

DOI: 10.1111/all.14293

## Definition, aims, and implementation of GA<sup>2</sup>LEN/HAEi Angioedema Centers of Reference and Excellence

To the Editor,

GA<sup>2</sup>LEN, the Global Allergy and Asthma European Network, and HAE international (HAEi), the global umbrella organization for the world's hereditary angioedema (HAE) patient groups, have launched their joint ACARE (Angioedema Center of Reference and Excellence) program, within GA<sup>2</sup>LEN's center of reference and excellence (CORE) initiative. Angioedema is a common, heterogeneous, often debilitating and chronic condition and is frequently a challenge for physicians and affected patients, especially patients suffering from recurrent attacks. Additionally, it can be a challenge for some patients to understand the underlying etiology of their angioedema (Table 1). GA<sup>2</sup>LEN's CORE networks, such as UCARE for urticaria and ADCARE for atopic dermatitis, help to improve the management of difficult-to-treat conditions. Here, we describe the aims, requirements, provisions, application process, audit, and accreditation

protocol for GA<sup>2</sup>LEN/HAEi ACAREs. ACAREs aim to provide excellence in angioedema management, increase the knowledge of angioedema through research and education, and promote advocacy activities that raise angioedema awareness. To become a certified ACARE, angioedema centers must fulfill 32 requirements, defined by specific provisions that will be assessed during an audit visit. The ACARE program will result in a strong network of angioedema specialists, promote angioedema research and awareness, and harmonize and improve angioedema management globally. ACAREs will expand access to modern angioedema medicines in countries where they are available and help to bring them to countries where they are not.<sup>1</sup>

This document summarizes the aims of GA<sup>2</sup>LEN/HAEi Angioedema Centers of Reference and Excellence (ACAREs) and elaborates the requirements that ACAREs must fulfill to become

**TABLE 1** Classification of angioedema

Bradykinin-mediated angioedema				Mast cell mediator-mediated angioedema		Unknown mediator
C1-INH deficiency/defect		C1-INH normal		IgE mediated	Non-IgE mediated	
Inherited	Acquired	Inherited	Acquired			
HAE-1	AAE-C1-INH	HAE nC1-INH (HAE-FXII, HAE-ANGPTI, HAE-PLG, HAE-KNG1, HAE-UNK)	AE due to medication that interferes with BK degradation, eg ACEi	Angioedema with or without wheals in patients with urticaria Anaphylaxis	Angioedema with or without wheals in patients with urticaria	Idiopathic AE

Abbreviations: AAE-C1-INH, acquired angioedema due to C1-inhibitor deficiency; ACEI-AE, angiotensin-converting enzyme inhibitor-induced angioedema; BK, bradykinin; HAE nC1-INH, hereditary angioedema with normal C1-inhibitor levels, either due to a mutation in factor XII (F12), angiotensin-converting enzyme 1 (ACE1), plasminogen (PLG), kininogen-1 (KNG1), or unknown (UNK) (HAE-FXII, HAE-ANGPTI, HAE-PLG, HAE-KNG1, HAE-UNK); HAE-1, hereditary angioedema due to C1-inhibitor deficiency; HAE-2, hereditary angioedema due to C1-inhibitor dysfunction.

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

© 2020 The Authors. *Allergy* published by European Academy of Allergy and Clinical Immunology and John Wiley & Sons Ltd

(A) GALEN HAEi Network of Excellence HAEi. Table with columns: Requirement, Objective, Sub-objective, No/Yes, C/A. Sections include: Information / Not up, Management, Research, Education, Advisory.

FIGURE 1 A and B, Audit checklist for GA2LEN/HAEi Angioedema Center of Reference and Excellence (ACARE) certification (A) and certificate awarded to GA2LEN/HAEi ACAREs upon a successful audit (B). A, The list shows and explains the requirements for becoming a GA2LEN/HAEi ACARE and the deliverables that are reviewed during the audit process. B, The certificate is awarded for 2 y and requires successful re-audit to be extended

certified. It also provides (see Appendix S1) background information on GA2LEN and HAEi, including HAEi member organizations and regional patient advocates, on why we need an Angioedema Center of Reference and Excellence (ACARE) program and network, and on the accreditation and certification process, governance and funding, and on the interaction with other GA2LEN networks of centers of reference and excellence. The protocols, aims, requirements, and provisions related to becoming a certified ACARE are based on (a) the experience of the GA2LEN UCARE network and (b) input from angioedema patients, general practitioners, and angioedema specialists.

What are the aims of GA2LEN/HAEi ACAREs? The aims of ACAREs are to set the global standard for excellence in comprehensive angioedema care through research, education, advocacy, and interaction among ACAREs. By serving as referral centers for the diagnosis and management of patients with angioedema, ACAREs will complement the local healthcare system. ACAREs aim to increase knowledge and awareness of angioedema.

What are the requirements for GA2LEN/HAEi ACAREs? ACAREs are required to demonstrate excellence in the management of angioedema, research activities, efforts in education, and advocacy activity. ACAREs need to fulfill 32 requirements, which are explained in the audit checklist (Figure 1A). This checklist includes specific deliverables for each requirement. For example, the requirement to know and follow international guidelines and consensus documents for angioedema (Requirement #16) entails that physicians and other ACARE healthcare professionals have read and understood the current versions of these guidelines and consensus documents and that their recommendations are implemented in their center.

These guidelines and consensus documents include, for example, the international WAO/EAACI guideline for HAE, the EAACI/GA2LEN/EDF/WAO guideline for urticaria, the International/Canadian hereditary angioedema guideline,2-5 the international consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency, the international consensus on the use of genetics in the management of HAE,6 and the international consensus and practical guidelines on the gynecologic and obstetric management of female patients with hereditary angioedema caused by C1 inhibitor deficiency.7 The deliverables for this requirement are that (a) current guideline and consensus document versions are present (paper or electronic version) at the center, (b) ACARE staff can answer questions on the recommendations these documents provide, and (c) ACARE physicians can show, upon request, by use of a patient file, that patient

(B) GALEN ACARE HAEi. Certificate text: 'The GALEN ACARE office hereby certifies that the Department and Center Name and for Name of Head of Center City Country has been externally audited and fulfills the GALEN HAEi quality criteria as a GALEN HAEi Angioedema Center of Reference and Excellence (GALEN HAEi ACARE). Date: 03/20/2019 Valid until: 03/20/2021' Includes logos for GALEN, ACARE, and HAEi.

management decisions are based on guideline recommendations (Figure 1B).

