

Definition, aims, and implementation of GA²LEN Urticaria Centers of Reference and Excellence

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Definition, aims, and implementation of GA²LEN Urticaria Centers of Reference and Excellence

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Key words: angioedema, center, excellence, management, urticaria

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3 **Title:** short and informative, length less than 100 characters (current: 81)

4 **Short title:** less than 50 characters (current: 46)

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6 **Abstract:** 250 words: background (including the aims of the study), methods (If space is short, report only
7 the primary outcomes), results, conclusions (current: 170)

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9 **Key words:** up to 5, listed in alphabetical order (current: 5)

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11 **Text** is limited to:

- 12 • less than 3,500 words not including abstract, figure legends and references (word count: 1671)
 - 13 • up to 45 references (current: 21)
 - 14 • up to 6 figures and/or tables (total) If longer, in the cover letter, reasons for increase in length, figure or
15 table number or reference number should be stated (current: 2 figures, 1 table)
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Abstract

GA²LEN, the Global Allergy and Asthma European Network, has recently launched a programme for the development, interaction and accreditation of centers of reference and excellence in special areas of allergy embedded in its overall quality management of allergy centres of excellence. The first area chosen is urticaria. Urticaria is a common and debilitating condition and can be a challenge for both patients and treating physicians, especially when chronic. Centers of reference and excellence in urticaria (UCAREs) can help to improve the management of hard to treat conditions such as urticaria. Here, we describe the aims, the requirements and deliverables, the application process, and the audit and accreditation protocol for GA²LEN UCAREs. The main aims of GA²LEN UCAREs are to provide excellence in urticaria management, to increase the knowledge of urticaria by research and education, and to promote the awareness of urticaria by advocacy activities. To become a certified GA²LEN UCARE, urticaria centers have to apply and fulfill 32 requirements, defined by specific deliverables that are assessed during an audit visit. The GA²LEN UCARE programme will result in a strong network of urticaria specialists, promote urticaria research, and harmonize and improve urticaria management globally.

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Peer Review

Background

GA²LEN - the Global Allergy and Asthma European Network - is a Network of Excellence of the leading European clinical and research facilities in the field of allergology and asthma. Its founding partners include the European Academy of Allergy and Clinical Immunology (EAACI) and the organization representing European patients with allergies and asthma (EFA). GA²LEN started under the European Union Sixth Framework Programme for Research, in 2004, to address the growing public health concern of allergic diseases. It has since grown to include 90 leading European partners and collaborating centers making GA²LEN one of the largest multidisciplinary networks of researchers in allergy and asthma worldwide. GA²LEN enhances the quality of research, integrates research and communicates the findings with the ultimate goal of reducing the burden of allergy and asthma for patients and for Europe's economy and society. GA²LEN aims to develop better health care and improve the quality of life for patients with allergies. GA²LEN also aims to promote training and education in the field of allergology, for example by its GA²LEN Allergy Schools and Masterclasses programme (1). Since its beginning, GA²LEN has set up criteria for centers of excellence in allergy. In 2015, GA²LEN launched an initiative to define, promote, and certify Centers of Reference and Excellence (COREs) for specific diseases. Led by the GA²LEN task force on urticaria (2), the GA²LEN Urticaria Centers of Reference and Excellence (UCARE) program is the first implementation of this GA²LEN CORE initiative, embedded in the overall GA²LEN quality management system of allergy centers of excellence (Table 1) (3).

Urticaria is a common and debilitating group of diseases characterized by recurrent wheals, angioedema, or both (4). The chronic forms of urticaria, i.e. chronic spontaneous urticaria and chronic inducible urticaria, with recurrent signs and symptoms for longer than 6 weeks and often many years, are especially troublesome and incapacitating. Despite recent advances such as the global harmonization of chronic urticaria classification and nomenclature, novel diagnostic tools and instruments, and better treatment options (5) (6) (7) (8) (9) (10) (11) (12) (13) (14) (15) (16) (17) (18), chronic urticaria can be a challenging condition for patients and their treating physicians. Typical challenges in the management of chronic urticaria include the long duration of disease, severe quality of life impairment, high rates of comorbidities including psychiatric and psychosomatic diseases, long delays in diagnosis due to multiple differential diagnoses, fluctuations in disease activity, and insufficient response to antihistamine treatment. Chronic spontaneous urticaria is also a challenge to our health care systems (19) (20).

Centers of Reference and Excellence for specific diseases can help to improve the management of challenging conditions such as urticaria. In addition to serving as referral and second opinion centers for hard to treat patients, centers of reference and excellence improve the understanding, management options, knowledge and awareness of diseases by research, clinical studies, education, and advocacy activities, respectively. Prominent examples of the benefit of centers of reference and excellence include the Centers of Excellence for Rare Diseases, Centers of Excellence for mitral valve surgery, and the European Competence Network of Mastocytosis (ECNM) Centers of Excellence and Reference Centers (21).

This document summarizes the aims of GA²LEN Urticaria Centers of Reference and Excellence (UCAREs), and it describes the requirements and provides the criteria that UCAREs have to fulfill to be certified as such. We also explain how to become a GA²LEN UCARE and the audit and certification process. The aims, requirements, and deliverables for GA²LEN UCAREs and the protocols for implementation and certification of GA²LEN UCAREs in and outside of Europe we provide are based on the work of the GA²LEN task force on urticaria as well as on input from CU patients and from general practitioners and specialists who treat CU patients.

