

## Consensus on the definition of disease control and response assessment in chronic urticaria

**Running title:** Control concept and response assessment in CU

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## Abstract

The concept of disease control and remission, and other key terms used in chronic urticaria (CU) such as flare-up, relapse, exacerbation or recurrence, are not fully clarified in the literature. Disease monitoring and treatment goals in clinical practice are not well established. After a qualitative appraisal of the evidence, we aim to find a consensus definition of CU control and remission, clarify key terminology, provide guidance on how to monitor the disease and establish treatment goals in clinical practice. To reach consensus, a modified Delphi consensus approach was used. Based on a literature review, a scientific committee provided 137 statements addressing controversial definitions and terms, available patient-reported outcomes (PROs), and recommendations on how to measure CU therapeutic objectives. The questionnaire was evaluated by 138 expert allergists and dermatologists. A consensus was reached on 105 out of the 137 proposed items (76.6%). The experts agreed that complete control and remission of CU could be defined as the absence of disease signs or symptoms while on treatment and in the absence of treatment, respectively. Consensus was not reached on the definition of other key terms such as flare up, exacerbation or recurrence. The panel agreed that the therapeutic objective of CU should be to achieve complete control. PROs that define the degree of CU control (complete, good, partial or absence of control) were established. An algorithm for disease assessment is provided. In conclusion, this work offers consensus definitions and tools that may be useful in the management of patients with CU.

**Key words:** Chronic Urticaria. Terminology as Topic. Patient Outcome Assessment. Recurrence. Consensus.

## Resumen

El concepto de control y remisión de la enfermedad, así como otros términos clave utilizados en la urticaria crónica (UC), como reagudización, recaída, exacerbación o recurrencia, no están totalmente aclarados en la literatura. Tampoco está bien establecido el seguimiento de la enfermedad y los objetivos del tratamiento en la práctica clínica. Tras una evaluación cualitativa de la evidencia, nos propusimos encontrar una definición consensuada de control y remisión de la UC, aclarar terminología clave, proporcionar orientación sobre cómo monitorizar la enfermedad y establecer objetivos de tratamiento en la práctica clínica. Para llegar a un consenso, se utilizó una técnica Delphi modificada. Basándose en una revisión de la literatura, un comité científico elaboró 137 aseveraciones que abordaban definiciones y términos controvertidos, el uso de *Patient Reported Outcomes* (PROs) y recomendaciones sobre cómo medir los objetivos terapéuticos en la UC. El cuestionario fue evaluado por 138 alergólogos y dermatólogos expertos. Se alcanzó un consenso en 105 de las 137 aseveraciones propuestas (76,6%). Los expertos estuvieron de acuerdo en que el control completo y la remisión de la CU podrían definirse como la ausencia de signos o síntomas de la enfermedad mientras se está en tratamiento y en ausencia de tratamiento, respectivamente. No se alcanzó un consenso sobre la definición de otros términos clave como reagudización, exacerbación o recurrencia. El panel estuvo de acuerdo en que el objetivo terapéutico de la CU debe ser lograr un control completo. Se establecieron los PRO que definen el grado de control de la CU (completo, bueno, parcial o ausencia de control). Además, se creó un algoritmo para la evaluación de la enfermedad. En conclusión, este trabajo ofrece definiciones y herramientas de consenso que pueden ser útiles en el manejo de los pacientes con CU.

**Palabras clave:** Urticaria crónica. Terminología como asunto evaluación del resultado de la atención al paciente. Recurrencia. Consenso.

## **Introduction**

Chronic urticaria (CU) is a common condition that markedly affects both patients' functioning and subjective well-being and has considerable patient and healthcare costs [1]. Point prevalence of CU, based on coding reports in health systems from different countries, ranges from 0.1 to around 1% globally [2]. CU affects mostly young and middle-aged women, usually lasts for several years (more than 1 year in 25-75% of patients) [3] and often more than 1 year is needed before effective management is implemented [3].