This publication marks our intent to start the implementation of the GA<sup>2</sup>LEN/HAEi ACARE initiative. Specialty centers for angioedema have started to apply to become ACAREs, and audits and certifications are ongoing (Figure 1B). We expect that most GA<sup>2</sup>LEN UCARE centers and many angioedema specialty centers will become ACAREs in the near future. We predict and hope that by 2022, GA<sup>2</sup>LEN/HAEi ACAREs will be established in every continent. This will result in a strong global network of angioedema specialists, promote angioedema research, and harmonize and improve angioedema management worldwide. GA<sup>2</sup>LEN and HAEi will measure the impact of ACAREs over time and document and report the benefits of this initiative. ACARE network activities and a current list of ACAREs are posted on the network's website ([www.acare-network.com](http://www.acare-network.com)).

#### ACKNOWLEDGMENTS

The GA<sup>2</sup>LEN/HAEi ACARE is supported by its twin network, the GA<sup>2</sup>LEN UCARE network ([www.ga2len-ucare.com](http://www.ga2len-ucare.com)). We thank Beate Schinzel for expert help with formatting and revising the manuscript as well as its submission.

#### CONFLICT OF INTEREST











Dr Maurer reports grants and personal fees from Allakos, personal fees from Aralaz, grants and personal fees from AstraZeneca, grants and personal fees from BioCryst, grants from Blueprint, grants and personal fees from CSL Behring, grants and personal fees from FAES, grants and personal fees from Genentech, grants from Kalvista, grants from Lilly, grants from Menarini, grants and personal fees from Novartis, grants from Leo Pharma, grants from Moxie, grants from Pharming, personal fees from Pharvaris, grants and personal fees from Roche, from Sanofi, grants and personal fees from Shire/Takeda, grants and personal fees from UCB, grants and personal fees from Uriach, outside the submitted work. Dr Aberer reports other from Takeda, other from CSL Behring, outside the submitted work. Dr Ansotegui reports personal fees from Mundipharma, personal fees from Roxall, personal fees from Sanofi, personal fees from MSD, personal fees from Faes Farma, personal fees from Hikma, personal fees from Astra Zeneca, personal fees from Stallergens, outside the submitted work. Dr Aygören-Pürsün reports personal fees from Adverum, grants and personal fees from BioCryst, grants and personal fees from CSL Behring, grants and personal fees from Kalvista, personal fees from Pharming, grants and personal fees from Shire/Takeda, during the conduct of the study. Dr Banerji reports grants from Takeda, BioCryst, personal fees from Takeda, BioCryst, CSL, Pharming, Pharvaris, Kalvista, outside the submitted work. Dr Aberer reports other from Takeda, other from CSL Behring, outside the submitted work. Dr Bernstein reports grants and personal fees from Shire/Takeda, grants and personal fees from CSL Behring, grants and personal fees from BioCryst, grants and personal fees from Kalvista, grants from IONIS, grants and personal fees from Novartis/Genentech, grants and personal fees from Astra Zeneca, grants and personal fees from Sanofi Regeneron, from HAEA MAB, during the














conduct of the study. Dr Betschel reports personal fees from CSL Behring, personal fees from Takeda/Shire, during the conduct of the study; personal fees from Octapharma, grants from Green Cross, personal fees from Novartis, personal fees from CADTH, outside the submitted work; and Chair of the Canadian Hereditary Angioedema Network. Dr Bork reports personal fees from CSL, personal fees from Shire, outside the submitted work. Dr Busse reports personal fees from CSL Behring, grants and personal fees from Shire, personal fees from Pharming, personal fees from Pearl Therapeutics, personal fees from BioCryst, personal fees from CVS Health, personal fees from Novartis, personal fees from Law offices of Levin, Riback, Adelman and Flangel, outside the submitted work. Dr Bygum reports grants and other from CSL Behring, grants and other from Shire/TAKEDA, other from ViroPharma, from HAE Scandinavia, outside the submitted work. Dr Caballero reports personal fees and other from BioCryst, personal fees, non-financial support and other from CSL-Behring, personal fees from Merck, personal fees and other from Novartis, personal fees from Octapharma, personal fees, non-financial support and other from Shire HGT, personal fees and other from Pharming NV, outside the submitted work. Dr Campos reports and Personal fees for consulting and lectures from Takeda. Dr Cancian served for Scientific Advisory Boards, and received travel grants, for/from CSL Behring and Shire-Takeda. His Institution (Department of Medicine, University of Padua, Italy) received grants from CSL Behring and Shire-Takeda. Dr Cohn reports personal fees from Takeda, personal fees from Pharming, personal fees from CSL, personal fees from BioCryst, outside the submitted work. Dr Craig reports grants, personal fees and other from CSL Behring, grants and personal fees from Dyax, grants, personal fees and other from Takeda, grants and personal fees from BioCryst, grants and personal fees from Pharming, personal fees from Grifols, grants and non-financial support from GSK, grants and non-financial support from Regeneron, grants and non-financial support from Novartis/Genentech, outside the submitted work; and On the Medical Advisory Board for HAE-A of America, AAAAI Board, ALA Mid Atlantic Board. Dr Dissemond reports grants and personal fees from Novartis, outside the submitted work. Dr Du-Thanh reports personal fees from SHIRE/T. Dr Ensina reports personal fees from NOVARTIS, personal fees and non-financial support from TAKEDA, personal fees from SANOFI, outside the submitted work. Dr Farkas reports grants and personal fees from CSL Behring, grants and personal fees from Shire/Takeda, grants and personal fees from Pharming, personal fees from BioCryst, personal fees from Kalvista, outside the submitted work. Dr Gimenez-Arnau reports grants and personal fees from URIACH, grants and personal fees from NOVARTIS, personal fees from DSANOFI, grants from CARLOS III FEDER, personal fees from FAES, personal fees from GSK, personal fees from ALMIRALL, personal fees from ASTRA ZENECA, outside the submitted work. Dr Fukunaga reports personal fees from A Takeda company (Shire), personal fees from CSL Behring, outside the submitted work. Dr Gompels reports other from Speaker at Novartis Urticaria conference 2019, outside the submitted work; and A member of the Immunology Clinical reference group. Dr Gower reports grants,

