台灣皮膚科醫學會

蕁麻疹定義、分類、診斷暨治療共識

2021年更新版

臺灣皮膚科醫學會
Taiwanese Dermatological Association

Taiwanese Dermatological Association consensus for the definition, classification, diagnosis and management of **urticaria**

蕁麻疹定義、分類、診斷暨治療共識 2021 年更新版

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簡介

本手冊將詳細描述台灣皮膚科醫學會 (TDA) 2021 年版蕁麻疹定義、分類、診斷暨治療共識的制定過程。TDA 共識的內容絕大部分是以歐洲過敏及臨床免疫學會 (EAACI)、歐盟贊助 Network of Excellence、全球過敏與氣喘網、歐洲皮膚科論壇，以及世界過敏組織所共同制定之 2018 年蕁麻疹指引為基礎 [1]。TDA 共識與較早期指引的主要差別在於它包含多項修訂內容，特別有益台灣的臨床醫師用於蕁麻疹的治療，因此這份共識可作為全台臨床醫師與其他醫療人員的重要參考資料。

蕁麻疹不僅對於病患，也會對整個健康照護體系造成巨大的負擔。蕁麻疹患者有較高的可能性會產生工作或日常活動中斷、睡眠障礙，以及生活品質不佳的困擾。此外，蕁麻疹已構成全球醫療照護資源利用的負擔並導致支出增加 [2]。在台灣也出現了相同情形；之前的調查顯示多數的慢性蕁麻疹 (CU) 病患在工作、日常活動、整體外觀、睡眠和人際關係等各方面皆受到疾病影響 [3]，不僅如此，台大朱家瑜等人也指出 CU 病患罹患包含甲狀腺、發炎性、風濕性與精神疾病在內之其他病況的風險較高 [4,5]，這些發現都證實了蕁麻疹對健康的重要影響。簡而言之，來自前面所提及與其他的台灣研究資訊，以及專業醫師的個人經驗，並參考上一段所列國際指引的補充資料，將加入此版 TDA 共識。

方法

我們為制訂新版 TDA 共識，成立了由多位台灣蕁麻疹專家共同組成的委員會；透過台灣各教學醫院與 TDA 推薦，共有 17 位在蕁麻疹治療上經驗豐富的皮膚科醫師受邀出席在台北舉辦的 TDA 共識會議。共識內容以專家群同意的 2018 年版 EAACI/ 全球過敏與氣喘網 / 歐洲皮膚科論壇 / 世界過敏組織指引為基礎，亦將各項特別針對台灣執業人士所做出的修訂納入考量。委員會針對各項修訂分別討論其支持性科學實證的品質（含透明度與明確標準），也討論了建議用藥的風險與效益。更新版的 TDA 共識除了修改前一版內容外，還加上來自新版 2018 EAACI 指引與其它台灣研究的新資訊 [1,3-7]，共識內容資訊經由出席 2021 年 3 月 27 日、5 月 22 日和 8 月 15 日所舉辦之 TDA 蕁麻疹共識會議的本國專家討論同意，且內文所有特定面向皆需獲得至少 75% 與會專家之認可。

結果

蕁麻疹的定義

蕁麻疹的特徵為突然出現的風疹塊、血管性水腫，或兩者兼具。

風疹塊通常具有下列三項特色：(1) 初始表現為大小不同的腫塊，有時會被反射性紅斑環繞，沒有表皮變化；(2) 發癢，或偶爾出現麻刺感或灼熱感；以及 (3) 稍縱即逝，皮膚通常在 24 小時內會恢復正常外觀。

血管性水腫有下列特性：(1) 突發性、明顯的紅斑性腫脹，或呈現膚色的真皮層下部和皮下組織腫脹，很常影響到黏膜下層；和 (2) 某些情況下會出現疼痛而非發癢。血管性水腫的緩解速度比風疹塊慢，可能會維持長達 72 小時。

根據發生頻率、持續時間和成因分類

蕁麻疹病例可依據其維持時間長短區分成急性或慢性，急性蕁麻疹定義為持續時間 ≤ 6 週的自發性風疹塊、血管性水腫或兩者均有，而慢性蕁麻疹 (Chronic urticaria, CU) 則定義為持續時間 > 6 週、突然發生的風疹塊和 / 或血管性水腫（經 93% 共識會議與會者認可）。**圖 1** 呈現急性和慢性之臨床分類流程與各種 CU 次分型，簡而言之，慢性蕁麻疹可因其外在誘發性因素之有無，再進一步分為慢性自發性蕁麻疹 (chronic spontaneous urticaria, CSU) 和慢性誘發性蕁麻疹 (chronic inducible urticaria, CIndU)。而慢性誘發性蕁麻疹可再因其外在誘發因素之不同再細分為各種不同的次分型，如水因性蕁麻疹、膽鹼性蕁麻疹、接觸性蕁麻疹等。

以蕁麻疹活性量表 (UAS) 和蕁麻疹控制檢測 (UCT) 評估疾病活性

蕁麻疹活性量表 (UAS) 系統是各個指引提議用於臨床照護和醫藥試驗中的一種簡單的評分系統，由於它曾在 Młynek 等人的研究中接受驗證，因此是建議用以評估自發性蕁麻疹疾病活性的方法 [8]，更精確地說，蕁麻疹活性 7 日量表（UAS7，補充**圖 1**）是

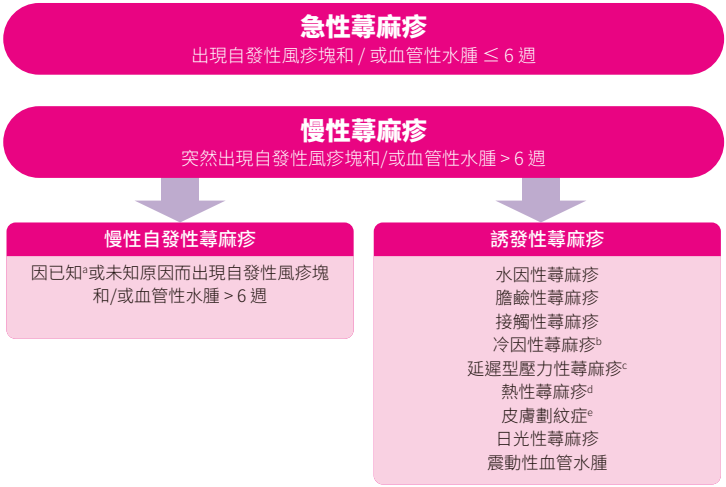

圖 1 慢性蕁麻疹次分型分類(出現風疹塊、血管性水腫,或兩者皆有)。本圖獲得 100% 共識會議與會者認可。[a] 例如自體反應性,即出現肥大細胞活化性自體抗體。[b] 別名「冷接觸性蕁麻疹」。[c]別名「壓力性蕁麻疹」。[d]別名「熱接觸性蕁麻疹」。[e]別名「人為蕁麻疹」和「皮膚劃紋性蕁麻疹」。

註:修改自 "Taiwanese Dermatological Association consensus for the definition, classification, diagnosis, and management of urticaria" by Chung WH, Chu CY, Huang YH, Wang WM, Yang CH and Tsai TF, 2016, J Formos Med Assoc. 2016 Nov;115(11):968-980.。Formosan Medical Association 2015 年版權所有。經許可改編。

EAACI 用於進行這類評估的標準方法。UAS 具備兩項不同優勢:(1) 因為被廣泛採用,使用 UAS 能直接比較全世界不同研究者的試驗和結果;與 (2) UAS 是以病患自行評估風疹塊和搔癢等關鍵症狀為根據,因為蕁麻疹的症狀強度變化頻繁,使這樣的自我評估更為可貴,像是每天由病患進行一次、每次持續數天的 24 小時自我評估量表,就能勾勒出最好的整體疾病活性全貌。

近來蕁麻疹控制檢測 (Urticaria control test, UCT) **(圖 2)** 已成為具有價值的病患疾病狀態評估方法,且已通過驗證,可判定所有型態 CU 的疾病控制程度 [9-11]。UCT 只有四個項目,且明確定義了疾病「控制良好」相對於「控制不佳」病患的切分點,故很適合用於常規臨床實務上的病患治療;疾病控制良好的分數切點為在 16 分中得到 12 分以上,有助於治療決策 [9]。

蕁麻疹的診斷

蕁麻疹主要是根據疾病症狀和徵象進行診斷。急性與慢性蕁麻疹之間的差異是風疹塊和 / 或血管性水腫的持續時間,疾病維持時間超過六週者定義為慢性蕁麻疹 **(圖 1)**。近年來,我們在辨識蕁麻疹的成因與不同類型 / 次分型方面有顯著的進步,舉例來說,Zuberbier 和 Maurer 提出了一些關於慢性自發性蕁麻疹 (CSU) 進展的大規模回顧 [12]。然而,針對這些問題所進行的多項研究得出之各種背後成因,其發生頻率變異度相當

UCT（蕁麻疹控制檢測）

1. 在過去四週內，蕁麻疹的**身體症狀**（**發癢、風疹塊**［**傷痕**］**和/或腫脹**）對您造成多大的困擾？

☐ 非常大 (0 分) ☐ 大 (1 分) ☐有些 (2 分) ☐ 很小 (3 分) ☐ 完全沒有 (4 分)

2. 在過去四週內，蕁麻疹對您的**生活品質**造成多大的影響？

☐ 非常大 (0 分) ☐ 大 (1 分) ☐有些 (2 分) ☐ 很小 (3 分) ☐ 完全沒有 (4 分)

3. 在過去四週內，您的蕁麻疹**治療不足以控制**蕁麻疹症狀的頻率為？

☐ 非常頻繁 (0 分) ☐ 頻繁 (1 分) ☐有時 (2 分) ☐ 很少 (3 分) ☐ 完全沒有 (4 分)