What are the aims of GA²LEN UCAREs?

The aims of GA²LEN UCAREs are to provide excellence in urticaria management, to increase the knowledge of urticaria by research and education, and to promote the awareness of urticaria by advocacy activities. GA²LEN UCAREs will serve as referral centers for the diagnosis and management of urticaria, and thereby complement the current efforts and pathways of health care communities to provide adequate care for urticaria patients. The interaction of GA²LEN UCAREs as a network will help to increase urticaria knowledge and management.

What are the requirements for GA²LEN UCAREs?

GA²LEN UCAREs are required to demonstrate excellence in the management of urticaria, research activities, efforts in education, and advocacy activity. Specifically, the following 32 requirements must be met (Fig. 1):

Infrastructure/setup

- Hospital setting
- Outpatient clinic with separate clinic hours for urticaria patients headed by expert
- Open to children and adult patients
- Team of dedicated staff, with specific urticaria training
- Multidisciplinary approach
- Accessibility and visibility
- Communication skills
- Quality management, structured and valid protocols of diagnosis and management
- Structured documentation, recording and archiving of patient data
- Critical incidence reporting and error management
- Assessment of patient satisfaction and unmet needs
- In team communication
- Active recruitment of research funding and support for educational activities and advocacy on urticaria
- Support of the UCARE network
- “Never give up” attitude

Management of urticaria

- Knowledge of and adherence to the EAACI/GA²LEN/EDF/WAO urticaria guideline
- Knowledge and use of current nomenclature and classification of urticaria
- Knowledge and use of guided history taking/anamnesis
- Knowledge and use of differential diagnostic algorithm
- Knowledge and use of standardized assessments and monitoring of disease activity, impact and control of disease
- Identification of comorbidities
- Provocation and threshold testing in CINDUs
- Knowledge and use of therapeutic algorithm
- Counseling

Clinical and Basic Research

- Scientific orientation
- Scientific activity
- Scientific productivity
- Clinical trials
- Participation in registry

Education

- Educational activities

Advocacy

- Increase awareness of urticaria
- Interaction with and support of patient organization(s)

Application process

Urticaria specialty centers in and outside of Europe can apply to become a GA²LEN UCARE by contacting GA²LEN (office@ga2len.net). GA²LEN encourages all urticaria centers to become UCAREs and to join the GA²LEN UCARE network. In their application, centers should describe their motivation to become a UCARE and provide information on how they fulfill the requirements by use of the checklist provided (Fig. 1). GA²LEN will review the application and schedule an audit visit. All 32 requirements have to be met. If it becomes clear, during the audit, that certain requirements are not (yet) fulfilled, GA²LEN will provide help and support to the center to address shortcomings and to achieve UCARE status. Upon successful audit, GA²LEN awards a two-year certificate (Fig. 2) that can be renewed upon successful re-audit. When GA²LEN UCAREs are located at GA²LEN centers or collaborating centers, this should ideally be done in parallel with the regular audits done to maintain GA²LEN Network of Excellence partner status. Certified GA²LEN UCAREs become members of the GA²LEN UCARE network and their head joins the UCARE audit and certification team. Certified GA²LEN UCAREs enjoy the benefits of being a member of the

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3 UCARE network (participation in network of excellence activities, multicenter projects, etc.). No
4 financial obligations to GA²LEN result from becoming or being a GA²LEN UCARE.
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8 **The audit and certification process**

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10 The audit and readit process involves an on site visit by at least one member of the GA²LEN
11 UCARE audit and certification team. The GA²LEN UCARE audit and certification team consists of all
12 members of the GA²LEN urticaria task force on urticaria and the heads of certified UCAREs. During
13 this audit visit, the center presents its facilities and team to the auditor(s), by working with the
14 audit checklist (Fig. 1). The audit visit is concluded by a collegial assessment and information by
15 the auditor on the results of the audit. Shortcomings, if identified, are discussed and strategies to
16 overcome them are jointly developed with the spirit of achieving the common goals of the UCARE
17 network. The team will receive a written audit report and the GA²LEN UCARE certificate (Fig. 2). In
18 case certain deliverables are missing or requirements were found to need work, the audit report
19 will contain specific recommendations and timelines to address this. GA²LEN will help centers to
20 achieve UCARE status.
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28 **What do urticaria specialty centers need to do to meet the requirements for GA²LEN UCAREs?**

29 All 32 requirements for GA²LEN UCAREs are explained in the audit checklist (Fig. 1), which includes
30 specific deliverables for each requirement. For example, the requirement to know and follow the
31 international EAACI/GA²LEN/EDF/WAO guideline for urticaria (Requirement #16) entails that
32 physicians and other UCARE health care professionals have read and understood the current
33 version of this guideline and that the guideline recommendations are implemented in their center.
34 The deliverables for this requirement are that 1) the current guideline version is present (paper or
35 electronic version) at the center, 2) that UCARE center staff can answer questions on the guideline
36 recommendations, and that 3) UCARE physicians can show, upon request, by use of a patient file,
37 that patients management decision are based on guideline recommendations (Fig. 1).
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45 **Outlook**

