

Use of Dapsone in the Treatment of Chronic Idiopathic and Autoimmune Urticaria

Sydney E. Liang, BS; Rachel Hoffmann, MD; Erik Peterson, BA; Nicholas A. Soter, MD

 Supplemental content

IMPORTANCE The first-line treatment for patients with chronic spontaneous urticaria (CSU), which is divided into idiopathic and autoimmune subtypes, consists of H₁-antihistamines. However, limited evidence guides the treatment of CSU after maximal therapy with antihistamines fails. Two randomized clinical trials suggest that dapsone may be a successful second-line therapy.

OBJECTIVE To evaluate the efficacy and safety of dapsone therapy in patients with CSU.

DESIGN, SETTING, AND PARTICIPANTS This retrospective medical record review included 79 patients with CSU treated with dapsone who presented to the tertiary care academic medical center at the New York University School of Medicine, New York, New York, from January 1, 2005, through April 15, 2017. Follow-up was completed on February 28, 2018. Data were analyzed from March 1 through May 31, 2018.

EXPOSURES Treatment with oral dapsone for CSU.

MAIN OUTCOMES AND MEASURES Efficacy of dapsone therapy for CSU was evaluated as improvement, complete response, and remission.

RESULTS Seventy-nine patients (65% women; mean [SD] age, 49.8 [16.1] years [range, 20-79 years]) were included in the analysis. Forty-five patients had chronic idiopathic urticaria and 34 had chronic autoimmune urticaria. Improvement in CSU was observed in 62 patients (78%) (36 [80%] with idiopathic and 26 [76%] with autoimmune disease) with dapsone. Mean (SD) time to improvement was 1.1 (1.0) months. A complete response was achieved in 29 (47%) of these 62 patients (16 [44%] with idiopathic and 13 [50%] with autoimmune disease). Mean (SD) time to complete response was 5.2 (5.2) months. Dapsone therapy was tapered in 21 patients after a mean (SD) of 2.4 (2.2) months and discontinued in 18. Ten patients experienced remission with no subsequent flares, even after dapsone therapy was discontinued with follow-up of 0.3 to 10.0 months. Sixteen patients experienced mild adverse effects. Two serious adverse effects were reported.

CONCLUSIONS AND RELEVANCE Results of this study suggest that dapsone is a useful and well-tolerated second-line therapy for patients with CSU in whom antihistamines and other first-line agents have failed.

JAMA Dermatol. doi:10.1001/jamadermatol.2018.3715
Published online November 21, 2018.

Author Affiliations: currently a medical student at New York University School of Medicine, New York, New York (Liang, Peterson); The Ronald O. Perleman Department of Dermatology, New York University School of Medicine, New York, New York (Hoffmann, Soter).

Corresponding Author: Nicholas A. Soter, MD, The Ronald O. Perleman Department of Dermatology, New York University School of Medicine, 240 E 38th St, 12th Floor, New York, NY 10016 (nicholas.soter@nyulangone.org).

Chronic spontaneous urticaria (CSU), which is divided into idiopathic and autoimmune subtypes, is a common and disabling disease.¹ The first-line treatment consists of second-generation H₁-antihistamines, which may be titrated up to 4 times the recommended dose.^{1,2} However, almost 50% of patients incompletely respond to antihistamines,³ and many other treatments are used.^{2,4}

Dapsone is a sulfone antibiotic with antimicrobial and anti-inflammatory properties.⁵ Only 2 small, randomized clinical trials exist on the use of dapsone in CSU.^{6,7} Owing to our experience as a referral center for many patients with CSU, we present a retrospective medical record review of 79 patients with CSU who were treated with dapsone.

Methods

This retrospective medical record review was approved by the institutional review board at New York University Langone Health, New York, New York, which waived the need for informed consent for the use of deidentified data. Individuals aged 18 to 89 years, diagnosed with CSU, and treated with dapsone from January 1, 2005, through April 15, 2017, were included. All patients (Table 1) underwent evaluation by one of us (N.A.S.) in his faculty practice or the resident clinic. A standardized urticaria history was completed on presentation (eFigure in the Supplement), and subsequent visits were performed or supervised by the same physician with similar questions asked. A serum chronic urticaria test was performed to diagnose autoimmune urticaria if the results were positive. All patients had laboratory testing for glucose-6-phosphate dehydrogenase levels before initiating dapsone therapy.