personal fees, research grants and other from Takeda/Shire/Dyax, research grants and other from BioCryst Pharmaceuticals, other from CSL Behring, other from Pharming, other from Fresenius kabi, outside the submitted work. Dr Grumach reports grants, personal fees and other from Shire/Takeda, personal fees and other from CSL Behring, outside the submitted work. Dr Hide reports grants and personal fees from Shire/Takeda, Mitsubishi-Tanabe, Taiho-yakuin, personal fees from CSL-Behring, BioCryst, Novartis, Teikoku-Seiyaku, Eizai, Kaken, Kyowahakkou-Kirin, grants from Glaxo-Smith-Klein, outside the submitted work. Dr Jakob reports grants, personal fees and non-financial support from Novartis, personal fees and non-financial support from Thermo Fisher Scientific, grants and personal fees from ALK-Abello, personal fees from Celgene, personal fees and non-financial support from Bencard/Allergy Therapeutics, personal fees from Allergopharma, outside the submitted work. Dr Kaplan reports other from Genentech, other from Novartis, other from Sanofi Aventis, other from BioCryst, outside the submitted work. Dr Katelaris reports grants and personal fees from CSL Behring, grants and personal fees from Takeda, grants from BioCryst, during the conduct of the study. Dr Kleinheinz reports personal fees from Novartis, during the conduct of the study; personal fees from Abbvie, personal fees from Leo GmbH, personal fees from Janssen, personal fees from Medac, personal fees from Galderma, personal fees from Celgene, personal fees from Bencard, outside the submitted work. Dr Kocatürk reports personal fees from Novartis, personal fees from Sanofi, outside the submitted work. Dr Longhurst reports grants and personal fees from BioCryst, grants, personal fees and non-financial support from CSL Behring, grants from Ionis, grants from Kalvista, personal fees from Pharming, grants, personal fees and non-financial support from Takeda, personal fees from GSK, personal fees from Octapharma, outside the submitted work. Dr MacGinnitie reports personal fees from BioCryst, personal fees from Shire, outside the submitted work. Dr Magerl reports personal fees from CSL Behring, personal fees from Shire/part of Takeda, personal fees from Novartis, personal fees from BioCryst, personal fees from KalVista, personal fees from Pharming, outside the submitted work. Dr Makris reports personal fees from Novartis, outside the submitted work. Dr Marsland reports grants and personal fees from Novartis, personal fees and non-financial support from Sanofi, personal fees from Galderma, personal fees from Roche, non-financial support from Almirall, outside the submitted work. I. Martinez Sagner has received honoraria, research funding, and travel grants from BioCryst, CSL Behring, Pharming, and Takeda/Shire, KalVista and/or served as a consultant and/or participated in advisory boards for these companies. Dr Metz reports personal fees from Moxie, personal fees from Novartis, personal fees from Roche, personal fees from Sanofi, personal fees from Shire, outside the submitted work. Dr Papadopoulos reports personal fees from Novartis, personal fees from Nutricia, personal fees from HAL, personal fees from MENARINI/FAES FARMA, personal fees from SANOFI, personal fees from MYLAN/MEDA, personal fees from BIOMAY, personal fees from AstraZeneca, personal fees from GSK, personal fees from MSD, personal fees from ASIT BIOTECH, personal fees from Boehringer Ingelheim, grants

from Gerolymatos International SA, grants from Capricare, outside the submitted work. Dr Reich reports personal fees from Abbvie, personal fees from Bioderma, personal fees from Chema Elektromet, personal fees from Galderma, personal fees from Bausch Health, personal fees from Janssen, personal fees from Leo Pharma, personal fees from Medac, grants and personal fees from Menlo Therapeutics, personal fees from Novartis, personal fees from Pierre-Fabre, personal fees from Trevi, personal fees from Kymab Limited, personal fees from MSD, personal fees from Metriopharm, personal fees from Drug Delivery Solutions, personal fees from Eli Lilly, outside the submitted work. Dr Riedl reports grants and personal fees from CSL Behring, grants and personal fees from Shire/Takeda, grants and personal fees from BioCryst, grants and personal fees from Pharming, personal fees from Pharvaris, personal fees from Adverum, personal fees from KalVista, personal fees from Attune, grants from Ionis, outside the submitted work; and US HAEA Medical Advisory Board Member - uncompensated. Dr Röckmann-Helmbach reports other from Pharming, during the conduct of the study. Dr Schmid-Grendelmeier reports personal fees from Takeda, during the conduct of the study. Dr Serpa reports speaker fees from Shire/Takeda, Novartis and Sanofi. Dr Sheikh reports other from Takeda, from CSL, outside the submitted work. Dr Smith reports personal fees from Takeda/Shire, personal fees from CSL/Behring, grants from Takeda/Shire, grants from BioCryst, outside the submitted work. Dr Soria reports personal fees from Novartis, personal fees from Sanofi Genzyme, personal fees from Abbvie, outside the submitted work. Dr Staubach reports personal fees and non-financial support from Takeda, personal fees and non-financial support from Shire, personal fees and non-financial support from Pharming, personal fees and non-financial support from CSL Behring, personal fees and non-financial support from Novartis, outside the submitted work. Dr Stobiecki reports personal fees from lectures given for CSL Behring, Takeda (Shire), personal fees from conducting clinical trials as a principal investigator for BioCryst, personal fees from consultant work for: BioCryst, CSL Behring, Takeda (Shire), Pharming, outside the submitted work. Dr Sussman reports grants and personal fees from Research grants from pharmaceutical companies. Novartis, Genentech, Amgen, Sanofi, CSL behring, Leo, Kedrion, Green Cross, DBV, Aimune. D'dConsulting and honoraria from Novartis, Novo, CSL Behring, Amgen., during the conduct of the study; grants from Novartis Pharmaceutical, grants from Genentech, grants from CSL behring, grants from Amgen, grants from Leo, grants from DBV, grants from Aimune, grants from Sanofi, non-financial support from Novartis, non-financial support from Novo, non-financial support from Pediapharm, non-financial support from Sanofi, grants from Kedrion, outside the submitted work. Dr Thomsen reports grants and personal fees from Novartis, grants and personal fees from Sanofi, grants and personal fees from UCB, grants and personal fees from Janssen, grants and personal fees from Abbvie, outside the submitted work. Dr Treudler reports personal fees from Shire-Takeda, personal fees from ALK-Abello, personal fees from Novartis, grants and personal fees from Sanofi-Genzyme, grants from Hautnetz Leipzig e.V., other from Fraunhofer Institut, outside the submitted