4. 整體而言，在過去四週內，您的蕁麻疹控制情況如何？

☐ 完全沒有控制 (0 分) ☐ 很差 (1 分) ☐尚可 (2 分) ☐ 不錯 (3 分) ☐ 非常好 (4 分)

*UCT分數介於 0 到 16 分
**<12：蕁麻疹控制不佳
***≥12：蕁麻疹控制良好

圖 2 用於評估各種形式之 CU 疾病狀態與判定疾病控制程度的UCT。本圖獲得100%共識會議與會者認可。UCT只有四個項目，且明確定義了疾病「控制良好」相對於「控制不佳」病患的切分點，很適合用於常規臨床實務上的病患治療。疾病控制良好的分數切點為在 16 分中得到 12 分。

大，這個結果可能至少在某種程度上是導因於全球各地區之間的差異，例如各個地區有不一樣的傳統食物及相異的各類感染盛行率。所以臨床醫師應牢記的重點在於「沒必要幫所有病人辨識和調查出所有可能的致病因子」。

病史 (圖 3)

在無需專注於辨識出所有可能致病因子的情況下，做出精確診斷的第一步驟就是徹底詢問病史，尤其針對疾病維持時間超過 6 週的病患。應詢問病患下列事項：

疾病特色

下列特色表現清單獲得 100% 共識會議與會者認可：(1) 發病時間；(2) 頻率 / 持續時間；(3) 日夜變化；(4) 發生時機與週末、節假日、季節、出國旅行的相關性；(5) 風疹塊的形狀、大小與分布；(6) 是否連帶血管性水腫；以及 (7) 連帶病灶的主觀症狀，例如發癢和疼痛。

病史

下列相關病史清單獲得 100% 共識會議與會者認可：(1) 家族和個人的蕁麻疹與異位性體質 (atopy) 病史；(2) 之前或目前的過敏、感染、內科疾病或其他可能成因；(3) 身心和精神疾病；(4) 與月經週期間的關聯性；(5) 吸菸習慣（尤其是使用芳香菸產品）；

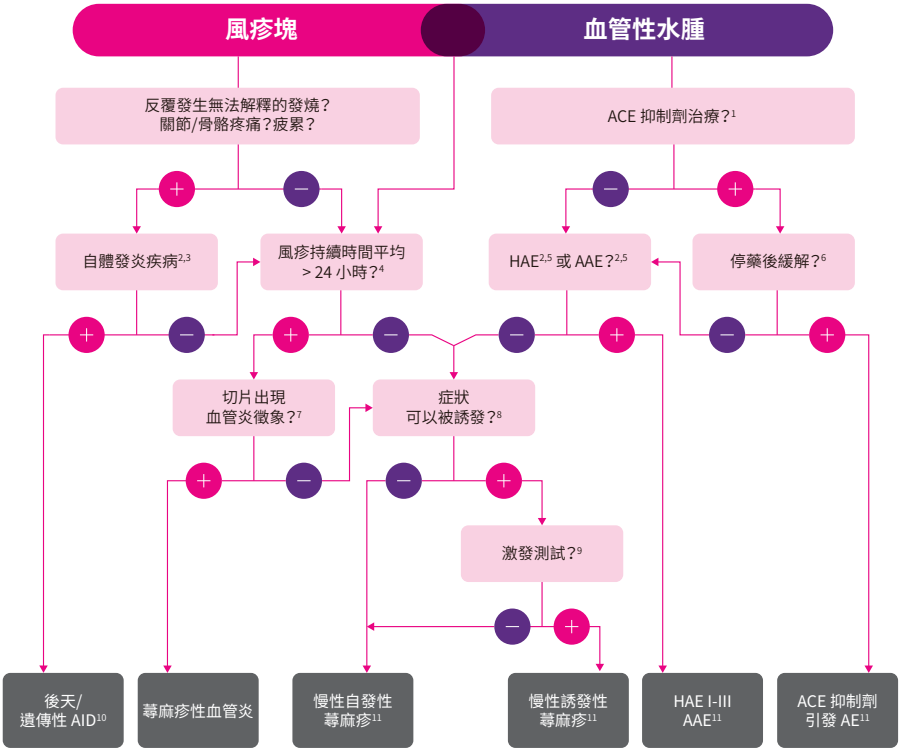

圖 3 針對出現風疹塊、血管性水腫或兩者皆有的病患之建議診斷流程。本圖獲得 100% 共識會議與會者認可。[a] 自體發炎疾病導因於不受控的先天免疫系統活化，包含 Schnitzler 症候群、全身性兒童特發性關節炎、cryopyrin 相關週期性症候群等。[1] 其他（新）藥物也可引發緩激肽 (bradykinin) 調控之血管性水腫。[2] 應詢問病患的詳盡家族史與發病年齡。[3] 檢測是否出現發炎標記（C-反應蛋白、紅血球沉降速率）上升情形，為成人檢測是否有副蛋白血症 (paraproteinemia)，觀察皮膚切片有無大量嗜中性球浸潤 (neutrophil-rich infiltrates)；當強烈懷疑時，進行遺傳性週期熱症候群（如 cryopyrin 相關週期性症候群）基因突變分析。[4] 應詢問病患：「您的風疹塊持續多久？」[5] 檢測補體 C4、C1-INH 值與功能；另外，若懷疑是 AAE，則檢測 C1q 和 C1-INH 抗體；若前述檢測結果無特殊發現但患者病史很像遺傳性血管性水腫，則進行基因突變分析。[6] 最長等待 6 個月，觀察是否緩解；應僅在家族史暗示診斷為遺傳性血管性水腫時，進行額外的 C1 抑制缺乏診斷性檢測。[7] 病灶皮膚切片是否顯現乳突和網狀真皮層小血管損傷和/或血管旁與間質部位類纖維蛋白沉積，暗示為 UV（蕁麻疹性血管炎）？[8] 應詢問病患：「您可以自行誘發出風疹塊嗎？」[9] 對於病史暗示診斷為誘發性蕁麻疹的病患，應根據國際共識建議，進行標準化激發測試。[10] 後天 AID 包括 Schnitzler 症候群、全身性兒童特發性關節炎與成人 Still 氏症；遺傳性 AID 包括 cryopyrin 相關週期性症候群，如家族性冷因性自體發炎症候群、Muckle-Well氏症候群和新生兒多系統發炎症候群，更罕見的 IgD 過高症候群與腫瘤壞死因子受體-α 相關週期性症候群。[11] 在某些罕見情況下，反覆性血管性水腫並非由肥大細胞調控因子或緩激肽調控，其背後病理機轉仍屬未知。某些作者將這種罕見病例稱為「特發性血管性水腫」。AAE = 因 C1 抑制缺乏而導致之後天血管性水腫；ACE-INH = 血管收縮素轉換酶抑制劑；AE = 血管性水腫；AH = 抗組織胺；AID = 自體發炎疾病；HAE = 遺傳性血管性水腫；IL-1 = 介白素 (interleukin)-1。註：取自 “The EAACI/GA²LEN/EDF/WAO guideline for the definition, classification, diagnosis and management of urticaria” by Zuberbier T, Aberer W, Asero R, Abdul Latiff AH, Baker D, Ballmer-Weber B, et al, 2018, Allergy, 73, p. 1393-1414. EAACI and John Wiley and Sons A/S 2018 年版權所有。經許可改編。

(6) 工作類型；(7) 嗜好；(8) 壓力（良性壓力和困擾）；(9) 之前的療法和治療反應；(10) 之前的診斷程序 / 結果；以及 (11) 無汗症或少汗症病史。

誘發風疹塊或血管性水腫的可能因子

目前已發現許多 CSU 病理生理學相關因子，包括自體免疫、對非類固醇消炎止痛藥 (NSAID) 與食物的假性過敏 (pseudoallergic) 反應，以及感染（病毒、寄生蟲和細菌）。在各項因子中，急性或慢性腸胃道感染（例如胃幽門螺旋桿菌 [Helicobacter pylori] 或海獸胃線蟲 [Anisakis simplex]）曾被指為 CU 的成因 [13]。下列致病因子清單獲得 100% 共識會議與會者認可：(1) 胃腸問題；(2) 被物理因素或運動所引發；(3) 使用藥物（例如 NSAID、血管收縮素轉換酶 [ACE] 抑制劑、注射劑、預防接種、荷爾蒙、瀉劑、栓劑、耳和眼部滴劑，與替代療法 [如中藥]）、毒品和局部麻醉；(4) 觀察到與食物和酒精飲料相關；以及 (5) 手術植入物和手術中事件。

生活品質

下列生活品質項目獲得 100% 共識會議與會者認可：採用如慢性蕁麻疹生活品質問卷 (CU-Q2oL) 等評估工具，評估與蕁麻疹和情緒影響相關的生活品質。

診斷的第二步驟是對病患進行理學檢查。依病史判定，必要時可執行診斷性激發測試 (provocation test)，涵蓋藥物、食物和物理測試；儘管如此，在多數情況下並不建議為了找出蕁麻疹的成因而進行深度且昂貴的整體篩檢。**圖 3** 呈現建議之蕁麻疹診斷流程，而**表 1** 則明確列出常見蕁麻疹次分型的建議診斷性檢測。簡言之，對於 CSU 病患的建議診斷性檢測包含血球分類計數、D-dimer 和 ESR 或 CRP。僅建議在根據病史而懷疑某些因子存在時，才進行延伸診斷性檢測，舉例來說，CSU 病患的功能性自體抗體可包括抗甲狀腺自體抗體、抗核抗體 (ANA)、抗 FcεRI 或抗 IgE 抗體等。