EAACI/GA2LEN/EuroGuiDerm/APAAACI guidelines cover the definition and classification of urticarial [1]. However, the concept of disease control and remission is not fully clarified by these and other guidelines [4–8] and different definitions can be found in the literature [1,9–11]. Other key terms such as flare-up, relapse, exacerbation or recurrence are commonly used in the literature and in clinical practice but there are no uniform criteria on what they exactly mean and to what extent they are interchangeable [12–15]. In addition, guidelines provide recommendations on the use of patient-reported outcomes (PROs) but no precise recommendations are given on the cut-off points that should guide treatment changes [1,4–8,16–18].

In this work, we aimed to find a consensus definition of CU control and remission and clarify key terminology related to disease relapse or recurrence. Additionally, we aimed to provide guidance on how to monitor the disease and how to optimize the use of PROs in the decision-making process during the clinical management of patients with CU.

## **Material and methods**

In this project, a qualitative appraisal of the scientific evidence and a consensus method (modified Delphi) were used [19]. A scientific committee, consisting of 10 experts with

recognized experience in the management of urticaria, was formed to lead the work. Details of the modified Delphi methodology used to reach consensus are shown in Table S1. In summary, after an exhaustive review of the literature and discussion, the scientific committee generated 137 debatable statements/items addressing the concept of control in CU and recommendations on how to monitor the disease activity and its impact. The questionnaire was assessed online by 138 expert allergists and dermatologists in two rounds.

### ***Literature search***

The literature search was focused on guidelines and reviews addressing CU management and monitoring. The search was carried out in the web sites of the main scientific societies of allergology and dermatology as well as in the main guideline repositories and in the PubMed database. In addition, a search was performed in PubMed with the following terms: "Chronic Urticaria"[Mesh] OR (Chronic Urticaria) AND (Control OR Remission OR Recovery of Function OR Disease Activity OR Urticaria Activity Score OR Urticaria Control Test). Guidelines and reviews of the last 5 years and clinical studies of the last 10 years in Spanish or English were assessed. We selected the articles that proposed definitions of CU control and remission or other terms such as relapse, recurrence, flare up or exacerbation. In addition, we selected guidelines addressing disease monitoring with emphasis in those that provided guidance on the use of PROs. The literature search was performed in July 2020. The details of the search are shown in Table S2. The evidence was qualitatively reviewed, summarized and presented to the scientific committee for the elaboration of the debatable items.

### **Results**

The questionnaire contained 137 items divided into 3 blocks addressing controversial definitions and terms related to CU (**Table S3**), available and recommended PROs in CU (**Table S4**) and recommendations on how to measure CU therapeutic objectives (**Table S5**). The questionnaire was submitted to a panel of 147 experts and 138 panellists responded to both rounds of

evaluation. After 2 rounds of evaluation, a consensus was reached on 105 out of the 137 proposed items (76,6%). Of them, 100 reached consensus on agreement and 5 on disagreement. Consensus was not reached on 32 items (**Table S3-S5**). Seven out of 8 items related to the best term to define reappearance of symptoms in an asymptomatic CU patient with or without treatment did not reach consensus (**Table S3**). Key terms used in chronic urticaria that need clarification and only one definition are summarised in **Table 1**.

**Figure 1** shows an algorithm for CU assessment that summarises the consensus on recommended PROs and tools to assess disease activity and control and quality of life (QoL) in clinical practice and when to use them. This algorithm includes consensus items from block II (**Table S4**). **Table 2** summarises definitions of CU control (complete, good, partial or absence of control), PROs that define this degree of control, time to confirm the degree of control in a patient with a biological or immunomodulatory therapy and some management recommendations. This table includes mostly consensus items from block III (**Table S5**) and some consensus items from block I related to the definition of disease control (**Table S3**).

## Discussion

In this article, we reviewed the concept of disease control and remission, and other key terms used in CU, and evaluated guidelines and reviews addressing monitoring and treatment goals in clinical practice. A panel of allergists/allergologists and dermatologists with extensive experience in the management of CU reached a consensus on the definition of CU control and remission. In addition, the experts reached a consensus on aspects related to the assessment and management of CU and provided insights on how to monitor and manage the disease according to the disease activity.

### ***Key terms used in CU that need clarification***

Regarding the terminology related to CU, despite the fact that the definition of CU is well established [1,16], it is surprising that there is no agreed definition in the literature of key concepts such as CU control and remission. The terms control and remission are sometimes considered interchangeable in the literature [9]. This lack of consensus on terminology also occurs in other fields of medicine such as rheumatic diseases [20].