work. Dr van Doorn reports personal fees from Leopharma, grants and personal fees from Novartis, personal fees from Abbvie, personal fees from BMS, personal fees from Celgene, personal fees from Lilly, personal fees from MSD, personal fees from Pfizer, personal fees from Sanofi-Genzyme, personal fees from Janssen Cilag, outside the submitted work. Dr Weber-Chrysochoou reports personal fees from Takeda and CSL Behring, outside the submitted work. Dr Zuberbier reports personal fees from AstraZeneca, personal fees from AbbVie, personal fees from ALK, personal fees from Almirall, personal fees from Astellas, personal fees from Bayer Health Care, personal fees from Bencard, personal fees from Berlin Chemie, personal fees from FAES, personal fees from HAL, personal fees from Leti, personal fees from Meda, personal fees from Menarini, personal fees from Merck, personal fees from MSD, grants and personal fees from Novartis, personal fees from Pfizer, personal fees from Sanofi, personal fees from Stallergenes, personal fees from Takeda, personal fees from Teva, personal fees from UCB, grants from Henkel, personal fees from Kryolan, personal fees from L'Oréal, outside the submitted work; and Organizational affiliations: Üommittee member: WHO-Initiative "Allergic Rhinitis and Its Impact on Asthma" (ARIA) Member of the Board: German Society for Allergy and Clinical Immunology (DGAKI) Member: European Centre for Allergy Research Foundation (ECARF) Secretary General: Global Allergy and Asthma European Network (GA2LEN) Member: Committee on Allergy Diagnosis and Molecular Allergology, World Allergy Organization (WAO). Other authors declare that they have no conflicts of interest.

Marcus Maurer<sup>1</sup>   
 Werner Aberer<sup>2</sup>  
 Rosana Agondi<sup>3</sup>  
 Mona Al-Ahmad<sup>4</sup>   
 Maryam Ali Al-Nest<sup>5</sup>   
 Ignacio Ansotegui<sup>6</sup>  
 Rand Arnaout<sup>7</sup>  
 Luisa Karla Arruda<sup>8</sup>   
 Riccardo Asero<sup>9</sup>   
 Emel Aygören-Pürsün<sup>10</sup>  
 Aleena Banerji<sup>11</sup>  
 Andrea Bauer<sup>12</sup>  
 Moshe Ben-Shoshan<sup>13</sup>  
 Alejandro Berardi<sup>14</sup>  
 Jonathan A. Bernstein<sup>15</sup>   
 Stephen Betschel<sup>16</sup>  
 Carsten Bindslev-Jensen<sup>17</sup>  
 Mojca Bizjak<sup>18</sup>   
 Isabelle Boccon-Gibod<sup>19</sup>  
 Konrad Bork<sup>20</sup>   
 Laurence Bouillet<sup>19</sup>   
 Henrik Balle Boysen<sup>21</sup>  
 Nicholas Brodzski<sup>22</sup>  
 Sigurd Broesby-Olsen<sup>17</sup>   
 Paula Busse<sup>23</sup>

Thomas Buttgerit<sup>1</sup>  
 Anette Bygum<sup>24</sup>   
 Teresa Caballero<sup>25</sup>  
 Régis A. Campos<sup>26,27</sup>  
 Mauro Cancian<sup>28</sup>  
 Ivan Chérrez-Ojeda<sup>29,30</sup>   
 Danny M. Cohn<sup>31</sup>  
 Célia Costa<sup>32</sup>  
 Timothy Craig<sup>33</sup>  
 Paulo Ricardo Criado<sup>34,35,36</sup>  
 Roberta F. Criado<sup>37</sup>  
 Dorottya Csuka<sup>38</sup>  
 Joachim Dissemond<sup>39</sup>  
 Aurélie Du-Thanh<sup>40</sup>  
 Luis Felipe Ensina<sup>41</sup>  
 Ragıp Ertaş<sup>42</sup>  
 José E. Fabiani<sup>43</sup>  
 Claudio Fantini<sup>44</sup>  
 Henriette Farkas<sup>38</sup>   
 Silvia Mariel Ferrucci<sup>45</sup>  
 Ignasi Figueras-Nart<sup>46</sup>  
 Natalia L. Fili<sup>47</sup>   
 Daria Fomina<sup>48,49</sup>  
 Atsushi Fukunaga<sup>50</sup>   
 Asli Gelincik<sup>51</sup>   
 Ana Giménez-Arnau<sup>52</sup>   
 Kiran Godse<sup>53</sup>  
 Mark Gompels<sup>54</sup>  
 Margarida Gonçalves<sup>55</sup>  
 Maia Gotua<sup>56</sup>   
 Richard Gower<sup>57</sup>  
 Anete S. Grumach<sup>58</sup>  
 Guillermo Guidos-Fogelbach<sup>59</sup>  
 Michihiro Hide<sup>60</sup>  
 Natalia Ilina<sup>61</sup>  
 Naoko Inomata<sup>62</sup>  
 Thilo Jakob<sup>63</sup>  
 Dario O. Josviack<sup>64</sup>  
 Hye-Ryun Kang<sup>65</sup>   
 Allen Kaplan<sup>66</sup>   
 Alicja Kasperska-Zajac<sup>67</sup>   
 Constance Katelaris<sup>68</sup>  
 Aharon Kessel<sup>69</sup>  
 Andreas Kleinheinz<sup>70</sup>  
 Emek Kocatürk<sup>71</sup>  
 Mitja Košnik<sup>18</sup>   
 Dorota Krasowska<sup>72</sup>  
 Kanokvalai Kulthanan<sup>73</sup>  
 M. Sendhil Kumaran<sup>74</sup>  
 José Ignacio Larco Sousa<sup>75</sup>  
 Hilary J. Longhurst<sup>76,77,78</sup>  
 William Lumry<sup>79</sup>  
 Andrew MacGinnitie<sup>80</sup> 