Dapsone therapy was initiated at 25 or 50 mg/d with the existing doses of antihistamines and titrated to a maximal individual effective dose in each patient by increments of 25 or 50 mg/d at intervals of 2 to 4 weeks. Response to treatment was based on patient interviews and results of physical examinations that were performed during office visits. Improvement was indicated by a decrease in pruritus, a decrease in the duration and number of wheals, a decrease in the number and frequency of CSU episodes, or a decrease in systemic symptoms. Complete response was defined by the complete absence of urticaria, angioedema, and systemic symptoms, and sustained complete response was defined as 2 or more consecutive months of complete response. After 2 months of sustained complete response, dapsone therapy was tapered by 25 or 50 mg/d at intervals of 2 to 4 weeks and, if possible, discontinued. Remission was defined as complete response with no subsequent flares up to the end of the medical record review on February 28, 2018.

Laboratory monitoring during treatment included a complete blood cell count, reticulocyte count, and comprehensive metabolic panel with each increase in dose of dapsone and approximately every 3 months after a stable dose was achieved. Unless otherwise indicated, data are expressed as mean (SD).

Key Points

Question What is the efficacy and safety of dapsone in the treatment of chronic spontaneous urticaria?

Findings In this medical record review, 79 patients with chronic idiopathic or autoimmune urticaria were treated with dapsone. Sixty-two patients experienced improvement, and of these, 29 achieved complete control.

Meaning Dapsone is an effective and well-tolerated second-line therapy for the treatment of chronic spontaneous urticaria.

Results

Our search yielded 155 medical records, of which 79 met inclusion criteria (28 men [35%] and 51 [65%] women; mean age, 49.8 [16.1] years). Table 1 displays patient characteristics. Forty-five patients had chronic idiopathic urticaria, 34 had chronic autoimmune urticaria, and 53 had concomitant angioedema. Seventy-one patients had more than 1 type of urticaria. The mean duration of urticaria at presentation was 37.5 (61.2) months (median, 12.0 months; range, 1.0-240.0 months).

Before initiating dapsone therapy, all 79 patients had been treated with 1 or more other agents. Prior treatments included first- and second-generation H₁-antihistamines, often as much as 4 times the recommended dose (79 [100%]), leukotriene inhibitors (55 [67%]), prednisone (37 [47%]), H₂ antagonists (28 [35%]), methylprednisolone (9 [11%]), omalizumab (6 [8%]), cyclosporine (5 [6%]), mycophenolate mofetil (3 [4%]), and/or nifedipine (1 [1%]). However, no patients experienced disease control with these treatments, alone or in combination.

The mean maximum dose of dapsone was 118.4 (44.1) mg/d (median, 125.0 mg/d; range, 25.0-200.0 mg/d), and the mean duration of dapsone therapy was 9.0 (13.7) months (median, 5.0 months; range, 0.5-72.0 months) (Table 2). Sixty-two patients (78%) experienced improvement with dapsone, which included 36 of 45 (80%) with idiopathic urticaria and 26 of 34 (76%) with autoimmune urticaria. The mean time to improvement was 1.1 (1.0) months (median, 1.0 month; range, 0.5-7.0 months).

Of the 62 patients who experienced improvement, 29 (47%) experienced a complete response of their CSU as well as concomitant physical urticarias with dapsone. This included 16 of 36 patients (44%) with idiopathic and 13 of 26 (50%) with autoimmune urticaria. The mean time to complete response was 5.2 (5.2) months (median, 4.0 months; range, <0.5 to 29.0 months). Twenty-seven of these patients (93%) had a sustained complete response, which was maintained a mean of 6.7 (4.0) months (median, 6.0 months; range, 2.0-16.0 months).

After a sustained complete response, dapsone therapy could be tapered in 21 of the 27 patients (78%). The mean interval from sustained complete response to initiation of dapsone tapering was 2.4 (2.2) months (median, 2.0 months; range, 0-6.5 months). Of the 6 patients for whom dapsone therapy was not tapered, 3 experienced a flare in the setting of decreasing antihistamine doses and 3 experienced subsequent CSU flares that prevented tapering and/or required initiation of a different therapy. Dapsone therapy was successfully discontinued in 18 of the 21

