Chronic spontaneous urticaria – a management pathway for patients with chronic spontaneous urticaria

Christian Termeer, Petra Staubach, Hjalmar Kurzen, Klaus Strömer, Rolf Ostendorf, Marcus Maurer

(1) Private Practice Stuttgart, Department of Dermatology, University of Freiburg
(2) Department of Dermatology, University Medicine Mainz
(3) Private Practice Freising, University Medicine Mannheim
(4) Private Practice Mönchengladbach
(5) Private Practice Zentderma Mönchengladbach
(6) Charité – University Medicine Berlin, Department of Dermatology, Venereology and Allergology

Introduction

According to recently published international S3 guidelines, urticaria is defined as a disease characterized by pruritic urticae, angioedema, or both [1, 2]. Acute and chronic forms are distinguished solely based on disease duration (longer or shorter than six weeks) [3]. In practice, acute urticaria is treated symptomatically with second-generation antihistamines and, if necessary, with short-term systemic corticosteroids; intensive workup is usually not performed, unless suggested by the patient’s history, for instance, in type I allergy.

Management becomes more difficult, when the patient presents repeatedly, and symptoms do not subside spontaneously or recur [4]. In chronic urticaria, guidelines distinguish between spontaneous and inducible forms, including physical urticaria, where the patient’s history frequently provides

Summary

Chronic spontaneous urticaria (CSU) is a common and challenging disease, especially with respect to healthcare provision in the context of the German statutory health insurance system. If treatment with second-generation antihistamines is unsuccessful, current guidelines recommend further therapeutic options. However, most of these are off-label. This discrepancy between treatment according to guidelines and the ability to prescribe drugs at the expense of the statutory health insurance (reimbursability) often leads to uncertainties in everyday clinical practice. In addition, physicians prescribing certain drugs are faced with the difficulty of measuring and documenting therapeutic success/outcome. Respective outcome measurement methods have not yet been established in daily practice. Using a consensus process, a working group, composed of dermatologists in private practice and specialized urticaria centers, has defined a practical pathway for the implementation of current treatment recommendations based on the 2014 S3 guidelines for urticaria. Here, we present a diagnostic and therapeutic management pathway for CSU. Further, we discuss prescription issues in daily practice, including updosing of antihistamines, with regard to cost-effectiveness and drug approval on the basis of published studies and current legislation.

Constituting the highest treatment level, the use of cyclosporine A, montelukast, and omalizumab, which has recently become available as therapeutic option, is reviewed. The urticaria control test (UCT) is presented as a valid outcome measure in routine practice. Our objective was to provide physicians in private practice with a practical guideline-based therapeutic decision tool, taking into account the requirements imposed by the statutory health insurance system. It is not meant to replace individualized history taking or treatment of this heterogeneous disease. Rather, we would like to suggest reference points for clinical diagnosis and treatment of CSU.
clues as to potential triggers. Other subgroups of inducible urticaria are cholinergic urticaria, aquagenic urticaria, and contact urticaria. Combinations of more than one subform are not rare.

Confirmation of the diagnosis by corresponding provocation tests is easy in inducible urticaria forms [5]. In rare and difficult cases, patients may be also referred to clinical centers. In everyday clinical practice, however, the spectrum of chronic spontaneous urticaria (CSU) much more relevant. Here, guidelines recommend workup and, if necessary, assessment of underlying inflammatory disorders. Naturally, as in any patient examination, a detailed history all comes to the fore. With respect to differential diagnoses of CSU, please refer to the relevant guidelines [1]. We set up an expert group, in order to develop simple recommendations for the practical implementation of the most recent international guidelines [1], suggesting a pathway for the diagnosis and therapy of CSU. This article represents the personal opinion and experience of the experts and should be understood as a practical addition to the guideline recommendations.

### Diagnosis of chronic spontaneous urticaria

For every patient who presents for the first time with a suspected diagnosis of CSU, three questions are important:

1. Is this CSU?
2. How severely is the patient affected?
3. What is the cause?

The first question is easily answered. We recommend using the simple and expedient algorithm in the current guidelines (Figure 1) [1–3]. Important differential diagnoses such as autoinflammatory syndromes, urticarial vasculitis,
Minireview Chronic spontaneous urticaria – a management pathway

Table 1 Tools for assessing disease activity, quality of life, and disease control in chronic spontaneous urticaria (CSU) patients.