- Markus Magerl<sup>1</sup>  
 Michael P. Makris<sup>81</sup>  
 Alejandro Malbrán<sup>82</sup>  
 Alexander Marsland<sup>83</sup>  
 Inmaculada Martinez-Saguer<sup>84</sup>  
 Iris V. Medina<sup>85</sup>  
 Raisa Meshkova<sup>86</sup>  
 Martin Metz<sup>1</sup>   
 Iman Nasr<sup>87</sup>   
 Jan Nicolay<sup>88</sup>  
 Chikako Nishigori<sup>89</sup>  
 Isao Ohsawa<sup>90</sup>  
 Kemal Özyurt<sup>91</sup>  
 Nikolaos G. Papadopoulos<sup>92</sup>   
 Claudio A. S. Parisi<sup>93</sup>  
 Jonathan Grant Peter<sup>94</sup>  
 Wolfgang Pfützner<sup>95</sup>   
 Todor Popov<sup>96</sup>  
 Nieves Prior<sup>97</sup>  
 German D. Ramon<sup>98</sup>  
 Adam Reich<sup>99</sup>  
 Avner Reshef<sup>100</sup>   
 Marc A. Riedl<sup>101</sup>   
 Bruce Ritchie<sup>102</sup>  
 Heike Röckmann-Helmbach<sup>103</sup>  
 Michael Rudenko<sup>104</sup>  
 Andaç Salman<sup>105</sup>   
 Mario Sanchez-Borges<sup>106</sup>   
 Peter Schmid-Grendelmeier<sup>107</sup>   
 Faradiba S. Serpa<sup>108</sup>  
 Esther Serra-Baldrich<sup>109</sup>  
 Farrukh R. Sheikh<sup>110</sup>  
 William Smith<sup>111</sup>  
 Angèle Soria<sup>112</sup>   
 Petra Staubach<sup>113</sup>  
 Urs C. Steiner<sup>114</sup>  
 Marcin Stobiecki<sup>115</sup>  
 Gordon Sussman<sup>116</sup>   
 Anna Tagka<sup>117</sup>   
 Simon Francis Thomsen<sup>118</sup>   
 Regina Treudler<sup>119</sup>  
 Solange Valle<sup>120</sup>  
 Martijn van Doorn<sup>121</sup>  
 Lilian Varga<sup>38</sup>   
 Daniel O. Vázquez<sup>122</sup>   
 Nicola Wagner<sup>123</sup>  
 Liangchun Wang<sup>124</sup>   
 Christina Weber-Chrysochoou<sup>107</sup>  
 Young-Min Ye<sup>125</sup>   
 Anna Zalewska-Janowska<sup>126</sup>  
 Andrea Zanichelli<sup>127</sup>  
 Zuotao Zhao<sup>128,129</sup>   
 Yuxiang Zhi<sup>130</sup> 
- Torsten Zuberbier<sup>131</sup>   
 Ricardo D. Zwiener<sup>132</sup>  
 Anthony Castaldo<sup>133</sup>
- <sup>1</sup>Department of Dermatology and Allergy, Dermatological Allergology, Allergie-Centrum-Charité, Charité—Universitätsmedizin Berlin, Berlin, Germany  
<sup>2</sup>Department of Dermatology, Medical University of Graz, Graz, Austria  
<sup>3</sup>University of São Paulo, São Paulo, Brazil  
<sup>4</sup>Microbiology Department, Faculty of Medicine, Kuwait University, Safat, Kuwait  
<sup>5</sup>Allergy and Immunology Section, Department of Medicine, Hamad General Hospital, Doha, Qatar  
<sup>6</sup>Department of Allergy and Immunology, Hospital Quiron Bizkaia, Bizkaia, Spain  
<sup>7</sup>King Faisal Specialist Hospital & Research Center, Al Faisal University, Riyadh, Saudi Arabia  
<sup>8</sup>Ribeirão Preto Medical School, University of São Paulo, São Paulo, Brazil  
<sup>9</sup>Ambulatorio di Allergologia, Clinica San Carlo, Paderno Dugnano (MI), Italy  
<sup>10</sup>Center for Children and Adolescents, University Hospital Frankfurt, Frankfurt, Germany  
<sup>11</sup>Division of Rheumatology, Allergy and Immunology, Massachusetts General Hospital, Boston, MA, USA  
<sup>12</sup>Department of Dermatology, University Allergy Center, University Hospital Carl Gustav Carus, Technical University, Dresden, Germany  
<sup>13</sup>Division of Allergy, Immunology and Dermatology, Department of Pediatrics, McGill University Health Center, Montreal, QC, Canada  
<sup>14</sup>Instituto de Asma, Alergia y Enfermedades Respiratorias, Corrientes, Argentina  
<sup>15</sup>Allergy Section, Division of Immunology, Department of Internal Medicine, Partner Bernstein Allergy Group, Partner Bernstein Clinical Research Center, University of Cincinnati, Cincinnati, OH, USA  
<sup>16</sup>Division of Clinical Immunology and Allergy, St. Michael's Hospital, University of Toronto, Toronto, ON, Canada  
<sup>17</sup>Department of Dermatology and Allergy Center, Odense University Hospital, Odense, Denmark  
<sup>18</sup>Division of Allergy, University Clinic of Respiratory and Allergic Diseases Golnik, Golnik, Slovenia  
<sup>19</sup>Clinical Immunology/Internal Medicine Department, National Reference Center for Angioedema, Grenoble University Hospital, Grenoble, France  
<sup>20</sup>Department of Dermatology, Johannes Gutenberg University Mainz, Mainz, Germany  
<sup>21</sup>HAE International (HAEi), Horsens, Denmark  
<sup>22</sup>Skåne University Hospital, Lund University, Lund, Sweden  
<sup>23</sup>Division of Clinical Immunology, Icahn School at Mount Sinai,