46 This publication marks the start of the implementation of the GA²LEN UCARE initiative. Several
47 specialty centers for urticaria, e.g. at the Charité, Berlin and at the Hospital del Mar, Barcelona
48 have already applied to become GA²LEN UCAREs, and audits and certifications are ongoing. We
49 expect that most GA²LEN centers and many urticaria specialty centers in an outside of Europe will
50 take this step in the near future. We predict and hope that by 2020, all countries in Europe and
51 many countries outside of Europe will have at least one GA²LEN UCARE. This will result in a strong
52 network of urticaria specialists, promote urticaria research, and harmonize and improve urticaria
53 management globally. The goal is to measure the impact of UCAREs over time and to document
54 the benefits of this initiative.
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Statement of contribution

All authors have contributed to the development of the UCARE programme and the manuscript.

Conflicts of interest

Marcus Maurer has received institutional funding for research and / honoraria for lectures and/or consulting from Almirall, FAES, Genentech, Moxie, MSD, Novartis, Sanofi, Takeda, UCB, and Uriach.

Martin Metz has been a speaker or consultant for Bayer, Dr. R. Pflieger, GSK, Moxie, Nerre, Novartis, Roche and Sanofi.

Jean Bousquet, Carsten Bindslev-Jensen, Kiran Godse, Michael Makris have no conflict of interest.

Walter Canonica has been a scientific consultant and/or speaker supported for the following commercial companies: A.Menarini, Faes, Lab.Guidotti-Malesci, Uriach, Novartis

Martin Church has been a speaker or consultant for Almirall, FAES Pharma, Menarini, Moxie, MSD, Novartis, UCB Pharma, Sanofi-Aventis and Uriach.

Michihiro Hide has received institutional funding for research and/honoraria for lectures and/or consulting from MSD, Novartis, GlaxoSmithKline, Tanabe-Mitsubishi, Kyowahakkou-Kirin, Taiho-Yakuhin, Teikoku-Seiyaku, Shionogi-Seiyaku and BayerYakuhin.

Emek Kocatürk has been a speaker and consultant for Novartis.

Markus Magerl has been a speaker or consultant for Almirall, Moxie, Novartis, and Uriach.

Sarbjit Saini: Research Interests-NIH, ITN/NIAID, Novartis, Astra-Zeneca; Consultant to Genentech, Medimmune, Novartis, Ono, Regeneron Organizational interests: AAAAI, UptoDate, Journal of Investigative Dermatology.

Zuotao Zhao has been a speaker for Novartis, Galderma, MSD, Pfizer, Stiefel, Astellas, Moxie Meda, Takeda, Bayer, GlaxoSmithKline, UCB, and ROTAM & Dr. Reddy's.

Torsten Zuberbier has received institutional funding for research and/or honoraria for lectures and/or consulting from Allergopharma, Ansell, Bayer Schering, DST, FAES Pharma, Fujisawa, HAL, Henkel, Kryolan, Leti Pharma, Menarini, Merck, MSD, Novartis, Procter & Gamble, Ranbaxy, Sanofi-Aventis, Schering Plough, Stallergenes, Takeda, UCB. In addition, he is a member of DDG, DGAKI, EAACI, EDF, GA²LEN, WAO.