In clinical trials, symptom control and symptom remission have been defined as Urticaria Activity Score 7 (UAS7)=0 while on treatment [9], but other definitions can be found, such as: “not being diagnosed with urticaria for at least 1 year during follow-up” [10], or “if a patient with CU never utilised medical services to treat urticaria for  $\geq 365$  days, even after using all the prescribed urticaria medicines” [11]. The definition of control is not homogeneous in the literature as well [21–24]. Our panel agreed that the definition of these two concepts is not clear in the literature and reached a consensus on their definitions. The panel considered that the concepts of CU control and remission are different: control refers to patients without CU signs or symptoms when on treatment, and remission when not on treatment. Accordingly, the panel agreed that complete control of CU could be defined as the absence of disease signs or symptoms while the patient is receiving treatment for it and remission can be defined as the total absence of disease signs or symptoms in the absence of treatment. In addition, there was an agreement on a definition of good, partial or absence of control mainly based on the intensity of disease symptoms or signs while on treatment, always taking into account the assessment of the clinical condition by both the treating physician and the patient (**Table 2**).

Recurrence and relapse are other terms with different interpretations in the literature. In clinical trials with omalizumab in chronic spontaneous urticaria (CSU), relapse has been defined as UAS7 greater than or equal to 16 after experiencing symptom control and withdrawal from initial therapy [14]. However, relapse has also been considered to be the reappearance of CSU

symptoms in complete responders and the increase in UAS7, compared to the value at the end of omalizumab treatment in partial responders [15]. In other studies, CU recurring at least 6 months after cessation of effective therapy and disappearance of prior CU symptoms is called recurrent CU instead of relapse [13]. In addition, in the Medical Subject Headings (MeSH) thesaurus (the National Library of Medicine's controlled vocabulary thesaurus used for indexing articles for the MEDLINE®/PubMed® database) the term recurrence is defined as the return of a sign, symptom, or disease after a remission and includes the terms recrudescence and relapse [25]. The panellists were requested to agree on the differences between relapse, recurrence and other related terminology such as flare-up or exacerbation. The questionnaire was provided in Spanish; therefore, the conclusions are not transposable into the English language. The panel did not reach an agreement on the best term to define the reappearance of symptoms in an asymptomatic CU patient while on treatment. The term with the highest degree of consensus (very close to agreement) is flare up ("*brote*" in Spanish) with much more degree of consensus than exacerbation ("*exacerbación*" in Spanish). In the MeSH thesaurus, symptom flare up is defined as a transient exacerbation of symptoms of an existing disease or condition [26] which is in line with our panel consensus. On the other hand, the panel agreed that the best term to define the reappearance of symptoms in an asymptomatic CU patient in the absence of treatment is relapse ("*recidiva*" in Spanish) rather than recurrence ("*recurrencia*" in Spanish). In conclusion, we propose to use the terms relapse and flare up (rather than exacerbation or recurrence) to describe the reappearance of symptoms in an asymptomatic CU patient in the absence of treatment or while on treatment, respectively. However, a consensus specifically designed in English would be necessary to make this recommendation applicable to the English-language literature.

### **CU monitoring**

Regarding the use of PROs, the panel agreed that there is a need to define which PROs are most indicated for use in daily clinical practice or whether there are specific situations where one instead of another can be used. Guidelines are not consistent in either what PROs should be performed in CU patients or when to perform them in the course of the disease [1,4,5,16,27,28]. In line with EAACI/GA2LEN/EuroGuiDerm/APAAACI guidelines [1], the panel agreed that in daily clinical practice it is advisable to use PROs to help us measure: CU activity, the degree of CU control and the QoL of patients with CU. Besides, EAACI/GA2LEN/EuroGuiDerm/APAAACI guidelines suggest the use of the UAS7 and the angioedema activity score (AAS) for assessing disease activity; the use of the urticaria control test (UCT), for assessing disease control; and the use of the chronic urticaria quality of life questionnaire (CU-Q2oL) and the angioedema quality of life questionnaire (AE-QoL), for assessing QoL impairment in patients with CSU [1]. The panel agreements are generally in line with these recommendations although they added some recommendations for chronic inducible urticaria (CINDU) assessment based in thresholds assessment with specific diagnostic tests (**Figure 1**). Considering the agreed items on the use of PROs, the scientific committee designed an algorithm that summarises the consensus on recommended PROs and tools to assess disease activity, disease control and QoL and when to use them (**Figure 1**). This algorithm can be a simple and useful tool in clinical practice when caring for a patient with CU.