慢性蕁麻疹的臨床治療

治療目標

如同上述，EAACI 指引建議採用病患的 UAS7 分數，作為評估 CU 疾病活性的簡單有效指標，另外，更新版的 EAACI 指引同樣指出治療目標應該是症狀完全緩解 [1]；在 TDA 共識會議中，EAACI 指引所陳述的這項治療目標正是討論主題的一部分。特別值得注意的是只有約 40% 的病患能達到代表症狀全部緩解的 UAS7 0 分，反之，將近 80% 的病人可達到 UAS7 ≤ 5 分，在多數情況下這一樣是代表非常顯著的進步。據此，TDA 共識會議與會者提出究竟應把治療目標訂為「全部症狀完全緩解」還是「UAS7 ≤ 5 分即可視為足夠」，經過一番討論後，最終決定應將治療目標訂為 UAS7 ≤ 5 分，且 UAS7 分數或對藥物之反應可用於判定治療是否有效 (經 100% 共識會議與會者同意)。同樣值得注意的是，不同病患、不同疾病及不同指引可以有不一樣的治療目標（例如病患可能覺得症狀只要緩解到可忍受，換言之生活品質有所改善的程度，就可以接受）。

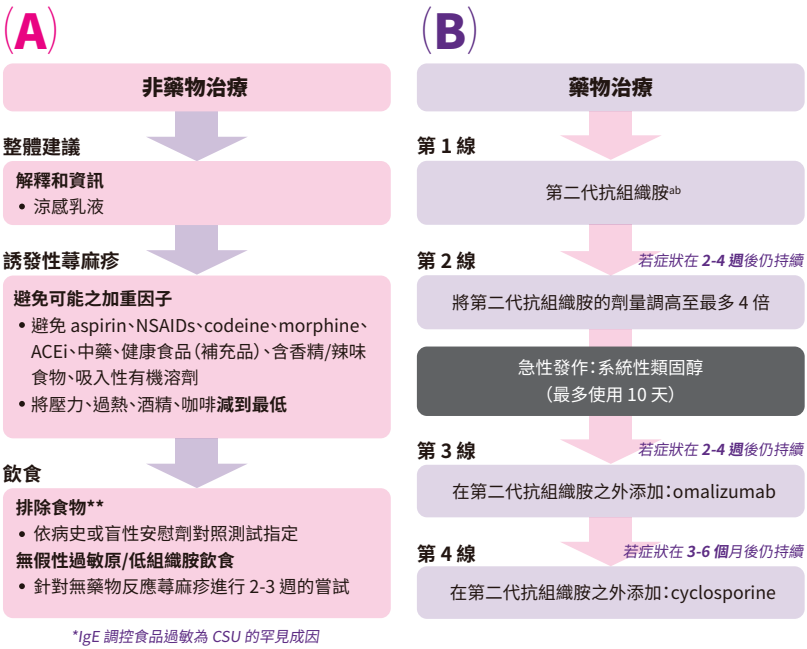

圖 4 建議治療流程包含慢性自發性蕁麻疹的 (A) 非藥物治療 (B) 藥物治療。經過討論後，本圖中各項目之修訂獲得 100%共識會議與會者認可。第一線 = 高品質實證：費用低且在全球皆可取得，由於半衰期更長、安全性表現極佳、療效良好，可每天用藥。第二線 = 高品質實證：費用低、安全性表現佳、療效良好。第三線和第四線為添加與第二代抗組織胺合併使用。Omalizumab = 高品質實證：費用高、安全性表現極佳、療效極佳。Cyclosporine = 高品質實證：費用中高、安全性表現中等、療效良好。[a] H1 抗組織胺和 omalizumab 為經核准之 CSU 治療 (FDA/EMA/TFDA)。[b] 參閱表 S1 核准使用年齡。ACEi = 血管收縮素轉換酶抑制劑；CSU = 慢性自發性蕁麻疹；FDA = 美國食品藥物管理局；EMA = 歐洲藥物管理局；TFDA = 台灣食品藥物管理署；NSAID = 非類固醇消炎止痛藥。

註：修改自 “Taiwanese Dermatological Association consensus for the definition, classification, diagnosis, and management of urticaria” by Chung WH, Chu CY, Huang YH, Wang WM, Yang CH and Tsai TF, 2016, J Formos Med Assoc. 2016 Nov;115(11):968-980. Formosan Medical Association 2015 年版權所有。經許可改編。

承上，**圖 4** 呈現 CSU 的建議治療流程，包括非藥物與藥物治療途徑。對於 CSU 的治療，應持續使用第二代抗組織胺 (sgAH)，而非視需求斷續使用，以減少疾病爆發情形，改善生活品質 [14,15]。與之相對，慢性誘發性蕁麻疹病患則可能獲益於視需求使用之斷續療法，尤其當誘發因子屬於計畫性或可預期時。目前已證實提高使用多種第二代抗組織胺藥物劑量的效益，包括 bilastine、cetirizine、desloratadine、ebastine、fexofenadine、levocetirizine 和 rupatadine[16-21](經 86% 共識會議與會者同意)。圖中同樣提供了關於可能會加重蕁麻疹的飲食、生理或情緒壓力以及環境因子的資訊，故應盡量避免這些因子或將其控制到最小 (經 100% 共識會議與會者同意)。值得提及的是台灣食品藥物管理署 (TFDA) 在 2014 年 12 月已核准以 omalizumab 治療對抗組織胺反應不理想之 CSU 病患。由於每個人的臨床反應與經濟考量均有差距，應以符合病患需求的方式量身打造個人化給藥間隔以及在延伸期間的持續治療。**附錄表 1** 提供可考慮用於特定 CU 病例之替代性藥物清單，包含來自 EAACI 蕁麻疹指引中各別藥物的研究實證強度及對應之 EAACI 建議

表 1 常見蕁麻疹次分型之建議診斷性檢測 [a]

類型	類型	常規診斷性檢測（建議）	為辨識誘發引子與排除可能鑑別診斷，適用時採取之延伸診斷計畫[b]（僅根據病史建議）
自發性蕁麻疹	急性自發性蕁麻疹 慢性自發性蕁麻疹	無 血球分類計數與 ESR 或 CRP 停用疑似成因藥物(例如 NSAID) D-dimer	無[c] (1)甲狀腺荷爾蒙與自體抗體 (2)自體血清皮膚檢測或嗜中性球活化測試 (3)第 I 型過敏 (IgE, MAST, CAP) (4)功能性自體抗體（ANA 等） (5)傳染病（如幽門螺旋桿菌） (6)病灶皮膚切片 (7)皮膚檢測，包括理學檢查 (8)類胰蛋白酶 (tryptase) [d] (9)持續 3 週無假性過敏原飲食
誘發性蕁麻疹	冷因性蕁麻疹	寒冷激發與閾值測試 (冰塊、冷水、冷風)	以血球分類計數與 ESR/CRP、冷沉澱蛋白 (cryoprotein) 排除其他疾病，尤其是感染
	延遲型壓力性蕁麻疹	壓力測試	無
	熱性蕁麻疹	熱激發與閾值測試	無
	日光性蕁麻疹	寒冷激發與閾值測試 UV、不同波常可見光與閾值測試	排除其他照光引發的皮膚病變
	皮膚劃紋症	誘發皮膚劃紋與閾值測試 (皮膚劃紋計)	血球分類計數、ESR/CRP
	震動性血管水腫	渦流測試	無
	水因性蕁麻疹	穿著與體溫相同溫度的溼衣服 20 分鐘	無
	膽鹼性蕁麻疹	運動與熱水浴激發	無
	接觸性蕁麻疹	皮膚激發測試 立即判讀之皮膚測試，例如點刺測試 (prick test)、新鮮過敏原點刺測試(prick-by-prick test)、貼布測試	無

表 1 常見蕁麻疹次分型之建議診斷性檢測。
ANA = 抗核抗體；CAP = Phadia Immunocap (Phadia CAP) 過敏原特異性 IgE 檢測；CRP = C-反應蛋白；ESR = 紅血球沉降速率；IgE = 免疫球蛋白 E；MAST = 多重特異性過敏原同步測試；NSAID = 非類固醇消炎止痛藥。
註：修改自 “Taiwanese Dermatological Association consensus for the definition, classification, diagnosis, and management of urticaria” by Chung WH, Chu CY, Huang YH, Wang WM, Yang CH and Tsai TF, 2016, J Formos Med Assoc. 2016 Nov;115(11):968-980. Formosan Medical Association 2015 年版權所有。經許可改編。

[a] 本表獲得 93 %共識會議與會者認可。
[b] 取決於疑似成因。
[c] 除非病患病史強烈暗示，例如過敏。
[d] 作為嚴重系統性疾病之指標。

等級相關資訊；同時納入英國過敏與臨床免疫學會對藥物的分級與適應症 [22-32]。

急性蕁麻疹的臨床治療

急性蕁麻疹與 CU 的不同之處在於持續時間長度不超過 6 週。蕁麻疹或血管性水腫的發作絕大部分侷限於皮膚（包含黏膜組織），但未連帶出現重大系統性症狀時所下的診斷。重要的是詢問病患是否出現嚴重過敏反應 anaphylaxis 的症狀並衛教他們這和蕁麻疹 / 血管性水腫不同，且有威脅生命的可能，症狀包含喘鳴 (wheezing)/ 咳嗽、嘔吐 / 腹瀉、頭暈 / 意識障礙或低血壓 / 心率變化。

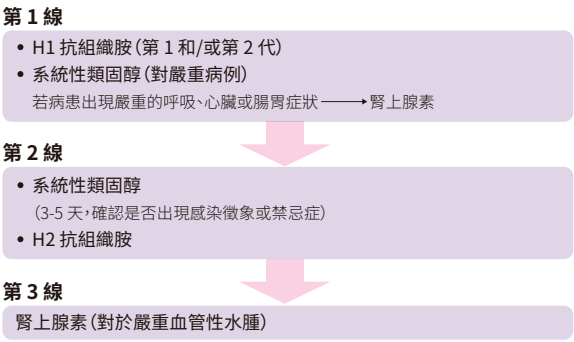

圖 5 急性蕁麻疹建議治療流程。本圖獲得 100% (21/21) 共識會議與會者認可。參閱表 S1 核准使用年齡。註：修改自 "Taiwanese Dermatological Association consensus for the definition, classification, diagnosis, and management of urticaria" by Chung WH, Chu CY, Huang YH, Wang WM, Yang CH and Tsai TF, 2016, J Formos Med Assoc. 2016 Nov;115(11):968-980. Formosan Medical Association 2015 年版權所有。經許可改編。