<table>
<thead>
<tr>
<th></th>
<th>For patients with urticae</th>
<th>For patients with angioedema</th>
<th>Prospective or retrospective</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease activity</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UAS</td>
<td>Yes</td>
<td>No</td>
<td>Prospective</td>
<td>[1, 8]</td>
</tr>
<tr>
<td>AAS</td>
<td>No</td>
<td>Yes</td>
<td>Prospective</td>
<td>[9]</td>
</tr>
<tr>
<td>Impairment of quality of life</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CU-QoL</td>
<td>Yes</td>
<td>No</td>
<td>Retrospective</td>
<td>[10]</td>
</tr>
<tr>
<td>AE-QoL</td>
<td>Nein</td>
<td>Yes</td>
<td>Retrospective</td>
<td>[11]</td>
</tr>
<tr>
<td>Disease control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UCT</td>
<td>Yes</td>
<td>Yes</td>
<td>Retrospective</td>
<td>[12]</td>
</tr>
</tbody>
</table>

Abbr.: UAS, Urticaria Activity Score; AAS, Angioedema Activity Score; CU-QoL, Chronic Urticaria Quality of Life Questionnaire; AE-QoL, Angioedema Quality of Life Questionnaire; UCT, Urticaria Control Test.

or bradykinin-mediated forms of angioedema (HAE, ACE inhibitor-induced angioedema) can be readily excluded with a few questions and tests [6]. In line with the guidelines, we also recommend a CBC with differential and an ESR in every patient with suspected CSU.

Current guidelines also recommend examining CSU patients for underlying causes only if the condition is severe and/or prolonged. In general, patients want and expect the cause to be investigated. We recommend looking only for frequent causes amenable to treatment. These are: 1. Chronic bacterial inflammation and 2. Food intolerances.

Standard tests in CSU (ESR/CRP, CBC with differential) as well as the patient history may provide important clues as to relevant chronic bacterial foci. Use of a standardized questionnaire is helpful (available free of charge at www.urtikaria.net/fileadmin/Patientenmaterial/PM_ANAMNESERFRAGEBOGEN.pdf). Because of the pruritus, testing for allergies is usually desired or even demanded by patients. In CSU, however, workup of lesions associated with inflammation and inflammation, which do not always cause symptoms, is much more frequent and relevant.

To detect inflammatory processes in principle, blood tests including CRP/ESR and CBC with differential can be useful. However, Helicobacter-associated gastritis is not necessarily always associated with CBC changes or an elevated CRP/ESR, or even causes symptoms. We therefore routinely recommend workup to rule out the following inflammatory conditions.

Established recommended measures for finding an infectious focus include:

- ENT (chronic sinusitis, tonsillitis, otitis media – possibly ASO test beforehand),
- Dentist (dental abscess, also insufficient tooth fillings),
- Gastroenterologist/internist/general practitioner (Helicobacter-associated gastritis; urea breath test or stool antigen test beforehand)

With respect to examining any underlying food intolerances, a pseudoallergen-free and histamine-free diet has proven useful. In many cases, symptoms disappear or markedly diminish on such a diet [7]. To keep costs in the practice under control, appropriate dietary recommendations have been developed with a dietician to pass on to patients; these are also available at http://www.urtikaria.net.

**Determination of disease severity and activity**

Determination of disease severity and activity is important for therapy and should be practicable for both patients and physicians. Five tools have been developed in recent years (Table 1): to determine disease activity, the urticaria activity score (UAS) [1, 8] and the angioedema activity score (AAS, for CSU patients with angioedema) [9] are used; to determine disease-related impairment of the quality of life, the Chronic Urticaria Quality of Life Questionnaire (CU-QoL, for CSU patients with wheals) [10] and the Angioedema Quality of Life Questionnaire (AE-QoL, for CSU patients with angioedema) [11] are used; to determine disease control, the urticaria control test (UCT) is used in all CSU patients [12].

© 2015 Deutsche Dermatologische Gesellschaft (DDG). Published by John Wiley & Sons Ltd. | JDDG | 1610-0379/2015
In daily practice, we recommend use of the UCT (Figure 2). The UAS7 and AAS are prospective instruments and therefore require patients to keep a diary. They are usually too complex for routine practice but may be helpful before starting a new therapy. The CU-Q20L and the AE-QoL may be used in addition [10, 11] but are also too complex for routine practice. The UCT can be obtained free of charge for noncommercial use at the office or hospital (http://www.urtikaria.net/fileadmin/unev/documents/UCT_GermanVersion_MOXIE.pdf).