In general, the panel agreed that it is advisable to measure CU disease activity and disease control by means of PROs on a routine basis. Conversely, there was no consensus on the need of QoL measuring routinely. This difference may be explained by the fact that tools to measure QoL are time consuming and hardly applicable in clinical practice where time is limited. In addition, CU activity is usually associated to QoL impairment [18,29], and the panel might have considered that QoL measuring is somewhat redundant and is better to prioritise the monitoring

of disease activity and control. On the other hand, EAACI/GA2LEN/EuroGuiDerm/APAAACI guidelines recommend that patients with CU should be assessed for disease activity, impact, and control at every visit [1]. Our panel recommended assessments at specific points in the course of the disease (**Figure 1**) and on a regular basis rather than at every visit. Again, a practical, down to earth point of view might explain the difference between panel opinion and guidelines.

### ***Therapeutic goals***

Considering CU therapeutic objectives, the panel reached a consensus on one key point that may guide the decision-making process when managing CU patients: the therapeutic objective of CU should be to achieve complete control of the disease. They also considered that if complete control is not achieved, after exhausting treatment alternatives, the therapeutic objective should be good control, trying to accomplish a minimum disease activity. Partial control is not an optimal therapeutic goal. Panellists agreed on the PROs thresholds recommended to define complete and good, or partial control of CU in clinical practice. This definition of CU control based on PROs may be more useful in clinical practice than the broad definition agreed previously in block I. The control definitions from these two perspectives are shown in **Table 2**. Additionally, this table shows the consensus on the timeframe needed to confirm the degree of control in a patient on treatment. The scientific committee considered that this timeframe applies only for a biological therapy. The scientific committee agreed that the required time to confirm the degree of control in a patient with standard-dose and up to fourfold standard-dose 2nd generation H1-antihistamine is shorter: 2-4 weeks respectively. This consideration is shown in **Table 2**. With regards to the absence of response, the panel considered that it should be defined as the absence of evident positive changes in the symptoms and QoL of the patient after starting treatment assessed by both the treating physician and the patient. The recommended time of absence of response to confirm that a patient with

treatment is a non-responder is 6 months. Again, the scientific committee considered that this time applies only to the biological therapy available for CU. The panel also agreed that there is not yet a specific percentage or threshold of any PROs that serves to definitively define the absence of a response, so there is a need to determine a specific percentage or threshold of some PROs to define the absence of response. Finally, the panel considered that the recommended time in the absence of CU signs and symptoms to confirm that a patient without treatment is in remission is 6 months.

In relation to QoL (regardless of the activity and / or level of disease control), the panel considered necessary to perform a QoL questionnaire (DLQI, CU-Q2oL...), actively investigate the sleep quality, mood state, the quality of personal interactions (family, friends, sexual and emotional life) and performance at work or school. These PROs and tools were added to **Figure 1** to make them easier to remember.

Finally, panellists agreed to perform a modification of the dosage regimen, or change the treatment, mainly in three situations: when the patient does not respond to treatment; when he/she presents a partial or a good response to treatment (but not a complete response), and more effective therapeutic alternatives are available; or when he/she has achieved a good or a complete response to treatment, but there is a treatment-related adverse event. The scientific committee summarised these consensus items as recommendations in **Table 1**.

There are several limitations of our work that must be noted, most of them related to the Delphi design. In this methodology is not possible to include the individual opinions of the panellists or discuss the statements in detail. In addition, the questionnaire is designed by a limited number of experts so some issues may be overlooked. The panel selection is another limitation of the Delphi methodology. However, the panellists were carefully selected, and we believe that their expertise is undoubted, and their opinion reflects the predominant opinion of other experts in this field. The possible influence of the scientific committee in the results is limited since they

did not take part in the voting process. Since the questionnaire was designed in Spanish, recommendations about terminology are not transposable to English language literature. Nevertheless, this local initiative may guide future international consensus focused on these inconsistencies in terminology.