急性蕁麻疹有很多可能成因，包括食物過敏 [33]、藥物疹（如 NSAID、ACE 抑制劑 [34] 和鴉片類藥物）、蟲咬反應、感染（如 EBV 或微小病毒 [parvovirus] B19 型）、自發性成因 [35]，或物理性蕁麻疹。舉例來說，在台灣，兒童首次急性蕁麻疹發作最常見的病因是感染 (48.4%)、食物 (23.5%)、自發性成因 (13.2%) 和藥物 (11.5%)[36]。基於預防和治療之目的，找出這些急性蕁麻疹的可能成因就相當重要。

急性蕁麻疹的治療包括避免和移除上述可能致病因子。在限制接觸這些可能誘發物後，針對持續性症狀的第一線治療是抗組織胺；在很嚴重的情況下，可能需要以口服皮質類固醇治療急性蕁麻疹和血管性水腫 **(圖 5)**。若症狀很嚴重且在接受抗組織胺後未見緩解，可考慮嘗試短時間口服皮質類固醇治療 (經 100% 共識會議與會者同意)，然而，常規使用口服皮質類固醇對急性蕁麻疹的效益仍不足以確認常規使用口服皮質類固醇優於抗組織胺。一項在台灣進行的小規模單臂開放性試驗顯示 omalizumab 可顯著改善急性蕁麻疹病患的症狀與生活品質，即便僅在少部分病患身上觀察到快速控制情形 。

針對嚴重血管性水腫，腎上腺素應作為第三線治療（在 H1 與 H2 抗組織胺及系統性類固醇之後）使用。特別注意，當病患出現嚴重呼吸道、心臟或腸胃道症狀時，腎上腺素應作為第一線療法；如尚未排除診斷是嚴重過敏反應 anaphylaxis 之可能性，也應處方腎上腺素。 為提供更多資訊，TDA 共識會議建立專為急性蕁麻疹所設計之建議治療流程。**(圖 5)**

特殊族群治療

老年病患

高齡 CSU 病患的主要特色在於風疹塊較少、血管性水腫發生機率較低、較少發生皮膚劃

紋症 (dermographism)、自體血清皮膚測試 (ASST) 陽性率較低，且性別分布均等[38]。老年人的共病症、多重用藥和器官功能不足使高齡蕁麻疹的治療變得非常困難[38,39]，徹底檢視並調整病患的藥物（包括 ACEI、Aspirin 和其他 NSAID）、避免誘發因子、治療共病症、確認腎臟與肝臟功能及調查是否有其他可能潛在之疾病（糖尿病、甲狀腺機能障礙、自體免疫疾病和惡性腫瘤）皆為治療成功的關鍵（參見**補充表 2** 之詳細資訊）。一般而言，為老年病患選擇藥物和劑量時應審慎思考，因可能產生藥物交互作用或不良反應，例如尿滯留、口乾、青光眼和中樞神經系統作用，這最常發生於第一代抗組織胺。此外，處方抗組織胺時也要將病患跌倒或發生交通事故的風險考量在內（參見**補充表 2 和 3** 之詳細資訊），同理，當老年病患使用 CSU 藥物的效益高於潛在風險時，就可考慮用藥。對於患有多種共病症或腎 / 肝功能不全的老年病患，基於安全性和有效性，可考慮使用 bilastine 和 omalizumab[38,40]。

腎或肝功能不全病患

對於肝腎功能不全的患者，尤其是洗腎患者（包括血液透析或是腹膜透析）需要考慮調整口服抗組織胺的藥物劑量。因為第一代抗組織胺的不適當鎮定作用，皆必須避免使用於嚴重肝腎功能疾病的患者。對於這些患者，比較建議謹慎使用第二代抗組織胺[41,42]。窄波紫外線 UVB(nbUVB) 治療對於抗組織胺治療無效的慢性蕁麻疹患者的臨床有效證據仍不足。但窄波 UVB 紫外線治療對於其他合併有系統性疾病的患者，包括肝腎功能不全，或是懷孕以及兒童慢性蕁麻疹患者皆是安全有效的治療[43]。

兒童病患

由於兒童對第一代抗組織胺不良反應較多，現已不建議讓年齡未滿 12 歲的孩童使用第一代抗組織胺 (fgAHs)。建議以適當劑量之無鎮靜作用的第二代抗組織胺作為未滿 12 歲病患之第一線治療（年齡與建議劑量參見**補充表 3**）。目前尚無分析年齡未滿 12 歲病患使用更高劑量第二代抗組織胺的隨機分配對照試驗 (RCT)。施用高達標準劑量 4 倍之第二代抗組織胺於 CSU 孩童看起來仍是安全的，但僅限於橫斷研究中證實過療效和耐受性者[44,45]。如同 EAACI 指引內容，我們也建議在使用第一線治療後症狀仍持續 2-4 週時，使用 4 倍核准劑量。和成人治療流程一樣，建議將 omalizumab 和 cyclosporine 當作第三線和第四線治療 (經 100% 共識會議與會者同意)。TFDA 並未核准以 omalizumab 治療 12 歲以下孩童的 CU，但核准其作為 6 歲以上孩童的氣喘治療。一項多中心回溯性病例系列報告指出 CSU 孩童對標準劑量 omalizumab 療法的反應佳，與成人反應率相當[46]。因此，omalizumab 對年齡大於 6 歲、第二線治療失敗的頑固性 CSU 兒童病患是可以考慮的一種方法。

懷孕婦女

原則上應以相同的方式考量對懷孕婦女的治療。通常考量到潛在風險與效益，處方的臨床醫師應避免對孕婦使用任何系統性治療，特別是在第一孕期；但於此同時，懷

孕婦女仍有權接受可行之最佳療法。對孕婦的 CSU 治療整體考量與一般族群類似，但我們應注意一些細節 (經 100% 共識會議與會者同意)。現在有些第二代抗組織胺不需處方簽就可購買，因此已被廣泛運用於治療過敏性鼻炎和蕁麻疹，可以想像許多孕婦都曾用過這些藥，尤其是在懷孕最早期（亦即在她們發現自己懷孕前）。關於在第一孕期暴露於 H1 抗組織胺一事，系統性回顧與整合分析文獻指出這並不會導致重大畸形或其他懷孕相關不良結果（自發性流產、早產、死產和低出生體重）的風險增加 [47]。當臨床適用時，在懷孕期間可小心地短期使用糖化皮質類固醇治療急性蕁麻疹或 CSU 急性發作。Betamethasone 和 dexamethasone 可穿過胎盤，在母親和胎兒體內的濃度相近；非氟化皮質類固醇（prednisone、methylprednisolone 和 hydrocortisone）大部分是經由胎盤 11β- 羥基類固醇脫氫酶代謝，進入胎兒血液循環的量非常少（小於總劑量的 10%）[48]，所以在懷孕期間較傾向使用非氟化皮質類固醇。即便如此，這些藥物的較高劑量暴露還是與早產、早期破水、子宮內胎兒生長遲滯、妊娠糖尿病、高血壓、子癲前症和子癲症相關 [49]。因故，當使用糖化皮質類固醇的時間較長時，應將劑量限制於 7.5 mg/ 天，且不可超過 20 mg/ 天。Cyclosporine 的資料大多來自接受器官移植者，這些人通常會比皮膚科病人使用更高的劑量（8–10 mg/kg/ 天）。Cyclosporine 並非動物或人類的致畸胎藥物，在從童年早期開始追蹤的世代研究中並未發現兒童出現長期神經發育、腎毒性或免疫功能的影響。然而 cyclosporine 可能會導致母體高血壓，且應保留作為嚴重疾病的救援療法 [50]。現在有越來越多報告是以 omalizumab 治療患有傳統療法效果不佳的 CSU 孕婦。現仍缺乏半衰期、關於新生兒 Fc 受體 (FcRn) 之藥物動力學，最重要的是亦缺乏懷孕時使用生物製劑安全性的調查與資訊。由於缺乏這些實證，有必要為了接受生物製劑治療的懷孕婦女，建立多專業合作方式、多中心登錄機制以進行長期追蹤、適合有生育能力女性之藥物試驗設計，以及更能充分呈現人類情況的實驗模型 [51]。FDA 將 omalizumab 歸類為 B 級藥物，這主要是根據以 omalizumab 治療氣喘病患之上市後前瞻性觀察性試驗 Xolair Pregnancy Registry (EXPECT) 所得的結果 [52]。文獻報告當時接受 omalizumab 治療的病患中，僅有 11 人懷孕 [53]；沒有證據指出懷孕病患及其嬰孩暴露於 omalizumab 與不良事件風險增加之間具有關聯性 [53,54]。儘管如此，在懷孕期間保持最高等級安全性這點至關重要，因此處方的臨床醫師應謹慎遵循共識指引內容行事。

哺乳婦女

當哺乳母親用藥時，所有的 H1 抗組織胺都會在母乳中有低濃度排出。此外，已知哺乳嬰孩在攝入轉移自乳汁的第一代抗組織胺後，有時會產生鎮靜效果。因故，應謹慎使用第一代抗組織胺，並應輔導家長監測孩子是否出現易怒或嗜睡之徵象，最好使用無鎮靜作用的第二代抗組織胺 [55]。哺乳時可以使用非氟化皮質類固醇，因為這些藥物比起其他藥物有較少的量分泌到乳汁中 (5–25%)[2]。若使用 cyclosporine 的母親選擇哺乳，則需要監測嬰孩有無出現 cyclosporine 中毒症狀，包括水腫、顫抖、多毛症、