Table 1. Patient Demographics and Characteristics

Characteristic	Data (n = 79)
Age at diagnosis, y	
Mean (SD)	49.8 (16.1)
Median (range)	53 (20-79)
Sex, No. (%)	
Men	28 (35)
Women	51 (65)
Duration of urticaria at presentation, mo ^a	
Mean (SD)	37.5 (61.2)
Median (range)	12 (1-240)
Diagnosis, No. (%)	
Chronic idiopathic urticaria	45 (57)
Chronic autoimmune urticaria ^b	34 (43)
Angioedema	53 (67)
Dermatographism	70 (89)
Delayed-pressure urticaria	18 (23)
Cholinergic urticaria	12 (15)
Other urticaria ^c	4 (5)
Prior treatments, No. (%) ^d	
H ₁ -antihistamines	79 (100)
Leukotriene inhibitors	55 (70)
Prednisone	37 (47)
H ₂ antagonist	28 (35)
Methylprednisolone	9 (11)
Omalizumab	6 (8)
Cyclosporine	5 (6)
Mycophenolate mofetil	3 (4)
Nifedipine	1 (1)

^a Several patients presented with acute urticaria, which persisted after presentation to become chronic urticaria.

^b Twenty-seven of the 34 patients with chronic autoimmune urticaria had a positive chronic urticaria test value recorded in their medical record; 7 had a positive chronic urticaria test value from at an outside institution before presentation.

^c Includes salicylate- and drug-induced urticaria.

^d No patients experienced control with these treatments alone or in combination.

patients (86%) in whom it was tapered. Three patients had a CSU flare in the setting of dapsone therapy tapering. Of the 18 patients who discontinued dapsone therapy, 10 (56%) experienced remission after dapsone therapy was discontinued during a mean follow-up time of 2.5 (3.1) months (median, 2.0 months; range, 0.25-10.0 months). Eight patients experienced a flare after dapsone therapy was discontinued.

Sixteen patients experienced predominantly mild adverse effects (Table 3). The most frequent adverse effect was an elevated reticulocyte count of greater than 4.9%, which was observed in 4 patients (5%) patients, with a mean increase of 4.8% (2.5%) (median, 3.6%; range, 2.9%-9.0%) (to convert reticulocyte count to proportion of red blood cells, multiply by 0.01). Three of these 4 patients also experienced a decrease in hemoglobin level of below or equal to 10.7 g/dL, with a mean decrease of 2.8 (0.6) g/dL (median, 3.0 g/dL; range, 2.0-3.4 g/dL) (to convert to grams per liter, multiply by 10.0). Two patients experienced serious adverse effects, one with methemoglobinemia and one with a drug reaction with eosinophilia and systemic symptoms, which required dapsone therapy cessation.

Discussion

Second-generation H₁-antihistamines, given at as many as 4 times the usual dose, are the first-line and most frequently used medications in CSU.^{1,2} However, in patients for whom maximal therapy with antihistamines fails, the level of evidence on which medication to subsequently base treatment is limited according to the latest guidelines from the European Academy of Allergy and Clinical Immunology, Global Allergy and Asthma European Network, European Dermatology Forum, and World Allergy Organization.²

Dapsone, an anti-inflammatory and immunomodulatory agent, is used to treat several dermatologic conditions, including CSU.⁵ Although dapsone's precise mechanism of action in CSU has not been fully elucidated, it has been proposed that dapsone acts by inhibiting prostaglandin and leukotriene activity, disrupting neutrophil adhesion molecules, suppressing neutrophil recruitment and activation signals,⁸ and interfering with the release or function of neutrophil lysosomal enzymes, such as myeloperoxidase.⁹

Only 2 small, prospective randomized clinical trials exist on the use of dapsone in CSU.^{6,7} In a 2008 nonblinded trial,⁶ the use of dapsone, 50 mg, with desloratadine, 10 mg (n = 38), was compared with desloratadine, 10 mg, alone (n = 27) in patients with chronic idiopathic urticaria. Among patients treated with dapsone, the authors found significant improvement in overall severity ($P < .001$) and in wheals and pruritus ($P < .001$) when compared with baseline. Complete response occurred in 9 of the 38 patients treated with dapsone (24%), with sustained complete response in 5 of those 9 (56%). No patients receiving antihistamine alone achieved a complete response.⁶ In a 2014 double-blind placebo-controlled trial,⁷ the use of dapsone, 100 mg/d, was examined in refractory chronic idiopathic urticaria, and significant improvement in overall severity ($P = .04$) and self-reported pruritus ($P = .047$) was detected with dapsone (n = 10) when compared with placebo (n = 12). Complete response occurred in 3 of the 10 patients treated with dapsone (30%) and in 0 of the 12 patients receiving placebo.⁷ Although both of these studies found significant improvement in overall severity and pruritus scores among patients treated with dapsone, they had short follow-up times of 6 months and 6 weeks, respectively; therefore, whether their complete responses were sustained in the long term was unknown. In addition, neither study included patients explicitly diagnosed with chronic autoimmune urticaria.^{6,7} To our knowledge, no studies have examined the use of dapsone in patients with chronic autoimmune urticaria in the literature.

