bitte begründen Sie Ihre Ausführungen; geben Sie ggf. zitierte Quellen in einer Referenzliste an.)*
Ich verweise hier auf ein Verfahren aus dem letzten Jahr, 2025-B-084, das die gleiche Fragestellung hatte (in Deutsch). Die Referenzliste ist aktualisiert worden. Die gegenwärtige Leitlinie (1) schlägt eine Stufentherapie vor, beginnend mit Antihistaminika der zweiten Generation, die nicht sedierend sind, diese bis zur vier-fachen Dosis gesteigert mit dem Hinweis, dass dies Off-Label ist. In der nächsten Stufe der gegenwärtig gültigen Leitlinie wird Omalizumab 300mg (entsprechend der Zulassung) bis zu 1200mg alle vier Wochen empfohlen und im Folgeschritt, falls hier kein ansprechen erfolgt, Cyclosporin A. In der neuen Leitlinie (2) wird neben Omalizumab auch die Gabe von Dupilumab und Remibrutinib als evidenzbasierte Therapie genannt, mit dem Hinweis, dass beide Substanzen noch nicht oder nur in einigen Ländern bisher zugelassen sind (in Deutschland ist keine der Substanzen zugelassen). Zusätzlich wären möglich Kombinationstherapien mit Cyclosporin A erläutert als auch alternative Behandlungen zu denen die Evidenzlage gering ist. Es muss zusammenfassend nämlich festgestellt werden, dass die jetzige Studienlage gezeigt hat, dass es keine etablierte Standardtherapie für Patienten gibt, die auf Antihistaminika nicht ansprechen, da bei der chronischen Urtikaria viele verschiedene Subtypen existieren, nicht nur Subtypen im Sinne der chronisch spontanen Urtikaria und der chronisch induzierbaren Urtikaria. Auch bei der chronisch spontanen Urtikaria gibt es in allen vorliegenden Studien Subgruppen von Non-Respondern und Complete-Respondern. Hier hat sich inzwischen pathophysiologisch gezeigt, dass es unterschiedliche Mechanismen sind, die die Quaddeln unterhalten. So zeigte sich beispielsweise in Studien, dass es bei einem Urtikaria Patienten mit einen hohen im Wert von Eosinophilen auch Benralizumab ein sinnvolles Medikament sein kann, obwohl es in Studien im Durchschnitt aller behandelten Patienten, keine signifikante Verbesserung gegenüber Placebo zeigt. Im Fazit macht es daher keinen Sinn, eine neuzuzulassende Substanz gegen einen Standard Präparat, wie es durch die alte Leitlinie suggeriert sein mag, Omalizumab zu prüfen, sondern wichtiger ist es, Subgruppenanalysen durchzuführen. Die neue Leitlinie schlägt daher vor kontinuierlich das Ansprechen auf Präparate zu überprüfen und gegebenenfalls das Präparat zu wechseln oder in höherer Dosierung zu verwenden.

Gibt es Kriterien für unterschiedliche Behandlungsentscheidungen in der o.g. Indikation, die regelhaft berücksichtigt werden? Wenn ja, welche sind dies und was sind in dem Fall die Therapieoptionen? *(Bitte begründen Sie Ihre Ausführungen; geben Sie ggf. zitierte Quellen in einer Referenzliste an.)*
Wie oben ausgeführt die differenzierten Komorbiditäten.

Referenzliste:

(1) Zuberbier T et al. S3-Leitlinie Urtikaria. Teil 2: Therapie der Urtikaria - deutschsprachige Adaption der internationalen S3-Leitlinie. J Dtsch Dermatol Ges. 2023 Feb;21(2):202-216. German. doi: 10.1111/ddg.14932_g. PMID: 36808444.

(2) Zuberbier T et al. The International Guideline for the Definition, Classification, Diagnosis and Management of Urticaria. Allergy. 2026 Feb 6. doi: 10.1111/all.70210. Epub ahead of print. PMID: 41649409.