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For Peer Review

References

1. Maurer M, Magerl M, Metz M, Siebenhaar F, Weller K, Krause K. Practical algorithm for diagnosing patients with recurrent wheals or angioedema. *Allergy* 2013;**68**(6):816-819.
2. Maurer M, Rosen K, Hsieh HJ, Saini S, Grattan C, Gimenez-Arnau A, et al. Omalizumab for the treatment of chronic idiopathic or spontaneous urticaria. *N Engl J Med* 2013;**368**(10):924-935.
3. Heinzerling L, Burbach G, van Cauwenberge P, Papageorgiou P, Carlsen KH, Lodrup Carlsen KC, et al. Establishing a standardized quality management system for the European Health Network GA2LEN. *Allergy* 2010;**65**(6):743-752.
4. Zuberbier T, Aberer W, Asero R, Bindslev-Jensen C, Brzoza Z, Canonica GW, et al. The EAACI/GA(2) LEN/EDF/WAO Guideline for the definition, classification, diagnosis, and management of urticaria: the 2013 revision and update. *Allergy* 2014;**69**(7):868-887.
5. Baiardini I, Pasquali M, Braido F, Fumagalli F, Guerra L, Compalati E, et al. A new tool to evaluate the impact of chronic urticaria on quality of life: chronic urticaria quality of life questionnaire (CU-QoL). *Allergy* 2005;**60**(8):1073-1078.
6. Magerl M, Borzova E, Gimenez-Arnau A, Grattan CE, Lawlor F, Mathelier-Fusade P, et al. The definition and diagnostic testing of physical and cholinergic urticarias--EAACI/GA2LEN/EDF/UNEV consensus panel recommendations. *Allergy* 2009;**64**(12):1715-1721.
7. Weller K, Groffik A, Magerl M, Tohme N, Martus P, Krause K, et al. Development and construct validation of the angioedema quality of life questionnaire. *Allergy* 2012;**67**(10):1289-1298.
8. Kaplan A, Ledford D, Ashby M, Canvin J, Zazzali JL, Conner E, et al. Omalizumab in patients with symptomatic chronic idiopathic/spontaneous urticaria despite standard combination therapy. *J Allergy Clin Immunol* 2013;**132**(1):101-109.
9. Maurer M, Bindslev-Jensen C, Schoepke N, Zuberbier T. Effects of a Novel GA(2)LEN Training Program on Urticaria on the Knowledge of General Practitioners in Saudi-Arabia. *World Allergy Organ J* 2011;**4**(2):45-46.
10. Maurer M, Weller K, Bindslev-Jensen C, Gimenez-Arnau A, Bousquet PJ, Bousquet J, et al. Unmet clinical needs in chronic spontaneous urticaria. A GA(2)LEN task force report. *Allergy* 2011;**66**(3):317-330.
11. Mlynek A, Vieira dos Santos R, Ardelean E, Weller K, Magerl M, Church MK, et al. A novel, simple, validated and reproducible instrument for assessing provocation threshold levels in patients with symptomatic dermatographism. *Clin Exp Dermatol* 2013;**38**(4):360-366; quiz 366.
12. Weller K, Groffik A, Magerl M, Tohme N, Martus P, Krause K, et al. Development, validation, and initial results of the Angioedema Activity Score. *Allergy* 2013;**68**(9):1185-1192.
13. Altrichter S, Salow J, Ardelean E, Church MK, Werner A, Maurer M. Development of a standardized pulse-controlled ergometry test for diagnosing and investigating cholinergic urticaria. *J Dermatol Sci* 2014;**75**(2):88-93.
14. Weller K, Groffik A, Church MK, Hawro T, Krause K, Metz M, et al. Development and validation of the Urticaria Control Test: a patient-reported outcome instrument for assessing urticaria control. *J Allergy Clin Immunol* 2014;**133**(5):1365-1372, 1372 e1361-1366.
15. Casale TB, Bernstein JA, Maurer M, Saini SS, Trzaskoma B, Chen H, et al. Similar Efficacy with Omalizumab in Chronic Idiopathic/Spontaneous Urticaria Despite Different Background Therapy. *J Allergy Clin Immunol Pract* 2015;**3**(5):743-750 e741.
16. Magerl M, Abajian M, Krause K, Altrichter S, Siebenhaar F, Church MK. An improved Peltier effect-based instrument for critical temperature threshold measurement in cold- and heat-induced urticaria. *J Eur Acad Dermatol Venereol* 2015;**29**(10):2043-2045.

- 1
2
3 17. Saini SS, Bindslev-Jensen C, Maurer M, Grob JJ, Bulbul Baskan E, Bradley MS, et al. Efficacy
4 and Safety of Omalizumab in Patients with Chronic Idiopathic/Spontaneous Urticaria who Remain
5 Symptomatic on H1 Antihistamines: A Randomized, Placebo-Controlled Study. *J Invest Dermatol*
6 2015;**135**(3):925.
7
8 18. Schoepke N, Abajian M, Church MK, Magerl M. Validation of a simplified provocation
9 instrument for diagnosis and threshold testing of symptomatic dermographism. *Clin Exp Dermatol*
10 2015;**40**(4):399-403.
11 19. Maurer M, Staubach P, Raap U, Richter-Huhn G, Baier-Ebert M, Chapman-Rothe N.
12 ATTENTUS, a German online survey of chronic urticaria patients highlighting the burden of disease,
13 unmet needs and real-life clinical practice. *Br J Dermatol* 2015.
14 20. Weller K, Maurer M, Grattan C, Nakonechna A, Abuzakouk M, Berard F, et al. ASSURE-CSU:
15 a real-world study of burden of disease in patients with symptomatic chronic spontaneous
16 urticaria. *Clin Transl Allergy* 2015;**5**:29.
17
18 21. Sánchez-Muñoz L, Morgado A, Álvarez-Twose I, Matito A, Garcia-Montero AC, Teodosio C,
19 et al. Diagnosis and classification of mastocytosis in non-specialized versus reference centres: a
20 Spanish Network on Mastocytosis (REMA) study on 122 patients. *Br J Haematol* 2015;**Oct 12**. doi:
21 **10.1111/bjh.13789**. [Epub ahead of print].
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Figure legends

Fig. 1 Audit checklist for GA²LEN Urticaria Center of Reference and Excellence (UCARE) certification

The list shows and explains the requirements for becoming a GA²LEN UCARE and the deliverables that are reviewed during the audit process.

Fig. 2 Certificate awarded to GA²LEN UCAREs upon successful audit

The certificate is awarded for 2 years and requires successful re-audit to be extended.