In our study, which to our knowledge contains the largest number of patients to date, we examined the efficacy of dapsone in patients with chronic idiopathic as well as autoimmune urticaria. Sixty-two of our patients (78%), specifically 36 (80%) with idiopathic and 26 (76%) with autoimmune urticaria, experienced improvement with dapsone after a mean of 1.1 (1.0) months. Twenty-nine patients (37%) achieved a complete response, which included 16 (36%) with idiopathic and 13 (38%) with autoimmune urticaria, which is greater than response rates with this agent and other second-line agents

Table 2. Dapsone Treatment Data

Treatment Data	Disease		
	Chronic Idiopathic Urticaria (n = 45)	Chronic Autoimmune Urticaria (n = 34)	Chronic Spontaneous Urticaria (n = 79)
Time to initiating dapsone therapy, mo			
Mean (SD)	15.7 (36.8)	8.2 (21.0)	12.5 (31.2)
Median (range)	5.0 (0.5-185.0)	3.8 (0.5-124.0)	4.0 (0.5-185.0)
Duration of dapsone therapy, mo			
Mean (SD)	10.0 (14.8)	7.7 (12.0)	9.0 (13.7)
Median (range)	5.5 (0.5-72.0)	3.5 (0.5-68.0)	5.0 (0.5-72.0)
Maximum daily dapsone dose, mg			
Mean (SD)	117.8 (44.6)	119.1 (43.3)	118.4 (44.1)
Median (range)	125.0 (25.0-200.0)	125.0 (50.0-200.0)	125.0 (25.0-200.0)
Improvement with dapsone, No./Total No. (%) ^a	36/45 (80)	26/34 (76)	62/79 (78)
Time to improvement, mo			
Mean (SD)	1.2 (1.2)	1.0 (0.6)	1.1 (1.0)
Median (range)	1.0 (0.5-7.0)	1.0 (0.5-3.0)	1.0 (0.5-7.0)
Complete response with dapsone, No./Total No. (%) ^b			
All	16/45 (36)	13/34 (38)	29/79 (37)
With improvement	16/36 (44)	13/26 (50)	29/62 (47)
Time to complete response, mo ^c			
Mean (SD)	5.0 (6.3)	5.6 (3.1)	5.2 (5.2)
Median (range)	3.8 (1.0-29.0)	5.0 (<0.5-12.0)	4.0 (<0.5-294.0)
Sustained complete response, No./Total No. (%) ^d			
All	14/45 (31)	13/34 (38)	27/79 (34)
With complete response	14/16 (87)	13/13 (100)	27/29 (93)
Duration of sustained complete response, mo			
Mean (SD)	7.2 (2.7)	6.2 (5.0)	6.7 (4.0)
Median (range)	8.0 (2.8-11.0)	4.0 (2.0-16.0)	6.0 (2.0-16.0)
Able to taper therapy, No./Total No. (%) with sustained complete response	11/14 (77)	10/13 (77)	21/27 (78)
Interval from sustained complete response to taper, mo			
Mean (SD)	3.0 (2.4)	1.9 (1.8)	2.4 (2.2)
Median (range)	2.0 (0-6.5)	1.3 (0-6.0)	2.0 (0-6.5)
Experienced flare with therapy taper, No./Total No. (%) able to taper	1/11 (9)	2/10 (20)	3/21 (14)
Able to discontinue, No./Total No. (%) with sustained complete response	10/14 (71)	8/13 (62)	18/27 (67)
Achieved remission, No./Total No. (%) ^e			
All	4/45 (9)	6/34 (18)	10/79 (13)
With complete response	4/16 (25)	6/13 (46)	10/29 (34)
Able to discontinue therapy	4/10 (40)	6/8 (75)	10/18 (56)
Remission follow-up time after discontinuing dapsone, mo			
Mean (SD)	1.1 (1.1)	3.4 (3.6)	2.5 (3.1)
Median (range)	0.8 (0-3.0)	2.0 (0.3-10.0)	2.0 (0.3-10.0)
Flare after discontinuing dapsone therapy, No./Total No. (%)			
All	6/45 (13)	2/34 (6)	8/79 (10)
With complete response	6/16 (38)	2/13 (15)	8/29 (28)
Able to discontinue therapy	6/10 (60)	2/8 (25)	8/18 (44)
Time to flare after discontinuing dapsone, mo			
Mean (SD)	3.3 (2.0)	1.8 (1.3)	2.9 (2.0)
Median (range)	2.5 (0.8-6.0)	1.8 (0.5-3.0)	2.5 (0.5-6.0)

^a Indicated by a decrease in pruritus, a decrease in duration and number of wheals, a decrease in number and frequency of chronic spontaneous urticaria episodes, or a decrease in systemic symptoms.