- New York, NY, USA
- <sup>24</sup>HAE Centre, Odense University Hospital, Odense, Denmark
- <sup>25</sup>Allergy Department, Hospital Universitario La Paz, IdiPaz, CIBERER U754, Madrid, Spain
- <sup>26</sup>Universidade Federal da Bahia, Salvador, Brazil
- <sup>27</sup>Serviço de Imunologia, Hospital das Clínicas Professor Edgard Santos, Salvador, Brazil
- <sup>28</sup>Department of Systems Medicine, University Hospital of Padua, Padua, Italy
- <sup>29</sup>School of Medicine, Universidad de Especialidades Espíritu Santo, Samborondón, Ecuador
- <sup>30</sup>RespiraLab, Research, Guayaquil, Ecuador
- <sup>31</sup>Department of Vascular Medicine, Amsterdam UMC, University of Amsterdam, Amsterdam, The Netherlands
- <sup>32</sup>Immunoallergology Department, Hospital de Santa Maria, Centro Hospitalar Universitário de Lisboa Norte (CHLN), EPE, Lisbon, Portugal
- <sup>33</sup>Department of Medicine and Pediatrics, Penn State University, Hershey, PA, USA
- <sup>34</sup>Faculdade de Medicina do ABC, Santo André, Brazil
- <sup>35</sup>Alergoskin Alergia e Dermatologia SS Ltda, Santo André, Brazil
- <sup>36</sup>UCARE Center, São Paulo, Brazil
- <sup>37</sup>Faculdade de Medicina do ABC (FMABC), Santo André, Brazil
- <sup>38</sup>3rd Department of Internal Medicine, Hungarian Angioedema Reference Center, Semmelweis University, Budapest, Hungary
- <sup>39</sup>Department of Dermatology, Venereology and Allergology, University of Essen, Essen, Germany
- <sup>40</sup>Service de Dermatologie-allergologie, CHU Montpellier, Montpellier Cedex 5, France
- <sup>41</sup>Division of Allergy, Clinical Immunology and Rheumatology, Department of Pediatrics, Federal University of São Paulo, São Paulo, Brazil
- <sup>42</sup>Department of Dermatology, Kayseri City Education and Research Hospital, Kayseri, Turkey
- <sup>43</sup>Private Practice, Lomas de Zamora, Argentina
- <sup>44</sup>Servicio de Alergia e Inmunología—Hospital Alende y Clínica Colón, Mar del Plata, Argentina
- <sup>45</sup>Ambulatorio di Dermatologia Allergologica e Professionale, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milano (MI), Italy
- <sup>46</sup>The Dermatology Department of the Hospital de Bellvitge, Universitat de Barcelona, Barcelona, Spain
- <sup>47</sup>Unidad Alergia e Inmunología Clínica, Hospital Público Materno Infantil, Salta, Argentina
- <sup>48</sup>Center of Allergy and Immunology, City Clinical Hospital No. 52, Moscow Ministry of Healthcare, Moscow, Russian Federation
- <sup>49</sup>Department of Allergology and Clinical Immunology, I.M. Sechenov First Moscow State Medical University, Moscow, Russian Federation
- <sup>50</sup>Division of Dermatology, Graduate School of Medicine, Kobe University, Kobe, Japan
- <sup>51</sup>Division of Immunology and Allergic Diseases, Department of Internal Medicine, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey
- <sup>52</sup>Department of Dermatology, Hospital del Mar, IMIM, Universitat Autònoma, Barcelona, Spain
- <sup>53</sup>Department of Dermatology, D Y. Patil University School of Medicine, Mumbai, India
- <sup>54</sup>Department of Immunology, North Bristol NHS Trust, Southmead Hospital, Bristol, UK
- <sup>55</sup>Clinica de Dermatologia, Centro Hospitalar Universitário Coimbra, Coimbra, Portugal
- <sup>56</sup>Center of Allergy and Immunology, Tbilisi, Georgia
- <sup>57</sup>Marycliff Clinical Research, Spokane, WA, USA
- <sup>58</sup>Clinical Immunology, Medical School, University Center Health ABC, Santo Andre, Brazil
- <sup>59</sup>National School of Medicine, Instituto Politécnico Nacional, Mexico City, Mexico
- <sup>60</sup>Department of Dermatology, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan
- <sup>61</sup>NRC Institute of Immunology FMBA, Moscow, Russia
- <sup>62</sup>Department of Environmental Immuno-Dermatology, Yokohama City University Graduate School of Medicine, Yokohama, Japan
- <sup>63</sup>Department of Dermatology and Allergy, University Medical Center Giessen (UKGM), Justus-Liebig-University Giessen, Giessen, Germany
- <sup>64</sup>Instituto de Medicina Respiratoria—Rafaela, Santa Fe, Argentina
- <sup>65</sup>Institute of Allergy and Clinical Immunology, Seoul National University Medical Research Center, Seoul, Korea
- <sup>66</sup>Medical University of South Carolina, Charleston, SC, USA
- <sup>67</sup>European Center for Diagnosis and Treatment of Urticaria, Zabrze, Poland
- <sup>68</sup>Immunology & Allergy Unit, Department of Medicine, Campbelltown Hospital, Campbelltown, NSW, Australia
- <sup>69</sup>Division of Allergy & Clinical Immunology, Rappaport Faculty of Medicine, Bnai Zion Medical Center, Technion, Haifa, Israel
- <sup>70</sup>Clinic for Dermatology, Elbe Kliniken Buxtehude, Buxtehude, Germany
- <sup>71</sup>Department of Dermatology, School of Medicine, Koç University, Koc, Turkey
- <sup>72</sup>Department of Dermatology, Venerology and Pediatric Dermatology, Medical University of Lublin, Lublin, Poland
- <sup>73</sup>Department of Dermatology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand
- <sup>74</sup>Department of Dermatology, Postgraduate Institute of Medical Education and Research, Chandigarh, India
- <sup>75</sup>Clinica San Felipe, Lima, Peru
- <sup>76</sup>Department of Immunology, Addenbrookes Hospital Cambridge University NHS Foundation Trust, Cambridge, UK
- <sup>77</sup>UCLH, London, UK
- <sup>78</sup>Addenbrooke's Hospital Cambridge and University College Hospital, London, UK
- <sup>79</sup>Allergy/Immunology Division, Department of Internal Medicine, University of Texas Southwestern Medical School,