### **Conclusions and recommendations**

In conclusion, in this work a consensus definition of CU control and remission is proposed and other key terminology issues are clarified. Additionally, it provides insights on how to monitor and manage CU according to the disease activity, emphasizing that the therapeutic objective of CU should be to achieve complete disease control. Gathering consensus items, the scientific committee developed an algorithm and a table that might be useful tools in clinical practice to optimize the decision-making process during the clinical management of patients with CU. Based on consensus items, the scientific committee propose the following main recommendations:

- Complete control of CU could be defined as the absence of disease signs or symptoms while the patient is receiving treatment for it and remission can be defined as the total absence of disease signs or symptoms in the absence of treatment.
- We propose to use the term relapse (rather than exacerbation) to describe the reappearance of symptoms in an asymptomatic CU patient in the absence of treatment.
- We propose to use the term flare up (rather than recurrence) to describe the reappearance of symptoms in an asymptomatic CU patient while on treatment.
- In daily clinical practice, it is advisable to use at least one PRO to help us measure CU activity, the degree of CU control and patients' QoL. An algorithm is proposed to help clinicians follow this recommendation.
- Complete CU control in clinical practice may be defined as:

- UAS7 = 0 (does not apply in CINDU and angioedema).
- UCT = 16.
- Absence of angioedema (ASS7 or ASS28 = 0) if there was a history of angioedema previously.
- Optimal quality of life (e.g., DLQI = 0-1).
- Good CU control in clinical practice may be defined as:
  - UAS7 1-6 (does not apply in CINDU and angioedema).
  - UCT ≥ 12.
  - Presence of angioedema (ASS7 or ASS28 > 0) that does NOT interfere with normal activity or does NOT have a high / significant impact on quality of life (if there was a history of angioedema previously).
  - Good quality of life (e.g., DLQI = 2-5).
- Partial CU control in clinical practice may be defined as:
  - Despite observing some clinical improvement, the patient continues with active disease by maintaining:
    - UAS7 > 6 (does not apply in CINDU and angioedema).
    - UCT < 12.
    - Presence of angioedema (ASS7 or ASS28 > 0) that interferes with normal activity or has a significant impact on quality of life (if there was a history of angioedema previously).
    - A significant impact on quality of life (e.g., DLQI > 5).
- Time to confirm the degree of complete, good or partial control in a patient with a biological therapy would be 3-6 months.
- The therapeutic objective of CU should be to achieve complete control of the disease. If complete control is not achieved, after exhausting treatment alternatives, the

therapeutic objective should be good control, trying to accomplish a minimum disease activity. Partial control is not an optimal therapeutic goal.

Further studies to determine whether these tools and recommendations are useful in clinical practice and how they may improve clinical practice are warranted.

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### **Conflict of interest**

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**Ignacio Jáuregui:** he has served as a consultant and/or received speaking fees at educational events from Novartis, Sanofi-Genzyme, AbbVie, and Leti Pharma; he has received congress fees from Menarini, and he has participated as principal investigator in observational trials sponsored by Novartis.

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**Joaquin Sastre:** reports having served as a consultant to Thermofisher, MEDA, Novartis, Sanofi, Leti, Faes Farma, Mundipharma, and GSK; having been paid lecture fees by Novartis, GSK, Stallergenes, Leti, and Faes Farma; as well as having received grant support for research from Thermofisher, Sanofi, and ALK.