高血壓和癲癇，且應密切追蹤嬰孩的血漿藥物濃度[56]。使用 omalizumab 時可允許哺乳，因為預期口服攝取後會破壞 omalizumab 的抗體結構[57]。通則還是應依個別病例的情況，考量哺乳婦女使用這些藥物的風險效益比，即當對母體的效益，也就是蕁麻疹的緩解大於嬰孩接受轉移自母乳之藥物可能導致的任何潛在風險時，通常可接受經考慮後使用藥物。話雖如此，仍應視需求，根據相關主管機關提供之最新建議，評估所有處方決策。請參考**補充表 3** 關於哺乳婦女使用各種藥物之相關具體建議。

討論與結論

在過去幾年間有許多原創研究對 CU 進行探討，凸顯出 CU 病患的特色，並討論台灣的 CU 治療[4-7]。這些研究擴展了我們對疾病的認識，且將重點放在台灣的實際情況。TDA 在目前的共識中整合納入這些對於台灣健康照護環境的特殊考量，並更新最近的蕁麻疹資訊，以提供醫師和病患最佳照護策略，提升蕁麻疹的照護品質。

除此之外，將來針對一系列相關主題（例如蕁麻疹的社會和經濟負擔、蕁麻疹疾病嚴重度和治療反應的生物標記，以及發展新的治療藥物）之研究工作應能讓日後的治療指引更為精細，藉此提升未來的照護品質。

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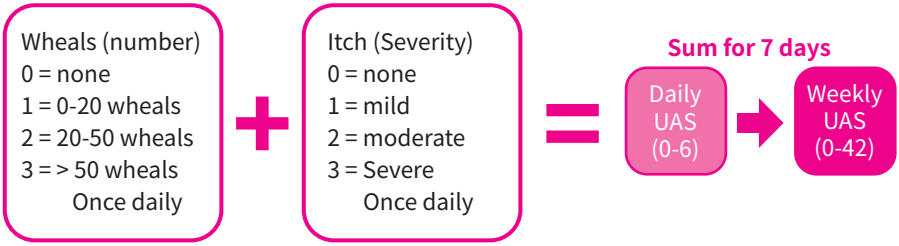
附錄

補充圖 1

UAS7 score

Score	Wheals	Itch
0 None	None	None
1 Mild	< 20 wheals/24 h	Mild (present, but not annoying or troublesome)
2 Moderate	20-50 wheals/24 h	Moderate (troublesome, but does not interfere with normal daily activity or sleep)
3 Intense	>50 wheals/24 h or large confluent area of wheals	Intense (severe itching, which is sufficiently troublesome to interfere with normal daily activity or sleep)



The UAS/UAS7 for assessing disease activity in CSU. Of the consensus attendees, 78.9% (15/19) approved this figure.Sum of scores: 0e6 for each day is summarized over 1 week (maximum 42). UAS is a diary-based, combined score of severity of itch and number of wheals (scale 0e6). CSU Z chronic spontaneous urticaria; UASZUrticaria Activity Score; UAS7 Z Urticaria Activity Score for 7 days. N Revision based on "Taiwanese Dermatological Association consensus for the definition, classification, diagnosis, and management of urticaria" by Chung WH, Chu CY, Huang YH, Wang WM, Yang CH and Tsai TF, 2016, J Formos Med Assoc. 2016 Nov;115(11):968-980.. Copyright 2015, Formosan Medical Association. Adapted with permission.

補充表 1

Alternative anti-inflammatory agents

Intervention	Subtance	Side effects
Widely used		
Anti-depressant	Doxepin	Constipation, nausea, xerostomia, dizziness, somnolence, urinary retention, upper respiratory infection, hypotension, sudden cardiac death, ventricular arrhythmia, agranulocytosis, anemia, leukopenia, thrombocytopenia, suicidal thoughts, suicide, nephrotoxicity
H1 histamine receptor antagonist and mast cell stabilizer	Ketotifen (Not listed in EAACI 2018)	Chills, cough, diarrhea, fever, general feeling of discomfort or illness, headache, joint pain, loss of appetite, muscle aches & pains, nausea, runny nose, shivering, sore throat, sweating, trouble sleeping, unusual tiredness or weakness, vomiting
H2-antihistamine	Ranitidine	Abdominal pain, constipation, diarrhea, headache, bradyarrhythmia, Stevens-Johnson syndrome, toxic epidermal necrolysis due to drug, necrotizing enterocolitis in fetus or newborn, thrombocytopenia, cholestatic hepatitis, hepatitis, liver function tests abnormal
Immunosuppressives	Methotrexate	Loss of appetite; nausea; vomiting; abdominal pain; impaired digestion; dyspepsia; inflammation & ulceration in mouth & throat; increase in level of liver enzyme; herpes zoster; effects on the blood, e.g., anemia, leukopenia, & thrombocytopenia; diarrhea; dry cough; shortness of breath; chest pain; fever; rashes; redness & itching; headache; tiredness; drowsiness
	Mycophenolate mofetil	Edema, hypertension, hyperglycemia ,abdominal pain, constipation, diarrhea, nausea, vomiting, musculoskeletal pain, headache, insomnia, serum blood urea nitrogen raised, serum creatinine raised, dyspnea, fever, gastric ulcer, gastrointestinal hemorrhage, gastrointestinal perforation, anemia, leukopenia, neutropenia, pancytopenia, pure red cell aplasia, thrombocytopenia, reactivation of hepatitis b viral hepatitis, reactivation of hepatitis c viral hepatitis, infectious disease, lymphoproliferative disorder following transplantation, opportunistic infection, sepsis, progressive multifocal leukoencephalopathy, renal impairment caused by polyomavirus, pleural effusion

Intervention	Subtance	Side effects
Leukotriene receptor antagonist	Montelukast	Abdominal pain, diarrhea, headache, otitis, otitis media, cough, nasal discharge, pharyngitis, sinusitis, upper respiratory infection, fever, influenza, eosinophilic granulomatosis with polyangiitis, disorientated, disturbance of attention, insomnia, memory impairment, stuttering, tic, tremor, aggressive behavior, agitation, anxiety, depression, dream disorder, hallucinations, irritability, nightmares, obsessive-compulsive disorder, restlessness, sleep walking disorder, suicidal behavior, suicidal thoughts
Miscellaneous	Hydroxychloroquine (EAACI 2018: infrequently used)	Feeling or being sick, loss of appetite, dizziness, ringing in the ears, headache, mood swings, fits, spasm of airways, muscle weakness, decreased reflexes, low platelets, bone marrow depression, abnormal nerve conduction, abnormal liver function, seen on blood tests, lowering of the blood glucose level, diarrhea, stomach pain, visual disturbances, vertigo, hearing loss, nervousness, psychosis, liver failure, itchy & raised rashes, muscle wasting, anemia, low white blood cells, general tissue swelling, problems with heart, conduction system, bleaching of hair/ hair loss
	Colchicine (EAACI 2018: infrequently used)	Diarrhea, nausea, vomiting, myelosuppression
Sulphones	Dapsne	Back, leg, or stomach pain;bluish fingernails, lips, or skin; difficult breathing; fever; loss of appetite; pale skin; skin rash; unusual tiredness or weakness
	Sulfasalazine	Pruritus, rash, abdominal pain, indigestion, loss of appetite, nausea, stomatitis, vomiting liver function tests abnormal, dizziness, headache, discolored urine, oligozoospermia, reversible, fever, myocarditis, erythroderma, Stevens-Johnson syndrome, toxic epidermal necrolysis, agranulocytosis, aplastic anemia, pure red cell aplasia, fulminant hepatic failure, hepatotoxicity, liver damage, hypersensitivity reaction, systemic lupus erythematosus, disorder of the central nervous system, myoneural disorder, kidney disease, male infertility, diffuse interstitial pulmonary fibrosis, pneumonia, sepsis

Intervention	Subtance	Side effects
Infrequently used		
Anabolic steroids	Danazol	Acne, weight increased, syncope, decreased HDL level, thromboembolic disorder, thrombophlebitis, adenoma of liver, cholestatic jaundice syndrome, elevated levels of transaminase & lactic acid dehydrogenase, hepatic failure, acute, jaundice, peliosis hepatis, cerebrovascular accident, pseudotumor cerebri, seizure
Anticoagulant	Warfarin	Alopecia, cholesterol embolus syndrome, tissue necrosis, calciphylaxis, tissue necrosis, upper gastrointestinal bleeding, hemorrhage, hemorrhage, hypersensitivity reaction, compartment syndrome, intracranial hemorrhage, intraocular hemorrhage
Antifibrinolytic	Tranexamic acid	Abdominal pain, diarrhea, nausea, anemia, arthralgia, backache, cramp, musculoskeletal pain, spasm, headache, migraine, nasal sinus problem, fatigue, thromboembolic disorder Anaphylactoid reaction, anaphylaxis, cerebral ischemia, retinal artery occlusion, thrombosis of retinal vein, visual disturbance, pulmonary embolism
Anabolic steroids	Danazol	Acne, weight increased, syncope, decreased HDL level, thromboembolic disorder, thrombophlebitis, adenoma of liver, cholestatic jaundice syndrome, elevated levels of transaminase & lactic acid dehydrogenase, hepatic failure, acute, jaundice, peliosis hepatis, cerebrovascular accident, pseudotumor cerebri, seizure
Anticoagulant	Warfarin	Alopecia, cholesterol embolus syndrome, tissue necrosis, calciphylaxis, tissue necrosis, upper gastrointestinal bleeding, hemorrhage, hemorrhage, hypersensitivity reaction, compartment syndrome, intracranial hemorrhage, intraocular hemorrhage