Dallas, TX, USA

- <sup>80</sup>Division of Immunology, Department of Pediatrics, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA
- <sup>81</sup>Allergy Unit "D. Kalogeromitros", 2nd Department of Dermatology and Venereology, University Hospital "Attikon", National and Kapodistrian University of Athens, Athens, Greece
- <sup>82</sup>Unidad de Alergia, Asma e Inmunología Clínica, Buenos Aires, Argentina
- <sup>83</sup>Department of Dermatology, The Urticaria Clinic, Salford Royal Foundation Trust, University of Manchester, Manchester, UK
- <sup>84</sup>Hemophilia Centre Rhine Main (HZRM), Moerfelden-Walldorf, Germany
- <sup>85</sup>Allergy and Clinical Immunology Department, Centro Médico Vitae, de Julio, Argentina
- <sup>86</sup>Department of Clinical Immunology and Allergology, Smolensk State Medical University, Smolensk, Russian Federation
- <sup>87</sup>Adult Immunology and Allergy Unit, Department of Medicine, Royal Hospital, Muscat, Oman
- <sup>88</sup>Klinik für Dermatologie, Universitätsklinikum Mannheim, Mannheim, Germany
- <sup>89</sup>Division of Dermatology, Kobe University Graduate School of Medicine, Kobe, Japan
- <sup>90</sup>Department of Internal Medicine, Saiyu Soka Hospital, Soka, Japan
- <sup>91</sup>Department of Dermatology, Faculty of Medicine, Kırşehir Ahi Evran University, Kırşehir, Turkey
- <sup>92</sup>Allergy Unit, 2nd Pediatric Clinic, National and Kapodistrian University of Athens, Athens, Greece
- <sup>93</sup>Adults and Pediatrics Allergy Unit, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina
- <sup>94</sup>Department of Medicine, University of Cape Town, Cape Town, South Africa
- <sup>95</sup>Department of Dermatology and Allergology, Allergy Center Hessen, University Clinic Marburg, Marburg, Germany
- <sup>96</sup>University Hospital Sv. Ivan Rilski, Sofia, Bulgaria
- <sup>97</sup>Allergy Department, Hospital Universitario Severo Ochoa, Madrid, Spain
- <sup>98</sup>Instituto de Alergia e Inmunología del Sur, Buenos Aires, Argentina
- <sup>99</sup>Department of Dermatology, University of Rzeszow, Rzeszów, Poland
- <sup>100</sup>Angioedema Center, Barzilai Medical Center, Ashkelon, Israel
- <sup>101</sup>Department of Medicine, University of California—San Diego, La Jolla, CA, USA
- <sup>102</sup>Departments of Medicine and Medical Oncology, University of Alberta, Edmonton, AB, Canada
- <sup>103</sup>Department of Dermatology and Allergology, University Medical Center Utrecht, Utrecht, The Netherlands
- <sup>104</sup>London Allergy and Immunology Centre, London, UK
- <sup>105</sup>Dermatology Department, Marmara University School of Medicine, Pendik Research and Training Hospital, Istanbul, Turkey
- <sup>106</sup>Allergy and Clinical Immunology Department, Centro Medico Docente La Trinidad, Caracas, Venezuela
- <sup>107</sup>Allergy Unit, Department of Dermatology, University Hospital of Zürich, Zürich, Switzerland
- <sup>108</sup>Hospital Santa Casa de Misericórdia de Vitória, Espírito Santo, Brazil
- <sup>109</sup>Dermatology Department, Hospital Sant Pau, Barcelona, Spain
- <sup>110</sup>Department of Medicine, King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia
- <sup>111</sup>Clinical Immunology and Allergy, Royal Adelaide Hospital, Adelaide, SA, Australia
- <sup>112</sup>Service de Dermatologie et Allergologie, Hopital Tenon, APHP, Sorbonne Université, Paris, France
- <sup>113</sup>Department of Dermatology, University Medical Center, Mainz, Germany
- <sup>114</sup>Department of Clinical Immunology, University Hospital Zurich, Zurich, Switzerland
- <sup>115</sup>Department of Environmental Allergology, Jagiellonian University Medical College Kraków, HAE Center, University Hospital, Kraków, Poland
- <sup>116</sup>Division of Allergy and Immunology, University of Toronto, Toronto, ON, Canada
- <sup>117</sup>First Department of Dermatology and Venereology, National and Kapodistrian University of Athens, "A. Syggros" Hospital, Referral Center of Occupational Dermatological Diseases, Athens, Greece
- <sup>118</sup>Department of Dermatology, Bispebjerg Hospital, Copenhagen, Denmark
- <sup>119</sup>Department of Dermatology, Venereology and Allergology and Leipzig Interdisciplinary Center of Allergology—Comprehensive Allergy Center, UMC Leipzig, Leipzig, Germany
- <sup>120</sup>Federal University of Rio de Janeiro, Rio de Janeiro, Brazil
- <sup>121</sup>Department of Dermatology, Erasmus MC, Rotterdam, The Netherlands
- <sup>122</sup>Clínica Privada Monte Grande, Buenos Aires, Argentina
- <sup>123</sup>Department of Dermatology, University of Erlangen, Erlangen, Germany
- <sup>124</sup>Dermatology Department of Sun Yat-sen Memorial Hospital, Guangzhou, China
- <sup>125</sup>Department of Allergy and Clinical Immunology, Ajou University School of Medicine, Suwon, Korea
- <sup>126</sup>Chair of Clinical Immunology and Rheumatology, Department of Psychodermatology, Medical University of Lodz, Lodz, Poland
- <sup>127</sup>Department of Biomedical and Clinical Sciences, Luigi Sacco Hospital, University of Milan, Milan, Italy
- <sup>128</sup>Department of Dermatology and Venereology, First Hospital, Peking University, Beijing, China
- <sup>129</sup>Beijing Key Laboratory of Molecular Diagnosis on Dermatoses, Beijing, China
- <sup>130</sup>Department of Allergy, Peking Union Medical College



Hospital &, Chinese Academy of Medical Sciences, Beijing, China

<sup>131</sup>Department of Dermatology and Allergy, Allergie-Centrum-Charité, Charité—Universitätsmedizin Berlin, Berlin, Germany

<sup>132</sup>Servicio de Alergia e Inmunología, Hospital Universitario Austral, Buenos Aires, Argentina

<sup>133</sup>HAE International (HAEi), Fairfax City, VA, USA

#### Correspondence

Marcus Maurer, Department of Dermatology and Allergy, Allergie-Centrum-Charité, Dermatological Allergology, Charité—Universitätsmedizin Berlin, Charitéplatz 1, D-10117 Berlin, Germany.