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Figure 1. GA²LEN Urticaria Centers of Reference and Excellence (UCARE): Requirements and deliverables

Audit Date: _____

Audited Center: _____

Auditor: _____

Last audit: _____



Infrastructure / Set up					
	Requirement	Explanation	Deliverable(s)	Yes /No	Cat.
1.	Hospital setting	Center needs to be in a hospital or affiliated with a hospital with inpatient facilities to allow for extended diagnostic work up and management of exacerbation	Evidence of hospital setting or affiliation with hospital	<input type="checkbox"/> <input type="checkbox"/> _____	B
2.	Outpatient clinic with separate clinic hours for urticaria patients headed by expert	Center needs to have designated and expert leadership (experienced specialist physician) and to offer a minimum number of consultation hours per week exclusive for urticaria patients	Lead by experienced physician (board certified specialist) ≥4h / week of dedicated urticaria clinic (physician contact time)	<input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____	A
3.	Open to children and adult patients	Centers need to be able to provide care for urticaria patients of any age, either by center staff or affiliated specialists	Evidence that urticaria patients of any age are provided with state of the art care	<input type="checkbox"/> <input type="checkbox"/> _____	A
4.	Team of dedicated staff, with specific urticaria training	Center staff needs to comprise more than one physician and at least one nurse. All center staff needs to be specifically and regularly trained in urticaria	≥2 physicians and ≥1 nurse Record of ≥1 urticaria training per staff member per year, e.g. GA ² LEN school on urticaria, urticaria CME activity, etc.	<input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____	A

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5.	Multidisciplinary approach	Center needs to be able to interact with other specialties for the management of comorbidities, the treatment of patients with differential diagnoses, and to perform extended diagnostics	Evidence of interaction with other specialists	<input type="checkbox"/> <input type="checkbox"/> _____	B
6.	Accessibility and visibility	Urticaria patients need to be able to find the center via information on the web; center needs to have referral network(s) of physicians; center needs to work with patient association(s), where applicable	Center clinic hours are posted on website Evidence of local referral network Evidence that patient organization recommends the center	<input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____	B
7.	Communication skills	Center staff needs to be able to communicate adequately with urticaria patients in national language and in English	Proof of adequate communication skills by interview with center staff	<input type="checkbox"/> <input type="checkbox"/> _____	B
8.	Quality management	Centers need to have Quality Management (QM) system in place, need to have written protocols and standard operating procedures (SOPs)	Evidence of presence of QM system Proof of presence and use of SOPs/ protocols	<input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____	B
9.	Structured documentation, recording and archiving of patient data	Centers needs to have in place and use a databank to record patient data. Databank needs to allow retrieval of information needed to address scientific questions	Patient databank ≥50 urticaria patients in databank/year	<input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____	B
10.	Critical incidence reporting and error management	Centers need to have and make use of an incidence report book documenting all critical incidents. Centers must analyze all reported incidents and take and document appropriate action	Evidence of presence and use of incidence report book and follow up and documentation of error reports by appropriate action	<input type="checkbox"/> <input type="checkbox"/> _____	B
11.	Assessment of patient satisfaction and unmet needs	Centers needs to regularly assess how satisfied their patients are with the work of the center and take appropriate action based on the outcome	Proof that ≥40 patients were asked about their satisfaction in last 12 months (preferably by questionnaire)	<input type="checkbox"/> <input type="checkbox"/> _____	B
12.	In team communication	Centers need to have regular meetings of staff to discuss projects and concepts. Decisions should be protocolled and followed by action where applicable.	Evidence of regular team meetings, at least once per month, on center logistics, projects and concepts	<input type="checkbox"/> <input type="checkbox"/> _____	B

13.	Active recruitment of research funding and support for educational activities and advocacy on urticaria	Centers needs to actively recruit extramural funding to support research, educational activities and/or advocacy on urticaria	Documentation of efforts to recruit funding (grant applications, donation programme)	<input type="checkbox"/> <input type="checkbox"/> _____	B
14.	Support of the UCARE network	Training and activities in auditing and certifying GA ² LEN UCAREs and interaction with other UCAREs	Letter of intent to serve as a GA ² LEN UCARE auditor and to contribute to other UCARE network activities	<input type="checkbox"/> <input type="checkbox"/> _____	A
15.	“Never give up” attitude	Staff needs to exhibit high motivation to help urticaria patients and show understanding that they may be the last resort of patients. Staff needs to convey to patients, that they are in good care and that the center will help them, however hard this may be.	Evidence of “never give up”-attitude by staff interview	<input type="checkbox"/> <input type="checkbox"/> _____	B

Management

	Requirement	Explanation	Deliverable(s)	Yes /No	Cat.
1.	Knowledge of and adherence to the EAACI/GA ² LEN /EDF/WAO urticaria guideline	All center staff members need to know the current version of the international EAACI / GA ² LEN / EDF / WAO guideline and their corresponding national guideline, if available. Center approach to urticaria needs to be based on guideline recommendations.	EAACI/GA ² LEN/EDF/WAO guideline is present (paper / electronic version ¹) Center staff can answer questions on the urticaria guideline recommendations Center physicians can show, by use of a patient file, that management decision are based on guideline recommendations	<input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____	A
2.	Knowledge and use of current nomenclature and classification of urticaria	Center staff needs to know and use the current urticaria classification and nomenclature	Evidence that staff uses current urticaria nomenclature and classification ¹ , e.g. by interview and/or patient file review	<input type="checkbox"/> <input type="checkbox"/> _____	A
3.	Knowledge and use of guided history taking/anamnesis	Structured history taking by center physicians is essential and a checklist can facilitate this	Checklist for history taking ¹ needs to be present and used as evidenced by interview or urticaria patient file review	<input type="checkbox"/> <input type="checkbox"/> _____	A
4.	Knowledge and use of differential diagnostic algorithm	Center physicians need to be aware of the differential diagnoses of chronic urticaria and know how not to miss them. The guideline algorithm can help with this.	Differential diagnostic algorithm ^{1,2} needs to be present and used as evidenced by interview or urticaria patient file review	<input type="checkbox"/> <input type="checkbox"/> _____	A