The UCT can be used in all forms of chronic urticaria and/or angioedema. It includes four questions that cover disease activity, quality of life as well as therapy and disease control, and rapidly detects whether the patient is optimally managed. Urticaria is regarded as controlled with a UCT score of ≥12 points and as uncontrolled with ≤11 points.

**Treatment of chronic spontaneous urticaria**

Symptomatic treatment of CSU is aimed at protecting patients from the occurrence of symptoms, that is to keep the disease in check until it resolves spontaneously (Treat the disease until it is gone). Under the motto “as little as possible, as much as necessary”, current guidelines recommend a three-step therapeutic approach: first, a second-generation antihistamine once daily; secondly, updosing of the second-generation antihistamine up to four times the daily dose; the third step consists of add-on therapy with omalizumab as approved treatment option for CSU or off-label therapy with cyclosporine A or montelukast.

We recommend the following therapeutic approach in CSU patients:

- Standard-dose second-generation antihistamine,
- In case of non-response: updosing up to four times the daily dose,
- In case of non-response after (a minimum of) two weeks or harmful adverse effects (off-label): switch to another second-generation antihistamine up to four times the daily dose,
- Non-response or harmful adverse effects: omalizumab (300 mg SQ every four weeks),
- Non-response: treatment with montelukast or cyclosporine A (off-label),
- Exceptional cases only: use of sedating antihistamines (benefit-risk profile),
- With restraint and for short periods only (10 days maximum): systemic corticosteroids.
Why is this recommended?

With respect to the highest treatment level, guideline recommendations are partially in the off-label area, which creates uncertainty among dermatologists regarding prescription at the expense of the statutory health insurers (GKV), since off-label prescriptions are again and again the subject of recourse and litigation. In a landmark decision by the Federal Social Court dated 19 March 2002 (B 1 KR 37/00 R), the criteria for reimbursement of medicinal products outside the approved indication by the statutory health insurers were established:

Treatment has to relate to a serious disease for which no other approved therapy is available or effective. There must be a reasonable prospect of treatment success on the basis of available medical data. Throughout Germany, medical services of statutory health insurers now uniformly define such data as sufficient, if there have been positive, randomized, double-blind and placebo-controlled studies or if the approval process of the drug in question has been initiated by the manufacturer.

Furthermore, the Bavarian Higher Social Court, in a decision dated 13 June 2006, distinguished between off-label use and the right of constitutional extension of healthcare benefits in terms of a beyond-label use. It established that to justify the right of extension of benefits for continued use of a drug in the same patient, the same drug and the same treatment, specific evidence of the severity of a disease may be sufficient in particular cases.

Off-label use of drugs and also their prescription at the expense of the GKV is accepted practice in the treatment of many dermatoses, especially rare disorders, and insurers have hardly ever raised any objections in the past. From a legal point of view, however, there is a liability risk for the prescriber; thus, in the coming years, it will be necessary to achieve greater legal certainty. Applications for reimbursement on a case-by-case basis are not reasonable for physicians working in the context of the statutory health insurance system. Appendix VI to section K of the Medicinal Products Guideline (version of March 28, 2014) is currently more than incomplete, as it only lists doxorubicin in Merkel cell carcinoma, immunoglobulins in dermatomyositis, and imiquimod for the treatment of anal dysplasia in HIV patients. Thus, less than 1% of relevant indications are mentioned in this appendix!

An initial inquiry to KV-Nordrhein (Regional Association of Statutory Health Insurance Physicians) resulted in a rather unsatisfactory solution (Figure 3). Similar cases are ultimately decided by health insurers in favor of cost aspects (http://www.spiegel.de/gesundheit/diagnose/amd-streitum-avastin-und-lucentis-verunsichert-patienten-a-846800.html). From both medical and financial reasons, we therefore initially recommend the pathway described below.

Step 1: antihistamines in the treatment of chronic urticaria

While first-generation H1 antihistamines were highly sedating due to their ability to enter the CSF, newer second-generation antihistamines (loratadine, desloratadine, cetirizine, levocetirizine, fexofenadine, ebastine, rupatadine, bilastine, mizolastine) hardly show any adverse effects affecting the central nervous system. The approved standard dose of second-generation antihistamines is one tablet per day;
updosing is beyond-label. In first-generation antihistamines, higher dosages were in-label on the basis of older drug approval conditions.

Current international guidelines expressly advise against the general use of sedating H1 antihistamines due to lower efficacy, shorter duration of action, numerous potentially severe adverse effects, and possible drug interactions, while costing the same overall. In individual cases, the sedating properties can be utilized.