^b Defined as complete absence of urticaria, angioedema, and systemic symptoms.

^c Includes 28 of the 29 patients who achieved complete response; 1 patient

achieved complete response in less than 0.5 months of dapsone therapy.

^d Defined as at least 2 consecutive months of complete response.

^e Defined as complete response with no subsequent flares to the end of medical record review.

reported in the literature.^{3,6,7} The mean time to complete response was 5.2 (5.2) months. In addition, 10 patients (13%), which included 4 (9%) with idiopathic and 6 (18%) with autoimmune urticaria, experienced remission of their disease with no subsequent flares, even after dapsone therapy discontinuation. Remissions were prolonged for as long as 16 months. Our

remission rate and durations are consistent with or greater than those reported in other studies with the use of dapsone.^{6,10-12} Thus, our study suggests that dapsone may be a remitting agent for some patients with CSU.

Dapsone was generally well tolerated. Most adverse effects were primarily mild, such as an elevation in reticulocyte

Table 3. Adverse Effects in 16 Patients^a

Adverse Effect	Data
Elevated reticulocyte count, No. (%)	4 (5)
Increase in reticulocyte count, %	
Mean (SD)	4.8 (2.5)
Median (range)	3.6 (2.9-9.0)
Decreased hemoglobin level, No. (%)	3 (4)
Decrease in hemoglobin level, g/dL	
Mean (SD)	2.8 (0.6)
Median (range)	3.0 (2.0-3.4)
Dizziness or light-headedness, No. (%)	4 (5)
Fatigue, No. (%)	3 (4)
Dyspnea, No. (%)	2 (2)
Elevated liver transaminase enzyme levels, No. (%)	2 (2)
Gastrointestinal tract symptoms, No. (%)	1 (1)
Decreased white blood cell count, No. (%)	1 (1)
Methemoglobinemia, No. (%) ^b	1 (1)
DRESS, No. (%)	1 (1)

Abbreviation: DRESS, drug reaction with eosinophilia and systemic symptoms.

SI conversion factors: To convert hemoglobin to grams per liter, multiply by 10.0; reticulocyte count to proportion of red blood cells, multiply by 0.01.

^a Sixteen patients experienced 22 total adverse effects; 5 experienced more than 1 adverse effect.

^b Methemoglobinemia was 8%, with associated chills, myalgia, and fatigue and was accompanied by a 3.6 g/dL decrease in hemoglobin and 5.2% increase in reticulocyte count at the time of discontinuing dapsone therapy.

count often associated with a decrease in hemoglobin level, and most did not require dapsone therapy discontinuation, which is consistent with other studies with this agent.^{6,7,13-16} These adverse effects are reversible and predictable, because approximately 80% of patients taking dapsone, 50 mg or greater, experience a drop of hemoglobin level of at least 1 g/dL.^{13,14}

One patient developed a drug reaction with eosinophilia and systemic symptoms, and another developed methemoglobinemia; these were considered serious adverse effects.

Our study has several limitations. Beyond the number of wheals and CSU episodes, disease severity was not quantitatively assessed using an objective measure. In addition, owing to the retrospective nature of our study, we did not have a control group, which makes it challenging to definitively distinguish between treatment response and the natural history of disease. Our study also describes a relatively small number of patients. However, one benefit of our study over other retrospective reviews is the consistency in treating physician throughout the study, because all patients were seen by the physician in his faculty practice or the resident clinic, and all patients had a standardized urticaria history taken on presentation.

Conclusions

Results of this study suggest that dapsone is an effective and well-tolerated second-line therapy for patients with refractory CSU, including the idiopathic and autoimmune subtypes. Of the 79 patients with CSU treated with dapsone at our center, 62 (78%) experienced improvement, 29 (37%) experienced a complete response, and 10 (13%) experienced remission of their CSU. For most patients, improvement occurred quickly, within approximately 1 month, and complete response occurred at approximately 5 months. Additional prospective studies are needed to further delineate the use of dapsone in the treatment of chronic idiopathic and autoimmune urticaria.