Intervention	Subtance	Side effects
Infrequently used		
Antifibrinolytic	Tranexamic acid	Abdominal pain, diarrhea, nausea, anemia, arthralgia, backache, cramp, musculoskeletal pain, spasm, headache, migraine, nasal sinus problem, fatigue, thromboembolic disorder Anaphylactoid reaction, anaphylaxis, cerebral ischemia, retinal artery occlusion, thrombosis of retinal vein, visual disturbance, pulmonary embolism
Immunosuppressives	Azathioprine (Not listed in EAACI 2018)	Black, tarry stools; bleeding gums; blood in urine or stools; chest pain; cough or hoarseness; fever or chills; lower back or side pain; painful or difficult urination; pinpoint red spots on the skin; shortness of breath; sore throat; sores, ulcers, or white spots on the lips or in the mouth; swollen glands; unusual bleeding or bruising; unusual tiredness or weakness
Immunomodulator	IVIG	Heart murmur, hypertension, hypotension, increased blood pressure, increased heart rate, increased systolic arterial pressure, peripheral edema, injection site reaction, pruritus, rash, swelling at injection site, urticaria, increased body temperature, aphthous ulcer of mouth, diarrhea, nausea, upper abdominal pain, vomiting, complication of infusion, arthralgia, muscle weakness, myalgia, pain in limb, spasm, asthenia, dizziness, headache, lethargy, migraine, otalgia, asthma, cough, nasal congestion, pain in throat, pharyngitis, pharyngolaryngitis, sinusitis, wheezing, dehydration, fatigue, fever, pain, rigor, shivering, chest discomfort, chest pain, myocardial infarction, tachycardia, hyponatremia, Hemolysis, hemolytic anemia, thrombosis, hepatitis c, anaphylaxis, backache, aseptic meningitis, acute renal failure, hypokalemic nephropathy, acute lung injury during and following administration of blood product, pulmonary embolism

Intervention	Subtance	Side effects
Miscellaneous	Autologous blood/ serum	NA
Photoehrapy	Narrow-band UV-B	NA
Psychotherapy	Holistic medicine	NA
Rarely used		
Anticoagulant	Heparin	Thrombocytopenia, increased liver aminotransferase level, hemorrhage, heparin-induced thrombocytopenia, heparin-induced thrombocytopenia with thrombosis, hypersensitivity reaction, non-traumatic spinal subdural hematoma
Miscellaneous	Anakinra	Injection site reaction, rash, diarrhea, gastroenteritis, nausea, vomiting, infectious disease, arthralgia, headache, nasopharyngitis, upper respiratory infection, fever, influenza-like illness, cardiorespiratory arrest, bacterial cellulitis, malignant melanoma, neutropenia, thrombocytopenia, anaphylaxis, hypersensitivity reaction, infectious disease, serious, malignant lymphoma, bacterial musculoskeletal infection, bacterial pneumonia, breast cancer, cancer, malignant lymphoma
	Anti-TNF-alpha	Injection site reaction, upper respiratory infection, congestive heart failure, erythema multiforme, malignant melanoma, necrotizing fasciitis, primary cutaneous vasculitis, skin cancer, squamous cell carcinoma of skin, Stevens-Johnson syndrome, toxic epidermal necrolysis, aplastic anemia, leukemia, pancytopenia, reactivation of hepatitis b viral hepatitis, autoimmune hepatitis, cancer, hepatosplenic T-cell lymphoma, hypersensitivity reaction, malignant lymphoma, demyelinating disease of central nervous system, multiple sclerosis, peripheral demyelinating neuropathy, seizure, transverse myelitis, optic neuritis, tuberculosis, infectious disease
	Camostat mesilate	NA
	Miltefosine	Pruritus, abdominal pain, decrease in appetite, nausea, vomiting, dizziness, somnolence, rash, Stevens-Johnson syndrome, diarrhea, melena, thrombocytopenia, hyperbilirubinemia, increased liver enzymes, arthritis, serum creatinine raised

Intervention	Subtance	Side effects
Miscellaneous	Mirtazapine	Constipation, xerostomia, asthenia, dizziness, disturbance in thinking, prolonged QT interval, Torsades de pointes, ventricular tachycardia, hyponatremia, serum cholesterol raised, serum triglycerides raised, weight gain, increased appetite, agranulocytosis, neutropenia, ALT/SGPT level raised, aspartate aminotransferase serum level raised, cirrhosis of liver, liver function tests abnormal, seizure, somnolence, angle-closure glaucoma, mania, suicidal thoughts, suicide, serotonin syndrome
	PUVA	NA
Very rarely used		
Immunosuppressive	Tacrolimus	Peripheral edema, alopecia, persistent erythema of skin, persistent erythema of skin, pruritus, rash, constipation, diarrhea, nausea, vomiting, anemia, leukocytosis, thrombocytopenia, headache, paresthesia, tremor, serum creatinine raised, increasing frequency of cough atrial fibrillation, cardiac arrest, cardiomegaly, congestive heart failure, hypertension, myocardial infarction, prolonged QT interval, diabetes mellitus, post-transplant, hyperkalemia, hypomagnesemia, gastrointestinal perforation, pure red cell aplasia, hepatitis, hepatotoxicity, anaphylaxis, infectious disease, lymphoproliferative disorder, malignant lymphoma, opportunistic infection, posterior reversible encephalopathy syndrome, seizure, acute renal failure, hemolytic uremic syndrome, nephrotoxicity, acute respiratory distress syndrome
Miscellaneous	Vitamin D Interferon alpha	Fatigue, headache, rigors, insomnia, anxiety, irritability, nervousness, depression, dizziness, pain, alopecia, growth suppression, nausea, vomiting, anorexia, abdominal pain, diarrhea, neutropenia, increased serum ALT, injection site reaction, weakness, myalgia, arthralgia, cough, flu-like symptoms, fever, lack of concentration, memory impairment, mood changes, skin rash, dermatitis, diaphoresis, xeroderma, eczema, weight loss, hypothyroidism, hyperthyroidism, decreased appetite, xerostomia, thrombocytopenia, lymphocytopenia, anemia, increased serum AST, liver decompensation, bacterial infection, back pain, blurred vision, epistaxis, upper respiratory tract infection, nasopharyngitis, dyspnea

補充表 2

CSU Management in Elderly patients

1. Considerations in geriatric age:

(1) Main characters of geriatric CSU: fewer wheals, lower rates of angioedema, less frequent dermographism, a lower frequency of ASST positivity, equal sex dstribution

(2) Review medication and avoidance of eliciting factors:

Medications which may cause urticaria	Consider shifting to
Angiotensin-converting enzyme inhibitors (ACEIs)	Angiotensin II receptor blockers (ARBs)
Aspirin	Clopidogrel Desensitization if aspirin is considered essential
other NSAIDs	Paracetamol An alternative class of NSAID A selective Cox-2 inhibitor

(3) Review comorbidities:

patients with a long QT interval, previous cardiac disease or are using drugs that prolong QT interval (anti-arrythmics, tricyclic anti-depressants, neuroleptics)6	Avoid first-generation H1 antihistamine1 Hydroxyzine Pamoate: QT prolongation and Torsade de Pointes have been reported (Micromedex) Cardiotoxicity is not reported for higher dose bilastine, cetirizine, desloratadine, ebastine, fexofenadine, levocetirizine, loratadine, mizolastine or rupatadine6
Currently taking drugs competing for the same hepatic cytochromes: antifungal azoles, macrolides, grapefruit juice and St. Johns Wort6	Avoid desloratadine, fexofenadine and ebastine6
Hepatic/Renal impairment6	No need for dose adjustment: bilastine, Omalizumab6,3
The high incidence of diabetes, dysthyroidism, autoimmune diseases and malignancies1	thyroid disease (Hashimoto’ s thyroiditis) 5 cancer (leukemia, breast, lung, colon and prostate cancers)4 infections (Helicobacter pylori, bacteria responsible for cystitis, sinusitis and abscesses)4 Female geriatric patients: higher incidence of rheumatoid arthritis, Sjo¨gren syndrome, celiac disease, type 1 diabetes mellitus, and systemic lupus erythematosus (diagnosed 10 years after urticaria)5 The underlying diseases could be masked by urticaria, or that urticaria itself could be the first clinical presentations of these diseases.1

2.Treatment consideration:

Avoid first-generation H1 antihistamines5	First-generation antihistamines have poor receptor selectivity with non-antihistamine activity and can pass blood-brain barrier leading to CNS effect. 5 (1)anticholinergic effects: urinary hesitancy, urinary retention, constipation, dry mouth, dry eyes, papillary dilatation, dizziness, impaired coordination, and memory dysfunction5 (2)α-adrenergic blockade: arrhythmias, peripheral vasodilatation, postural hypotension lead to the aggravation of concomitant diseases, such as prostatic hypertrophy, bladder neck obstruction, narrow-angle glaucoma, and heart disease. 5 (3)Impairment of CNS function: falls, inattention, disorganized speech, altered consciousness, delirium, drowsiness, sedation, somnolence, fatigue, dizziness, headache, decreased reaction time, dyskinesia, confusion, and agitation5
Nonsedating new-generation antihistamines	The second-generation antihistamines (sg-AHs) that are relatively non-sedating5 Use lowest treatment dosages to prevent the risk of falls (sleepiness or kinetic instability) 1 Bilastine is a safe, well tolerated, nonsedating and effective with no need for dose adjustment in renal/hepatic impaired patients, and has no anticholinergic effects/cardiotoxicity8
Steroids1	Prescribed only during exacerbations of CSU Used as short as possible corticosteroid-associated AEs: memory impairment, diabetes, cataract, osteoporosis, peptic ulcer5 Closely monitor blood pressure and glucose level
Cyclosporine	Efficacious particularly in patients with low IgE6 Prescribed only during exacerbations of CSU 1 Used as short and lowest therapeutic dose as possible. 5 Dose-dependent and timedependent AEs (arterial hypertension, kidney damage, hirsutism, gingival hyperplasia, dyslipidemia) limit its use 5,6 Require careful monitoring on blood pressure and renal function 5 Should be used with extreme attention in the elderly5 Cyclosporine has multiple drug interactions5
Omalizumab3	safe and effective in elderly patients with multiple comorbidities3 No need for dose adjustment for age or impaired renal/liver functions5 Can be considered for difficult-to-treat CSU and/or chronic inducible urticaria5
Montelukast	generally safe in the geriatric population, but has been outlined the risk of recurrent myocardial infarction in male subjects4, 5