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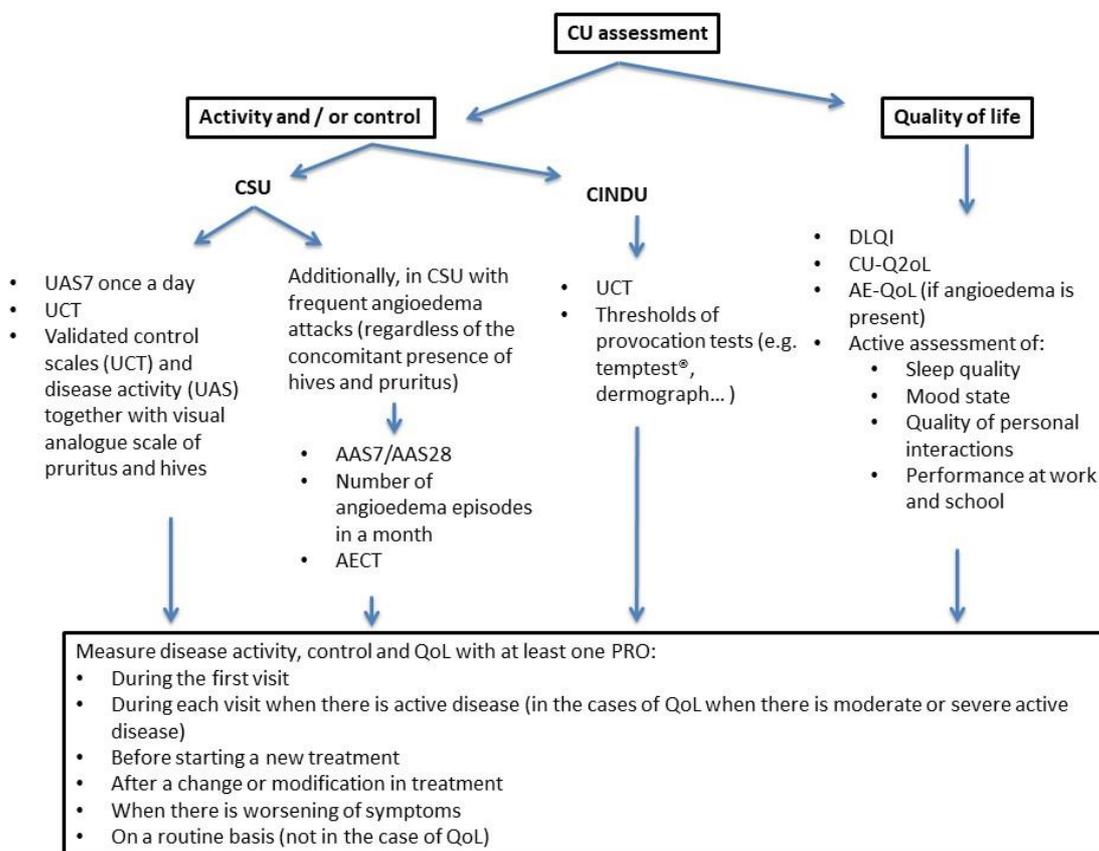
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Figure 1. Algorithm for chronic urticaria assessment.



AAS: Angioedema Activity Score; AECT: Angioedema Control Test; AE-QoL: Angioedema Quality of Life Questionnaire; CINDU: Chronic inducible urticaria; CSU: Chronic spontaneous urticaria; CU: Chronic urticaria; CU-Q2oL: Chronic Urticaria and Quality of Life Questionnaire; DQLI: Dermatology Quality of Life Index; PRO: Patient-reported outcome; QoL: Quality of life; UAS: Urticaria Activity Score; UCT: Urticaria Control Test.

**Table 1. Key terms used in chronic urticaria that need clarification and a single definition.**

The best term to define the total absence of signs or symptoms of the disease when on treatment
<ul style="list-style-type: none"><li>• Control*</li></ul>
The best term to define the total absence of signs or symptoms of the disease in the absence of treatment
<ul style="list-style-type: none"><li>• Remission*</li></ul>
The proposed term to define the reappearance of symptoms in an asymptomatic CU patient while on treatment (but has not reached a consensus).
<ul style="list-style-type: none"><li>• Flare up</li></ul>
<ul style="list-style-type: none"><li>• Break out</li></ul>
<ul style="list-style-type: none"><li>• Exacerbation</li></ul>
The best term to define the reappearance of symptoms in an asymptomatic CU patient in the absence of treatment:
<ul style="list-style-type: none"><li>• Relapse*<sup>¶</sup></li></ul>
<ul style="list-style-type: none"><li>• Recurrence</li></ul>
<ul style="list-style-type: none"><li>• Recidivate</li></ul>

*\*Terms that reached a consensus.*

*<sup>¶</sup>The panel reached a consensus on the term "relapse" as "recidiva" in Spanish.*