In general, we regard the sedating properties of H1 antihistamines as a major problem in clinical practice, since second-generation products are not entirely devoid of these features, either. Especially when updosing, we therefore categorically recommend providing the patient with written information, particularly with respect to driving, operating machines, or engaging in similar activities (information sheet as download: www.urtikaria.net à Links, Up-/Downloads).

It should be noted that the sedating effect is very individual and lasts longer than the antihistamine effect. In practice, this means that especially regular and long-term use of antihistamines can be problematic for patients in their daily life and also as regards full performance capability, since the sedating effects are cumulative. In this case, we recommend switching quickly to a different agent, if necessary, more than once. A brief sick leave from work for one or two days may sometimes be necessary (for example, truck drivers).

To assess the efficacy of individual agents, we generally advise against mixed treatments – this agent in the morning, the other in the evening. Studies show that there is no advantage in combining antihistamines. Updosing should optimally be done using one agent, for example, at a dose of 2 tablets twice daily.

Other adverse effects such as cardiotoxicity or hepatotoxicity occur at placebo level. As regards toxicological safety, it has been shown for several products that a dose as high as nine to ten times the normal dose is tolerated without any problems. For this reason, off-patent H1 antihistamines have become over-the-counter drugs.

When treating the various forms of urticaria in outpatient settings, some particularities have to be noted.

- **Approved for all forms of urticaria are:** desloratadine, levocetirizine, rupatadine, ebastine, mizolastine, bilastine.
- **Approved for chronic spontaneous urticaria are:** loratadine, cetirizine, fexofenadine 180 mg.
- **Approved for children are:** (check SPC for various forms of administration)
  - 12 months and older: desloratadine,
  - 2 years and older: cetirizine, levocetirizine, loratadine, rupatadine,
  - 12 years and older: fexofenadine, mizolastine, bilastine.

- **Approved in pregnancy and lactation:** (based on data provided by Embryotox)
  - 1st choice: loratadine and cetirizine,

No data available for rupatadine, ebastine, bilastine, and mizolastine.

According to current international guidelines, every form of urticaria should initially be treated with a single dose of a modern second-generation antihistamine. In acute urticaria, over-the-counter products should first be prescribed on a “green prescription form” for economic reasons. If these are not tolerated or ineffective, a prescription antihistamine can be prescribed at the expense of the statutory health insurer.

Regardless of any previous treatments, any approved antihistamine can be prescribed in severe recurrent urticaria at the expense of the statutory health insurance (in accordance with the exception clause of the medicinal product guidelines 16.4.5. https://www.g-ba.de/downloads/83–691–323/AM-RL-I-OTC-2013–06–05.pdf). In this case, either the diagnosis or “according to exception clause AMR 16.4.5.“ must be noted on the prescription form for OTC products.

**Step 2: Updosing of antihistamines**

In one-half of chronic urticaria patients, the standard antihistamine dose is not sufficient to achieve full symptom control. For this reason, higher doses of common second-generation antihistamines have been routinely used for many years. This is also reflected in the current international guidelines.

Studies regarding the efficacy of higher doses are sparse. Most of them were conducted in small patient cohorts over a short period of time and in different forms of urticaria [13, 14].

**Cetirizine**

In 11 patients with cholinergic urticaria, Zuberbier et al. (1996) [15] found the double daily dose of 20 mg given for three weeks to be more effective than placebo. Similar results were obtained by Kameyoshi in an open-label study with 21 CSU patients [6] and by Okubo in nine of 51 patients who were treated with 10 mg for three weeks and given twice this dose, if they did not respond [16]. Asero investigated a similarly small number of 22 patients who had not responded to the conventional dose of 10 mg; in only one of 22 patients, the response was improved by increasing the dose to 30 mg for two weeks [17]. In summary, there is no evidence for the use of cetirizine at a dose of 40 mg (four times the daily dose). However, there is data for updosing to 20 to 30 mg.
Desloratadine and levocetirizine

Regarding desloratadine, Siebenhaar [18] showed a significantly improved cold tolerance in 30 patients with cold urticaria treated with 20 mg for 7 days, compared with the approved dose of 5 mg. Magerl et al. arrived at similar results in a study with 28 patients [19].