5.	Standardized assessments and monitoring of disease activity, impact and control of disease	The use of instruments for assessing disease activity, impact and control allows for standardized measurements and monitoring of patients can help to optimize urticaria management.	UAS7 ^{1,3} , AAS ^{4,5} , CU-Q ₂ oL ⁶ , AE-QoL ^{5,7} , UCT ^{5,8,9} need to be present and used At least one of them needs to be used in 80% of chronic urticaria patients	<input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____	A
6.	Identification of comorbidities and underlying causes	Center needs to have access to and use measures to identify comorbidities and causes of chronic spontaneous urticaria, for example autoreactivity/autoimmunity, infections, etc. including biopsies	Evidence that diagnostic measures for urticaria comorbidities and underlying causes are used, e.g. ASST, BAT, biopsy, etc	<input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____	A
7.	Provocation and threshold testing in CINDUs	Provocation testing and threshold assessment are important in the diagnostic workup of CINDUs. SOPs are needed as is the use of appropriate instruments / protocols such as dermatographometers ^{5,10} / TempTest ^{®11} , pulse controlled ergometry ¹²	Standardized documentation of provocation and threshold testing ¹³ Instrument / techniques are available and used as evidenced by patient file reviews	<input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____	A
8.	Knowledge and use of therapeutic algorithm	Center physicians need to know and use therapeutic guideline algorithm, for example use of non-sedating antihistamines, up dosing of non-sedating antihistamines, restrictive use of glucocorticosteroids, use of step 3 therapies.	Evidence that staff uses current therapeutic algorithm ¹ for the treatment of chronic urticaria patients, e.g. by interview and/or patient file review	<input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____	A
9.	Counseling	Counseling of patients and their families, for example on triggers of exacerbation, stress, avoidance of non-steroidal anti-inflammatory drugs, daily life issues can help to optimize urticaria management	Evidence that urticaria patients receive counseling, e.g. by interview and/or patient file review	<input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____	A

Research					
	Requirement	Explanation	Deliverable(s)	Yes /No	Cat.
1.	Scientific orientation	Center staff needs to be up-to-date with the literature on urticaria, especially on pathogenesis, for example by participation in journal club, attending annual meetings of scientific societies, membership in research societies, for example EMBRN, ESDR, EAACI	Evidence of knowledge of the current urticaria literature, e.g. by interview	<input type="checkbox"/> <input type="checkbox"/> _____ <input type="checkbox"/> <input type="checkbox"/> _____	A

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2.	Scientific activity	Research activities in basic science, clinical science, translational science, epidemiology, and/or public health	Evidence of scientific activities and projects on urticaria	<input type="checkbox"/> <input type="checkbox"/> _____	A
3.	Scientific productivity	Center needs to show that its research activities result in publications and other scientific output	0.5 peer reviewed paper on urticaria per year per center physician	<input type="checkbox"/> <input type="checkbox"/> _____	A
4.	Clinical trials	Center needs to participation in clinical trials, pharma- and/or investigator-initiated; diagnostic and/or therapeutic trials	0.5 trials in urticaria per year per center physician	<input type="checkbox"/> <input type="checkbox"/> _____	A
5.	Participation in registry	Registries can help to better understand urticaria. Center needs to participate in international, national, and/or regional registry activities, e.g. CURE ¹⁴	Evidence that center contributes to a urticaria registry	<input type="checkbox"/> <input type="checkbox"/> _____	A

Education

	Requirement	Explanation	Deliverable(s)	Yes /No	Cat.
1.	Educational activities	Center needs to contribute to the education of other specialists, e.g. dermatologists, allergists, ER-physicians, non-specialists such as general practitioners and family physicians, medical students, residents, patients, and the general public	Evidence of 1 educational activity on urticaria per year for physicians and 1 per year for patients	<input type="checkbox"/> <input type="checkbox"/> _____	A

Advocacy

	Requirement	Explanation	Deliverable(s)	Yes /No	Cat.
1.	Increase awareness of urticaria	Centers need to increase awareness and knowledge of urticaria, for example by contributing to UrticariaDay ⁶ , support of the Urticaria Network ³ .	Evidence of 1 advocacy /awareness activity on urticaria per year	<input type="checkbox"/> <input type="checkbox"/> _____	A
2.	Interaction with and support of patient organization(s)	Patient organizations can help to improve the management of urticaria and urticaria patients	Evidence of interaction with urticaria patient organization	<input type="checkbox"/> <input type="checkbox"/> _____	A

Comments:

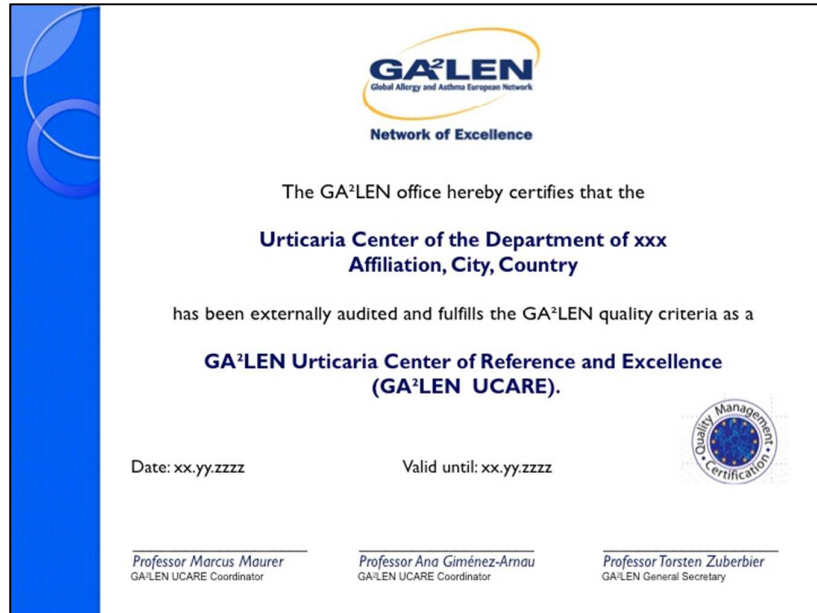
- Audit result:**
- All requirements fulfilled, center will receive certificate
 - Most requirements fulfilled, except for:
Center will receive certificate upon providing:
 - Re-audit in ____ months

Categories (Cat.): Requirements of the category A are specific for UCAREs, whereas requirements of the category B are part of the GA²LEN Centers of Excellence Quality Management and Certification programme. Category B requirements do, therefore, not need to be audited, if the urticaria center is part of an audited and certified GA²LEN Center of Excellence.

References: 1 = Zuberbier T et al. The EAACI/GA²LEN/EDF/WAO Guideline for the definition, classification, diagnosis and management of urticaria: The 2013 revision and update. Allergy 2014; 69: 868-87; 2 = Maurer, M., Magerl, M., Metz, M., Siebenhaar, F., Weller, K., and Krause, K.: Practical algorithm for diagnosing patients with recurrent wheals or angioedema. Allergy 2013a: 68; 816-819; 3 = www.urtikaria.net; 4 = Weller, K., Groffik, A., Magerl, M., Tohme, N., Martus, P., Krause, K., Metz, M., Staubach, P., and Maurer, M.: Development, validation and initial results of the angioedema activity score (AAS). Allergy 2013: 68; 1185-1192; 5 = www.moxie-gmbh.de; 6 = Baiardini I, Pasquali M, Braidò F, Fumagalli F, Guerra L, Compalati E, Braga M, Lombardi C, Fassio O, Canonica GW. A new tool to evaluate the impact of chronic urticaria on quality of life: chronic urticaria quality of life questionnaire (CU-QoL). Allergy. 2005; 60: 1073-8; 7 = Weller, K., Groffik, A., Magerl, M., Tohme, N., Martus, P., Krause, K., Metz, M., Staubach, P., and Maurer, M.: Development and construct validation of the angioedema Quality of Life Questionnaire (AE-QoL). Allergy 2012: 67; 1289-1298; 8 = Weller, K., Groffik, A., Church, M. K., Hawro, T., Krause, K., Metz, M., Martus, P., Casale, T., Staubach, P., and Maurer, M.: Development and validation of the urticaria control test - a patient reported outcome instrument for assessing urticaria control. J. Allergy Clin. Immunol. 2014: 133; 1365-1372; 9 = www.urticariady.org; 10 = www.htz.biz; 11 = www.couarge-khazaka.de; 12 = Altrichter, S., Salow, J., Ardelean, E., Church, M. K., Werner, A., and Maurer, M.: Development of a standardized pulse-controlled ergometry test for diagnosing and investigating cholinergic urticaria. J. Dermatol. Sci. 2014; 75; 88-93; 13 = Magerl, M., Borzova, E., Giménez-Arnau, A., Grattan, C. E. H., Lawlor, F., Mathelier-Fusade, P., Metz, M., Mlynek, A., and Maurer, M.: The definition and diagnostic testing of physical and cholinergic urticarias - EAACI/GA²LEN/EDF/UNEV consensus panel recommendations. Allergy 2009: 64; 1715-1721; 14 = www.urticaria-registry.com.

Abbreviations: AAS = Angioedema activity score; AE-QoL = Angioedema quality of life questionnaire; ASST = Autologous serum skin test; BAT = Basophil activation test; CAT = categories; CINDU = Chronic inducible urticaria; CME = Continued medical education; CURE = Chronic urticaria registry; CU-QoL = Chronic urticaria quality of life questionnaire; EAACI (The European Academy of Allergy and Clinical Immunology (www.EAACI.org); EMBRN = European mast cell and basophil research network (www.embrn.eu); ER = Emergency room; ESDR = European Society for Dermatological Research (www.esdr.org); GA²LEN = Global Allergy and asthma European Network; QM = Quality management, SOP = standard operating procedure; UAS7 = Urticaria activity score 7 (for seven consecutive days); UCARE = Urticaria Center of Reference and Excellence; UCT = Urticaria control test.