*CU: Chronic urticaria.*

**Table 2. Definitions of chronic urticaria control and management recommendations.**

	<b>Complete CU control</b>	<b>Good CU control</b>	<b>Partial CU control</b>	<b>Absence of CU control</b>
<b>Definition</b>	Absence of signs or symptoms of the disease while the patient is receiving treatment for it.	Decrease of the symptoms or signs with treatment at an appropriate level as judged by both the physician and the patient.	Decrease in the intensity of the symptoms or signs of the disease with treatment, but without reaching an adequate level according to the opinion of the doctor and the patient and without reaching a normal quality of life.	Absence of evident positive changes in the symptoms and quality of life of the patient after starting treatment (taking into account the evaluation of the clinical condition made by the treating physician and the assessment made by the patient).
<b>PROs that define the degree of CU control in clinical practice*</b>	<ul style="list-style-type: none"> <li>• UAS7 = 0 (does not apply in CINDU and angioedema).</li> <li>• UCT = 16.</li> <li>• Absence of angioedema (ASS7 or ASS28 = 0) if there was a history of angioedema previously.</li> <li>• Optimal quality of life (E.g., DLQI = 0-1).</li> </ul>	<ul style="list-style-type: none"> <li>• UAS7 1-6 (does not apply in CINDU and angioedema).</li> <li>• UCT ≥ 12.</li> <li>• Presence of angioedema (ASS7 or ASS28 &gt; 0) that does NOT interfere with normal activity or does NOT have a high / significant impact on quality of life (if there was a history of angioedema previously).</li> <li>• Good quality of life (e.g., DLQI = 2-5).</li> </ul>	<ul style="list-style-type: none"> <li>• Despite observing some clinical improvement, the patient continues with active disease by maintaining:               <ul style="list-style-type: none"> <li>○ UAS7 &gt; 6 (does not apply in CINDU and angioedema).</li> <li>○ UCT &lt; 12.</li> <li>○ Presence of angioedema (ASS7 or ASS28 &gt; 0) that interferes with normal activity or has a significant impact on quality of life (if there was a history of angioedema previously).</li> <li>○ A significant impact on quality of life (e.g., DLQI &gt; 5).</li> </ul> </li> </ul>	There is not yet a specific percentage or threshold of any PROs that serves to definitively define the absence of a response.

Time to confirm the degree of control in a patient with standard-dose 2nd generation H1-antihistamine**	2 weeks	2 weeks	2 weeks	2 weeks
Time to confirm the degree of control in a patient with up to fourfold standard-dose 2nd generation H1-antihistamine**	4 weeks	4 weeks	4 weeks	4 weeks
Time to confirm the degree of control in a patient with a biological therapy**	3-6 months	3-6 months	3-6 months	6 months
Recommendations	<ul style="list-style-type: none"> <li>• A modification of the dosage regimen or change of a treatment is recommended if there is a treatment-related adverse event.</li> <li>• If a decrease in the dosage regimen of a well-tolerated treatment in a patient with a complete response is desired, it is recommended to lower the dosage regimen when the patient presents a complete response for <math>\geq 3</math> -6 months.</li> <li>• If a well-tolerated treatment is to be withdrawn in a patient with a complete response, it is</li> </ul>	<ul style="list-style-type: none"> <li>• A modification of the dosage regimen or change of a treatment is recommended: <ul style="list-style-type: none"> <li>○ When the patient has achieved a good response to treatment (but not a complete response), and more effective therapeutic alternatives are available.</li> <li>○ Or there is a treatment-related adverse event.</li> </ul> </li> <li>• It is not recommended to withdraw the treatment or lower the treatment dosage in a patient who has a good response (but not a complete response) and the treatment is well tolerated.</li> </ul>	A modification of the dosage regimen or change of a treatment is recommended	A modification of the dosage regimen or change of a treatment is recommended

	recommended to withdraw it when the patient presents a complete response for $\geq 6$ months.			
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\*To assess the degree of control (complete control, good control, or partial control) it is recommended to use a validated questionnaire and complement it with an assessment by the treating physician, taking into account the patient's assessment of their clinical condition as well.

\*\* [Scientific committee recommendation do not specifically addressed in the questionnaire.](#)

AAS: Angioedema Activity Score; CINDU: Chronic inducible urticaria; CU: Chronic urticaria; DQLI: Dermatology Quality of Life Index; UAS: Urticaria Activity Score; UCT: Urticaria Control Test.