A study by Staeva et al. in 2010 [14] provided evidence for the efficacy of higher doses in CSU. Eighty patients received a regular dose of either desloratadine or levocetirizine for four weeks. If they did not respond, the dose was subsequently increased weekly to 10 to 20 mg or, if there was no improvement, they were switched to the other drug. Four patients became asymptomatic with 5 mg of desloratadine, seven patients with 10 mg of desloratadine and one patient with 20 mg desloratadine. Twenty-eight patients did not show any improvement. For this group of patients, switching to 20 mg of levocetirizine brought improvement in seven more patients. Of the 40 patients who had initially received levocetirizine, nine became asymptomatic with 5 mg, eight with 10 mg and five with 20 mg. Switching to 20 mg of desloratadine did not relieve any more patients of their symptoms.

Prescription of desloratadine and levocetirizine at the expense of the statutory health insurance can be problematic, as the two products have been pharmacologically classified by the drug report as analogous or “me-too” preparations. Prescription of cetirizine and loratadine is therefore recommended according to the efficiency principle in accordance with the exception clause described above. It should be noted, however, that, regarding chronic urticaria and updosing, available data for desloratadine and levocetirizine is better than for loratadine and cetirizine.

Fexofenadine

In the largest placebo-controlled dose-finding trials [20, 21], 439 and 418 CSU patients were treated with 0, 40, 120, 240, or 480 mg daily for four weeks. Both studies showed a better response for all groups compared with placebo, but 240 mg or 480 mg did not yield better effects than lower doses. Godse et al. studied the response of 37 CSU patients to treatment with up to 540 mg of fexofenadine (three-fold dose) [22]. Eleven patients became asymptomatic using the standard dose (180 mg), twelve of 26 patients after updosing to 360 mg, and of the remaining 14 patients, 13 became asymptomatic on 540 mg after four weeks.

Rupatadine

Several large studies also examined rupatadine at various doses: in 330 CSU patients, a significant reduction of 57.5% (p < 0.005) and 63.3 % (p = 0.0001) in the pruritus score compared with placebo (44.9 %) was found after use of 10 and 20 mg rupatadine for four weeks. The regular rupatadine dose of 10 mg led to fewer adverse effects [23]. Another large study in 277 patients did not reveal any differences in efficacy between 10 and 20 mg of rupatadine [24]. In a pooled sub-group analysis, however, a statistically significant reduction in pruritus was found [25]. In summary, there is evidence of a somewhat greater effect of the higher rupatadine dose of 20 mg.

Ebastine

Peyri et al. studied ebastine 10 mg and placebo in 204 CSU patients. In the ebastine group, pruritus and wheal formation were significantly less pronounced compared with placebo. In a study by Magerl et al., ebastine at a dose of 20 mg was investigated in cold urticaria. Ebastine 20 mg proved to be significantly more effective than placebo in 22 patients [26].

Bilastine

In a double-blind, placebo-controlled study, Krause et al. showed that treatment of patients with cold urticaria with bilastine 80 mg led to a significantly better response compared with the standard dose (20 mg) [27]. During treatment with 80 mg of bilastine, 19 of 20 patients exhibited improvement and twelve patients were asymptomatic compared with seven patients using the standard dose. The higher dose was not associated with an increase in undesirable effects such as increased sedation.

Summary

According to study data, there is a tendency for greater efficacy at higher doses. Switching to a different antihistamine appears reasonable in case of poor response or occurrence of adverse effects. Sedating first-generation antihistamines should only be used in exceptional cases.

Step 3: Treatment of antihistamine-refractory chronic spontaneous urticaria

Omalizumab

If patients do not sufficiently respond to second-generation antihistamines, the current S3 guidelines recommend the use of omalizumab 300 mg SQ in CSU (ICD 10: L50.8 or L50.1 and/or angioedema ICD10: T78.3), given at four-week intervals. The approval of omalizumab and guideline recommendations are based on the results of five double-blind placebo-controlled studies with more than 1,000 patients [28–32].
Minireview Chronic spontaneous urticaria – a management pathway

In CSU patients, all studies showed a rapid response to treatment with omalizumab 300 mg, leading to marked reduction in disease activity. Up to 70% of patients treated with omalizumab became asymptomatic. Clinical experience in the treatment of CSU patients outside clinical studies confirms the high efficacy of omalizumab and shows that treatment using this drug in CSU patients is very safe [33, 34]. In CSU studies, omalizumab exhibited a similar safety profile to placebo. For the treatment of asthma, fever is listed as a very common adverse effect, while headache, upper abdominal pain, and reactions at the injection site such as swelling, erythema, pain and pruritus are listed as common adverse effects. We like to emphasize that the treatment of CSU does not result in cure. Therapy should therefore be continued for the duration of the disease.