補充表 3

Detailed information of recommended urticaria treatment agents 2nd generation antihistamine for urticaria

Second generation H1 antihistamines		Approved Age	Pregnancy category	Breastfeeding
Cetirizine	FDA	≧ 6 mon	B	Excreted in human milk and NOT recommended
	EMA	≧ 2 yrs	NA	NA
	TFDA	≧ 3 yrs	NA	NA
	Micromedex	≧ 6 mon	Fetal risk cannot be ruled out	Infant risk cannot be ruled out
Levocetirizine	FDA	≧ 6 mon	B	Excreted in human milk and NOT recommended
	EMA	NA	NA	NA
	TFDA	≧ 6 yrs	NA	NA
	Micromedex	≧ 6 mon	Fetal risk cannot be ruled out	Infant risk cannot be ruled out

Metabolism/ dose for hepatic impairment	Elimination/dose for renal impairment	Contraindications
Dosing adjustment may be necessary in patients with hepatic impairment	Dosing adjustment is necessary in patients with moderate or severe renal impairment and in patients on dialysis	Should not be used in patients who have shown a previous hypersensitivity to this medication or any of its inactive ingredients or to hydroxyzine
NA	NA	
NA	NA	
Not extensively metabolized by the liver No dosage adjustment is necessary for hepatic impairment	Approximately 60% of dose is excreted in the urine through unchanged form No dosage adjustment is necessary for renal impairment	
Dosing adjustment is only necessary in hepatically impaired patients if concomitant renal impairment is present	Dosage adjustment is recommended	Should not be used in patients with end-stage renal disease or patients undergoing hemodialysis. Should not be used in children 6 months to 11 years of age with impaired renal function. Should not be used in patients who have shown a previous hypersensitivity to this medication or any of its inactive ingredients or to cetirizine
NA	NA	
NA	NA	
Less than 14% of a dose of levocetirizine is metabolized in the liver No dosage adjustment is necessary for hepatic impairment	Approximately 80% of dose is excreted in the urine through unchanged form Dose adjustments is needed based on Ccr	

Second generation H1 antihistamines		Approved Age	Pregnancy category	Breastfeeding
Fexofenadine	FDA	≧ 6 yrs	C	There are no adequate and well-controlled studies in women during lactation. Because many drugs are excreted in human milk, caution should be exercised when fexofenadine hydrochloride is administered to a nursing woman
	EMA	NA	NA	NA
	TFDA	≧ 6 yrs	NA	NA
	Micromedex	≧ 6 yrs	NA	Infant risk is minimal
Desloratadine	FDA	≧ 6 mon	C	Excreted in human milk and NOT recommended
	EMA	> 12 yrs (tablets)	NA	NA
	TFDA	> 12 yrs	NA	NA
	Micromedex	≧ 6 mon	Fetal risk cannot be ruled out	Infant risk cannot be ruled out
Ebastine	FDA	NA	NA	NA

Metabolism/ dose for hepatic impairment	Elimination/dose for renal impairment	Contraindications
No dosage adjustment is required	Dosage adjustment is recommended	
NA	NA	Should not be used in patients who have shown a previous hypersensitivity to this medication or any of its inactive ingredients
NA	NA	
Only around 1% of the dose is metabolized in the liver No dosage adjustment is necessary for hepatic impairment	Approximately 11% of dose is excreted in the urine Dose adjustments is needed for renal impairment	
Dosage adjustment is recommended	Dosage adjustment is recommended	
NA	NA	Should not be used in patients who have shown a previous hypersensitivity to this medication or any of its inactive ingredients or to loratadine.
NA	NA	
Extensively metabolized in the liver Dosage adjustment is necessary for hepatic impairment	Approximately 40% of dose is excreted in the urine Dose adjustments is needed for renal impairment	
NA	NA	

Second generation H1 antihistamines		Approved Age	Pregnancy category	Breastfeeding
	EMA	NA	NA	NA
	TFDA	Adult only	Fetal risk cannot be ruled out	Infant risk cannot be ruled out
	Micromedex	Adult only	NA	NA
Loratadine	FDA	＜ 2 yrs need to ask doctor	B	Micromedex: Infant risk is minimal
	EMA	≧ 2 yrs	NA	NA
	TFDA	≧ 2 yrs	NA	NA
	Micromedex	＜ 2 yrs need to ask doctor	Fetal risk cannot be ruled out.	Infant risk is minimal

FDA ＝ U.S. Food and Drug Administration
EMA ＝ European Medicines Agency
TFDA ＝ Taiwan Food and Drug Administration

Metabolism/ dose for hepatic impairment	Elimination/dose for renal impairment	Contraindications
NA	NA	
Metabolized by CYP3A4 to active metabolite	Around 63% of the dose has been shown to be excreted by renal	Hypersensitivity to ebastine
Metabolized by CYP3A4 to active metabolite	Around 40% of the dose has been shown to be excreted by renal	
Patients with severe irment should be administered a lower initial dose because they may have reduced clearance of loratadine	Dosage adjustment is recommended	
NA	NA	Should not be used in patients who have shown a previous hypersensitivity to this medication or any of its inactive ingredients
NA	NA	
Extensively metabolized in the liver	Approximately 80% of dose is excreted in the urine	

Immunomodulatory treatment for urticaria

Immunomodulatory treatment		Approved Age	Pregnancy category	Breastfeeding
Omalizumab	FDA	≥ 12 yrs	B	Not been studied and is expected that it will be present in human milk. (It is not known whether Omalizumab is present in human breast milk; however, IgG is present in human milk in small amounts. Exercise caution when administering Xolair to a nursing woman.)
	EMA	≥ 6 yrs (Asthma)	NA	It is unknown whether omalizumab is excreted in human milk. Omalizumab should not be given during breast-feeding
	TFDA	≥ 12 yrs	Fetal risk cannot be ruled out	Infant risk cannot be ruled out
	Micromedex	≥ 12 yrs	Fetal risk cannot be ruled out	Infant risk cannot be ruled out
Cyclosporine	FDA	off-label use for chronic urticaria Although no adequate and well-controlled studies have been conducted in children, patients as young as 6 months of age have received the drug with no unusual adverse effects	C	Not known if it is excreted in human milk. (Cyclosporine is present in breast milk. Because of the potential for serious adverse drug reactions in nursing infants from cyclosporine, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.)
	EMA	NA	NA	NA

Metabolism/ dose for hepatic impairment	Elimination/dose for renal impairment	Contraindications
No dosage adjustment is required (Not mentioned)	No dosage adjustment is required (Not mentioned)	
There have been no studies on the effect of impaired renal or hepatic function on the pharmacokinetics of omalizumab. While no particular dose adjustment is recommended for these patients, Xolair should be administered with caution	There have been no studies on the effect of impaired renal or hepatic function on the pharmacokinetics of omalizumab. While no particular dose adjustment is recommended for these patients, Xolair should be administered with caution	Should not be used in patients who have shown a previous hypersensitivity to this medication or any of its inactive ingredients
No dosage adjustment is required	No dosage adjustment is required	
Omalizumab is cleared via IgG and partially degraded by the liver	Excretion not through renal	
Dose reduction may be necessary in patients with severe liver impairment. (The clearance of cyclosporine may be significantly reduced in severe liver disease patients. Dose reduction may be necessary in patients with severe liver impairment to maintain blood concentrations within the recommended target range.)	Nephrotoxic potential, careful monitoring of renal function is recommended. (cyclosporine dosage should be reduced if indicated.)	Should not be used in patients receiving concomitant PUVA or UVB therapy, methotrexate or other immunosuppressive agents, coal tar or radiation therapy, or in patients with abnormal renal function, uncontrolled hypertension, or malignancies
NA	NA	

Immunomodulatory treatments		Approved Age	Pregnancy category	Breastfeeding
Cyclosporine	TFDA	off-label use for chronic urticaria	Fetal risk cannot be ruled out.	Because of the potential for serious adverse drug reactions in nursing infants from cyclosporine, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother
	Micromedex	≥ 9 years (off-label use for chronic urticaria)	Fetal risk cannot be ruled out	Infant risk cannot be ruled out

Metabolism/ dose for hepatic impairment	Elimination/dose for renal impairment	Contraindications
NA	NA	Should not be used in patients receiving concomitant PUVA or UVB therapy, methotrexate or other immunosuppressive agents, coal tar or radiation therapy, or in patients with abnormal renal function, uncontrolled hypertension, or malignancies
Patients with severe hepatic impairment may require lower doses of cyclosporine to maintain cyclosporine blood concentrations in the recommended range	Elimination of unchanged cyclosporine does not appear to be different in patients with advanced renal failure as compared with those with normal kidney function. Modification of initial dosing regimens are probably not required	

Detailed information of alternative urticaria treatment agents

1st generation antihistamine for urticaria

First generation H1 antihistamines		Approved Age	Pregnancy category	Breastfeeding
Chlorpheniramine	FDA	≥ 6 yrs	B	NA
	EMA	NA	NA	NA
	TFDA	≧ 2 yrs	NA	NA
	Micromedex	≥ 6 yrs	Fetal risk cannot be ruled out	Infant risk cannot be ruled out
Diphenhydramine	FDA	Infant or older	B	NA
	EMA	NA	NA	NA