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5 **Figure 2. Certificate awarded to GA²LEN UCAREs upon successful audit**
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Table 1: Criteria and Performance indicators for GA²LEN Allergy Centers

Criteria	Explanation	Performance indicator
Practice of official guidelines (e.g. WHO, EAACI)	Diagnosis and treatment should be based on evidence and consented guidelines	Guidelines exist for two relevant diseases
Compliance with guidelines/clinical pathways for two relevant diseases	Diagnosis and treatment should be based on evidence and consented guidelines	More than 80% of patients diagnosed/treated in compliance with guideline/pathway for e.g. allergic rhinitis, asthma, urticaria
Basic allergology training of doctors	Continuous medical education ensures standard of care	≥6 sessions/year
Basic allergology training of nurses	Continuous medical education ensures standard of care	≥3 sessions/year
Emergency intervention training of doctors and nurses	Repeating emergency interventions keeps knowledge up to date	≥1 sessions/year
Critical incidence reporting/ root cause analysis	Critical incidents (e.g. anaphylactic reactions, application of wrong medication/allergen extract or wrong dose) are reported, discussed, and the causes are analyzed. Actions to avoid future incidents are taken if necessary	Incidence report book documenting all incidents for internal and anonymous follow-up. Includes description and analysis of incidents and actions that have been taken for the future
Appointed internal responsible for quality issues (quality manager)	Contact person for quality matters and coordination of quality initiatives	Name of quality manager
Practice of first expired first out (FEFO)	Storage and use of medication and extracts as to minimize expiration of drugs/extracts	Yes, practiced
Controls of expiration dates of all extracts and medication used	Control to ensure quality of drugs/extracts	One check per month
Temperature logs for all fridges	Control to ensure quality of drugs/extracts	Daily check (manual or electronic alarm)
Availability of equipment for emergency intervention	Control to ensure effective emergency intervention if needed	Daily check
Practice of guidelines (e.g. WHO, ARIA, Gina)	Diagnosis and treatment should be based on evidence and consented guidelines	Guidelines used for all treated diseases if available
Full spectrum of allergology available	Coverage of all disease aspects including systemic allergic disease (anaphylaxis, food allergy, drug allergy)	Medical care for dermatological, pediatric and lung diseases
Quality control of diagnosis/treatment (patient record review)	Retrospective quality checks ensure elimination of errors	10 patient record reviewed per month by head of department or senior staff member
Quality control of documentation in patient record	Notes in patient records with date and abbreviation of doctor/nurse who has documented	More than 90% of notes are dated and carry name of care provider
Written protocols and manuals for testing and other procedures (standard operating procedures)	Protocols exist (can also be as reference to an article or standard book) and employees are aware of them to ensure standardization of procedures	Protocols for skin prick test, skin patch test, intracutaneous testing, lung function, nasal provocation, application of immunotherapy, food and drug provocation test
Excellence knowledge of allergology by team leaders	Maximum knowledge of team leaders ensures setting right guidelines and principles for medical care	Collegial interview with structured interview guidelines by telephone with other team leader on allergologic cases. Assignment of random interviewer by GA ² LEN office.
Structured curriculum for allergology training	Structured training (including theoretical and practical knowledge and skills) of registrars/junior doctors ensures standard of training	Structured curriculum, e.g. UEMS curriculum for allergology or national curricula
Allergology knowledge of doctors	Up-to-date knowledge of doctors ensures complying with right guidelines and principles of medical care	Six internet-based questions for doctors to be answered once per year
Basic allergology training of nurses	Continuous medical education ensures standard of care	≥4 sessions/year
Allergology knowledge of nurses	Up-to-date knowledge of nurses ensures complying with right guidelines and principles of medical care	Four internet-based questions for nurses to be answered once per year
Emergency intervention training of doctors and nurses	Repeating emergency interventions keeps knowledge up to date	Participation in one emergency situation per year (training session or while on duty)
Training of doctors for diagnostic and therapeutic guidelines	Continuous medical education ensures standard of care	1 session/year
Communication skills in English language	Health care for European citizens not speaking native language ensured by availability of English speaking nurse and doctor on demand	Possibility to ask questions in English
Critical assessment of scientific literature	High quality care is ensured by continuous education with peer reviewed articles	Assessment of one centrally provided Non-European article (in cooperation with Cochrane) by all researchers

Academic research	Participation in research ensures growth of body of knowledge and critical evaluation of results	At least 0.5 articles per year in a peer reviewed journal per researcher per year
Claim management	Continuous evaluation of claims and actions taken consequently ensure quality improvement in service delivery	Number of claims and number of actions taken
Patient interviews for evaluation of facility	Feedback from patients on quality of care (including access, safe services, confidentiality, informed choice, comfort, continuity of care up) and subsequent changes ensure service improvements	40 patients interviewed in last 12 months (possibly by questionnaire)

Based on Heinzerling et al., 2010

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