Email: marcus.maurer@charite.de

[Correction Statement: Correction added on 20 May 2020 after first online publication: the author name has been corrected to Emel Aygören-Pürsün in this version.]

#### ORCID

Marcus Maurer  <https://orcid.org/0000-0002-4121-481X>  
 Mona Al-Ahmad  <https://orcid.org/0000-0003-3720-7032>  
 Maryam Ali Al-Nesf  <https://orcid.org/0000-0001-9354-0214>  
 Luisa Karla Arruda  <https://orcid.org/0000-0002-7505-210X>  
 Riccardo Asero  <https://orcid.org/0000-0002-8277-1700>  
 Jonathan A. Bernstein  <https://orcid.org/0000-0002-3476-1196>  
 Mojca Bizjak  <https://orcid.org/0000-0003-2595-468X>  
 Konrad Bork  <https://orcid.org/0000-0002-6084-4577>  
 Laurence Bouillet  <https://orcid.org/0000-0001-8245-4767>  
 Sigurd Broesby-Olsen  <https://orcid.org/0000-0002-1558-8471>  
 Anette Bygum  <https://orcid.org/0000-0002-3004-0180>  
 Ivan Cherez-Ojeda  <https://orcid.org/0000-0002-1610-239X>  
 Henriette Farkas  <https://orcid.org/0000-0003-2929-1721>  
 Natalia L. Fili  <https://orcid.org/0000-0003-0327-3963>  
 Atsushi Fukunaga  <https://orcid.org/0000-0003-2026-8154>  
 Asli Gelincik  <https://orcid.org/0000-0002-3524-9952>  
 Ana Giménez-Arnau  <https://orcid.org/0000-0001-9548-5423>  
 Maia Gotua  <https://orcid.org/0000-0003-2497-4128>  
 Hye-Ryun Kang  <https://orcid.org/0000-0002-2317-4201>  
 Allen Kaplan  <https://orcid.org/0000-0002-6566-4743>  
 Alicja Kasperska-Zajac  <https://orcid.org/0000-0002-2000-0070>  
 Mitja Košnik  <https://orcid.org/0000-0002-4701-7374>  
 Andrew MacGinnitie  <https://orcid.org/0000-0002-9451-3733>  
 Martin Metz  <https://orcid.org/0000-0002-4070-9976>  
 Iman Nasr  <https://orcid.org/0000-0003-0346-9675>  
 Nikolaos G. Papadopoulos  <https://orcid.org/0000-0002-4448-3468>

Wolfgang Pfützner  <https://orcid.org/0000-0002-8721-724X>  
 Avner Reshef  <https://orcid.org/0000-0002-3324-7072>  
 Marc A. Riedl  <https://orcid.org/0000-0003-3460-1544>  
 Andaç Salman  <https://orcid.org/0000-0002-6407-926X>  
 Mario Sanchez-Borges  <https://orcid.org/0000-0002-9308-6418>  
 Peter Schmid-Grendelmeier  <https://orcid.org/0000-0003-3215-3370>  
 Angèle Soria  <https://orcid.org/0000-0002-8726-6658>  
 Gordon Sussman  <https://orcid.org/0000-0002-2202-2513>  
 Anna Tagka  <https://orcid.org/0000-0003-3307-6522>  
 Simon Francis Thomsen  <https://orcid.org/0000-0002-4838-300X>  
 Lilian Varga  <https://orcid.org/0000-0002-5484-364X>  
 Daniel O. Vázquez  <https://orcid.org/0000-0001-9864-0783>  
 Liangchun Wang  <https://orcid.org/0000-0002-5169-2751>  
 Young-Min Ye  <https://orcid.org/0000-0002-7517-1715>  
 Zuotao Zhao  <https://orcid.org/0000-0002-9595-6050>  
 Yuxiang Zhi  <https://orcid.org/0000-0001-7539-6650>  
 Torsten Zuberbier  <https://orcid.org/0000-0002-1466-8875>

#### REFERENCES

- Perego F, Wu MA, Valeriva A, et al. Current and emerging biologics for the treatment of hereditary angioedema. *Expert Opin Biol Ther.* 2019;19(6):517-526.
- Betschel S, Badiou J, Binkley K, et al. The International/Canadian hereditary angioedema guideline. *Allergy Asthma Clin Immunol.* 2019;15:72.
- Farkas H, Martinez-Saguer I, Bork K, et al. International consensus on the diagnosis and management of pediatric patients with hereditary angioedema with C1 inhibitor deficiency. *Allergy.* 2017;72(2):300-313.
- Maurer M, Magerl M, Ansotegui I, et al. The international WAO/EAACI guideline for the management of hereditary angioedema—the 2017 revision and update. *World Allergy Organ J.* 2018;11(1):5.
- Zuberbier T, Aberer W, Asero R, et al. The EAACI/GA(2)LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria. *Allergy.* 2018;73(7):1393-1414.
- Germenis AE, Margaglione M, Pesquero JB, et al. International consensus on the use of genetics in the management of hereditary angioedema. *J Allergy Clin Immunol Pract.* 2020;8:901-911.
- Caballero T, Farkas H, Bouillet L, et al. International consensus and practical guidelines on the gynecologic and obstetric management of female patients with hereditary angioedema caused by C1 inhibitor deficiency. *J Allergy Clin Immunol.* 2012;129(2):308-320.

#### SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.