ARTICLE INFORMATION

Accepted for Publication: August 26, 2018.

Published Online: November 21, 2018.

doi:10.1001/jamadermatol.2018.3715

Author Contributions: Ms Liang and Dr Soter had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: All authors.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: All authors.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Liang.

Administrative, technical, or material support:

Liang, Peterson, Soter.

Supervision: Hoffmann, Soter.

Conflict of Interest Disclosures: None reported.

REFERENCES

- Maurer M, Weller K, Bindslev-Jensen C, et al. Unmet clinical needs in chronic spontaneous urticaria: a GA²LEN task force report. *Allergy*. 2011;66(3):317-330. doi:10.1111/j.1398-9995.2010.02496.x
- 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: the 2017 revision and update. *Allergy*. 2018;73(7):1393-1414. doi:10.1111/all.13397
- Kaplan AP. Diagnosis, pathogenesis, and treatment of chronic spontaneous urticaria. *Allergy*

Asthma Proc. 2018;39(3):184-190. doi:10.2500/aap.2018.39.4121

4. Mehta A, Godse K, Patil S, Nadkarni N, Gautam M. Treatment of refractory chronic urticaria. *Indian J Dermatol*. 2015;60(3):230-237. doi:10.4103/0019-5154.156325

5. Zhu YI, Stiller MJ. Dapsone and sulfones in dermatology: overview and update. *J Am Acad Dermatol*. 2001;45(3):420-434. doi:10.1067/mjd.2001.114733

6. Engin B, Ozdemir M. Prospective randomized non-blinded clinical trial on the use of dapsone plus antihistamine vs antihistamine in patients with chronic idiopathic urticaria. *J Eur Acad Dermatol Venereol*. 2008;22(4):481-486. doi:10.1111/j.1468-3083.2007.02510.x

7. Morgan M, Cooke A, Rogers L, Adams-Huet B, Khan DA. Double-blind placebo-controlled trial of dapsone in antihistamine refractory chronic idiopathic urticaria. *J Allergy Clin Immunol Pract*. 2014;2(5):601-606. doi:10.1016/j.jaip.2014.06.004

8. Debol SM, Herron MJ, Nelson RD. Anti-inflammatory action of dapsone: inhibition of neutrophil adherence is associated with inhibition of chemoattractant-induced signal transduction. *J Leukoc Biol*. 1997;62(6):827-836. doi:10.1002/jlb.62.6.827

9. Bozeman PM, Learn DB, Thomas EL. Inhibition of the human leukocyte enzymes myeloperoxidase and eosinophil peroxidase by dapsone. *Biochem*

Pharmacol. 1992;44(3):553-563. doi:10.1016/0006-2952(92)90449-5

10. Boehm I, Bauer R, Bieber T. Urticaria treated with dapsone. *Allergy*. 1999;54(7):765-766. doi:10.1034/j.1398-9995.1999.00187.x

11. Cassano N, D'Argento V, Filotico R, Vena GA. Low-dose dapsone in chronic idiopathic urticaria: preliminary results of an open study. *Acta Derm Venereol*. 2005;85(3):254-255.

12. Noda S, Asano Y, Sato S. Long-term complete resolution of severe chronic idiopathic urticaria after dapsone treatment. *J Dermatol*. 2012;39(5):496-497. doi:10.1111/j.1346-8138.2011.01310.x

13. Byrd SR, Gelber RH. Effect of dapsone on haemoglobin concentration in patients with leprosy. *Lepr Rev*. 1991;62(2):171-178.

14. Grindulis KA, McConkey B. Rheumatoid arthritis: the effects of treatment with dapsone on hemoglobin. *J Rheumatol*. 1984;11(6):776-778.

15. Seth S, Khan DA. The comparative safety of multiple alternative agents in refractory chronic urticaria patients. *J Allergy Clin Immunol Pract*. 2017;5(1):165-170.e2. doi:10.1016/j.jaip.2016.08.010

16. Vancine-Califani SM, De Paula EV, Ozelo MC, Orsi FL, Fabri DR, Annichino-Bizzacchi JM. Efficacy and safety of dapsone as a second-line treatment in non-splenectomized adults with immune thrombocytopenic purpura. *Platelets*. 2008;19(7):489-495. doi:10.1080/09537100802315110