Practical information

Omalizumab is administered subcutaneously (2 pre-filled syringes) in both upper arms at a dose of 150 mg each. Prior clinical or hematological tests are not necessary. As with specific immune therapy, the patient should not show any signs of infection at the time of injection. Study results and practical experience from the last seven years with respect to omalizumab therapy in urticaria have not shown any relevant adverse effects; in particular, no anaphylactic reactions have been observed. Post-injection observation of the patient at the office is recommended. According to experience made by large German study centers involved in this publication, we recommend an observation period analogous to specific immune therapy.

In patients with both spontaneous and inducible urticaria, omalizumab therapy is also possible, if the spontaneous component predominates. Purely inducible forms of antihistamine-resistant urticaria (ICD10: L50.0 Allergic urticaria, L50.2 Urticaria due to cold or heat, L 50.3 Factitious urticaria, L50.4 Mechanical urticaria, L 50.5 Cholinergic urticaria, L 50.6 Contact urticaria) can only be treated with off-label omalizumab; written approval by the health insurer must be obtained prior to treatment.

Corticosteroids may be used in acute exacerbations. We expressly point out that this therapy should be limited to a maximum period of ten days. The short-term dose should be 0.5–1 mg of prednisolone equivalent. Tapering is usually not necessary when used for 3–5 days.

Other possible off-label treatments in all forms of chronic urticaria include montelukast and cyclosporine A.

Montelukast

Montelukast is available in doses of 4, 5, and 10 mg and should be taken at night. Drug approval in asthma specifies a dose of 4 mg for > 6 months up to 5 years, 5 mg for 6–14 years, and 10 mg for > 15 years and adults. A cheap generic is available. Adverse effects are rare and include depression, dizziness, diarrhea and vomiting.

Some studies [35] with small patient cohorts show different response rates in chronic urticaria when given in addition to antihistamines. The medication is not approved for urticaria, however, and available data do not meet the health insurers’ requirements as outlined above, as randomized, placebo-controlled studies are lacking. We therefore consider montelukast an off-label medication to be used, if the above-mentioned treatment options for chronic urticaria fail.

Cyclosporine A

Cyclosporine A is a calcineurin inhibitor that inhibits T-cell activation. It is used mainly as an immunosuppressant agent in organ transplantation. Though available as a generic, the drug is expensive. In dermatology it is approved for treatment of severe forms of psoriasis and atopic dermatitis ICD 10: L40.0/L20.9. The risk of adverse effects increases with the length of use and includes hepatic and renal damage, high blood pressure, hirsutism, and irreversible gingival hyperplasia.

Several studies have confirmed cyclosporine to be effective when given in addition to antihistamines. Doses of 4 mg/kg body weight or less were used in these studies [26]. The duration of use should not exceed three months. The medication is not approved for urticaria, and available data do not meet the aforementioned requirements of health insurers, as randomized, placebo-controlled studies are lacking. We therefore consider cyclosporine A an off-label medication to be used, if the above-mentioned treatment options for chronic urticaria fail.

Conflict of interest

Christian Termeer is or was a consultant and/or speaker for the following companies: Almirall Hermal, Novartis, Leo Pharma and Biofrontera. Petra Staubach is or was a consultant and/or speaker for the following companies: Novartis, Pohl-Boskamp and Viopharma. Hjalmar Kurzen is or was a consultant and/or speaker for the following companies: Novartis, AbbVie, Dr. Pfleger, Almirall Hermal and Janssen-Cilag. Klaus Strömer is or was a consultant and/or board member for the following companies: Novartis. Rolf Ostendorf is or was a consultant and/or speaker for the following companies: Novartis, Leo and Biofrontera. Marcus Maurer is or was a consultant and/or speaker for the following companies: Almirall Hermal, FAES, Genentech, GSK, Merckle Recordati, Novartis, Sanofi Aventis, MSD, UCB and Uriach.

© 2015 Deutsche Dermatologische Gesellschaft (DDG). Published by John Wiley & Sons Ltd. | JDDG | 1610-0379/2015
Correspondence to

Prof. Dr. med. Marcus Maurer
Charité – Universitätsmedizin Berlin
Klinik für Dermatologie, Venerologie und Allergologie
Charitéplatz 1
10117 Berlin
Germany
E-mail: marcus.maurer@charite.de

References
Minireview Chronic spontaneous urticaria – a management pathway

Query/ Note to the author:

Q1: Please check the listing, it has been modified.
Q2: Reference?
Q3: What “AIS” stands for?