Metabolism/ dose for hepatic impairment	Elimination/dose for renal impairment	Contraindications
Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	Should not be used for the following conditions: Hypersensitivity to antihistamines; stenosing peptic ulcer; narrow-angle glaucoma; symptomatic prostatic hypertrophy; asthma; bladder neck obstruction; pyloroduodenal obstruction; MAO therapy; in newborn or premature infants and in breast-feeding mothers
NA	NA	
NA	NA	
Extensively metabolized in the liver to inactive metabolite	Approximately 50% of dose is excreted as inactive metabolites with 3% to 18% occurring as unchanged drug	
Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	Should not be used in neonates, premature infants, or nursing mothers. Because of the risk of local necrosis, should not be used as a local anesthetic. Also contraindicated for the following conditions: Hypersensitivity to diphenhydramine hydrochloride and other antihistamines of similar chemical structure
NA	NA	

First generation H1 antihistamines		Approved Age	Pregnancy category	Breastfeeding
Diphenhydramine	TFDA	≧ 2 yrs	NA	NA
	Micromedex	Infant or older	Fetal risk cannot be ruled out	Infant risk cannot be ruled out
Hydroxyzine	FDA	≧ 6 yrs (but no indication for urticaria)	C	NA
	EMA	NA	NA	NA
	TFDA	≧ 30 months	NA	NA
	Micromedex	≧ 6 yrs	Fetal risk cannot be ruled out	Infant risk cannot be ruled out
Brompheniramine	FDA	Both adult & pediatric	C	NA
	EMA	NA	NA	NA
	TFDA	≧ 3 yrs	NA	NA
	Micromedex	Brompheniramine should not be	NA	Infant risk cannot be ruled out

Metabolism/ dose for hepatic impairment	Elimination/dose for renal impairment	Contraindications
NA	NA	Should not be used in neonates, premature infants, or nursing mothers. Because of the risk of local necrosis, should not be used as a local anesthetic. Also contraindicated for the following conditions: Hypersensitivity to diphenhydramine hydrochloride and other antihistamines of similar chemical structure
Approximately 50% of dose is metabolized in the liver to inactive metabolites	Urinary excretion of total metabolites represented 64% of a dose in single dose studies and 49% after multiple doses	
Patients with impaired hepatic function should be administered a lower dosage and dosing frequency	Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	Should not be used in early pregnancy or by nursing mothers. Should not be used by patients who have shown a previous hypersensitivity to any component of this medication. Hydroxyzine Pamoate: Prolonged QT interval (Micromedex)
NA	NA	
NA	NA	
Metabolized by liver	NA	
Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	Should not be used for the following conditions: Hypersensitivity to brompheniramine; focal central nervous system lesions; concurrent MAO therapy
NA	NA	
NA	NA	
NA	NA	

First generation H1 antihistamines		Approved Age	Pregnancy category	Breastfeeding
Buclizine	FDA	Adults only	B	NA
	EMA	NA	NA	NA
	TFDA	≧ 3 yrs	NA	NA
	Micromedex	Adults only	Fetal risk cannot be ruled out	Infant risk cannot be ruled out
Carbinoxamine	FDA	≧ 2 yrs	C	NA
	EMA	NA	NA	NA
	TFDA	≧ 3 yrs	NA	NA
	Micromedex	≧ 2 yrs	Fetal risk cannot be ruled out	Infant risk has been demonstrated
Clemastine	FDA	≥ 6 yrs	B	NA
	EMA	NA	NA	NA
	TFDA	≥ 3 yrs	NA	NA
	Micromedex	≥ 6 yrs	Fetal risk cannot be ruled out	Infant risk cannot be ruled out.

Metabolism/ dose for hepatic impairment	Elimination/dose for renal impairment	Contraindications
Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate.	Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate.	Should not be used for the following conditions: Hypersensitivity to Buclizine; early pregnancy
NA	NA	
NA	NA	
NA	NA	
Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate.	Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate.	Should not be used in children less than 2 years of age; concomitant MAOI therapy; hypersensitivity to carbinoxamine; breastfeeding mothers
NA	NA	
NA	NA	
Carbinoxamine is extensively metabolized in the liver	Carbinoxamine maleate is excreted in the urine as inactive metabolites	
Therapy with antihistamines should be administered cautiously in such patients. Lower	Therapy with antihistamines should be administered cautiously in such patients. Lower	Should not be used in, hypersensitivity to clemastine products, lactation, lower respiratory tract symptoms, MAOI therapy, newborn or premature infants
NA	NA	
NA	NA	
No enzyme inducing effects	Urinary excretion is the main route of elimination for clemastine	

First generation H1 antihistamines		Approved Age	Pregnancy category	Breastfeeding
Cyclizine	FDA	≥ 6 yrs	B	NA
	EMA	NA	NA	NA
	TFDA	≥ 3 yrs	Fetal risk cannot be ruled out	Cyclizine could be secreted in Breast milk. Using cyclizine in patients with breastfeeding is not recommended
	Micromedex	≥ 6 yrs	Available evidence on cyclizine shows that the malformation rate is no more than that normally observed in pregnancies	Infant risk cannot be ruled out
Cyproheptadine	FDA	≥ 2 yrs	B	NA
	EMA	NA	NA	NA
	TFDA	≥ 2 yrs	NA	NA
	Micromedex	≥ 2 yrs	Fetal risk cannot be ruled out	Infant risk cannot be ruled out
Dexchlorpheniramine	FDA	≥ 2 yrs	B	NA
	EMA	NA	NA	NA
	TFDA	≥ 2 yrs	NA	NA
	Micromedex	≥ 2 yrs	Fetal risk cannot be ruled out	Infant risk cannot be ruled out

Metabolism/ dose for hepatic impairment	Elimination/dose for renal impairment	Contraindications
No enzyme inducing effects	Urinary excretion is the main route of elimination for clemastine	
Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	
NA	NA	Hypersensitivity to cyclizine
NA	Around 66% of the dose has been shown to be excreted by renal	
Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	Should not be used in angle-closure glaucoma, bladder neck obstruction, elderly, debilitated patients, hypersensitivity to cyproheptadine and other drugs of similar chemical structure, MAOI therapy, newborn or premature infants, nursing mothers, pyloroduodenal obstruction, stenosing peptic ulcer ,symptomatic prostatic hypertrophy
NA	NA	
NA	NA	
Around 57% of the dose has been metabolized by liver	At least 40% of the dose has been shown to be excreted in the urine	
Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	Therapy with antihistamines should be administered cautiously in such patients. Lower initial dosages may be appropriate	Hypersensitivity to dexchlorpheniramine products, including racemic chlorpheniramine
NA	NA	
NA	NA	
Dexchlorpheniramine is rapidly and extensively metabolized in the liver to inactive metabolite	Approximately 50% of dose is excreted as inactive metabolites with 3% to 18% occurring as unchanged drug	

First generation H1 antihistamines		Approved Age	Pregnancy category	Breastfeeding
Mequitazine	FDA	NA	NA	NA
	EMA	NA	NA	NA
	TFDA	≥ 2.5 yrs	Fetal risk cannot be ruled out	NA
	Micromedex	NA	NA	NA
Oxatomide	FDA	NA	NA	NA
	EMA	NA	NA	NA
	TFDA	≥ 2 yrs	Fetal risk cannot be ruled out	Infant risk cannot be ruled out
	Micromedex	NA	NA	NA
Piprinhydrinate	FDA	NA	NA	NA
	EMA	NA	NA	NA
	TFDA	≥ 3 yrs	NA	NA
	Micromedex	NA	NA	NA
Promethazine	FDA	Labels are not available from FDA	C	NA
	EMA	NA	NA	NA
	TFDA	≧ 2 yrs	NA	NA
	Micromedex	≥ 2 yrs	Fetal risk cannot be ruled out.	Infant risk cannot be ruled out

Metabolism/ dose for hepatic impairment	Elimination/dose for renal impairment	Contraindications
NA	NA	
NA	NA	Should not be used in patients with hypersensitivity to mequitazine and phenothiazine derivatives, MAOI therapy, glaucoma and dysuria
NA	NA	
NA	NA	
NA	NA	
NA	NA	
Metabolized by CYP3A4 & CYP2D6	Around 40% of the dose has been shown to be excreted by renal	Hypersensitivity to oxatomide
NA	NA	
NA	NA	
NA	NA	Should not be used in patients with hypersensitivity to piprinhydrinate, emphysema, bronchitis, COPD, glaucoma and dysuria
NA	NA	
NA	NA	
NA	NA	Should not be used in pediatric patients less than two years of age. Should not be used in patients in comatose states, or in patients who have shown a previous hypersensitivity to this medication or to other phenothiazines. Should not be used in the treatment of lower respiratory tract symptoms including asthma
NA	NA	
NA	NA	
Extensively metabolized in the liver	Around 64% of dose excreted as unchanged drug in urine	

Other treatment for urticaria

Other treatments		Approved Age	Pregnancy category	Breastfeeding
Montelukast	FDA	≥ 6 mon	B	Not known if it is excreted in human milk. (It is not known if montelukast is excreted in human milk.)
	EMA	NA	NA	NA
	TFDA	≥ 6 mon	Only use when necessary	Need for caution
	Micromedex	≥ 6 mon	Fetal risk cannot be ruled out	Infant risk cannot be ruled out

Metabolism/ dose for hepatic impairment	Elimination/dose for renal impairment	Contraindications
No dosage adjustment is required. (No dosage adjustment is required in patients with mild-to-moderate hepatic insufficiency.)	No dosage adjustment is required. (No dosage adjustment is recommended in patients with renal insufficiency.)	
NA	NA	Should not be used in patients who have shown a previous hypersensitivity to this medication or any of its inactive ingredients
NA	NA	
Extensively metabolized in the liver via CYP2C8 No dosage adjustment is necessary for hepatic impairment	Less than 0.2% of dose is excreted in the urine No dose adjustments is needed for renal impairment	

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