

## Supplementary Text

### Draize scale

The Draize scale has four components. Hemorrhage/petechiae is scored on a scale of 0–5, erythema is scored on a scale of 0–4, edema is scored on a scale of 0–4, and pruritus is scored on a scale of 0–2 (see chart below).

<b>Score</b>	<b>Hemorrhage/petechiae</b>	<b>Erythema</b>	<b>Edema</b>	<b>Pruritus</b>
0	No hemorrhage/petechiae	No erythema	No edema	No pruritus
1	≤5 isolated petechiae	Very slight erythema	Very slight edema	Occasional pruritus
2	>5 isolated petechiae	Well-defined erythema	Slight edema	Constant pruritus
3	Many petechiae	Moderate/severe erythema	Moderate edema	
4	Spots of blood on the surface	Severe erythema	Severe edema	
5	Frank bleeding			

**Supplementary Table 1. Components of the 40 mg/0.8 mL and 40 mg/0.4 mL Adalimumab Formulations**

<b>40 mg/0.8 mL Formulation</b>	<b>40 mg/0.4 mL Formulation</b>
<ul style="list-style-type: none"><li>• Adalimumab</li><li>• Mannitol</li><li>• Polysorbate 80</li><li>• Water for injection</li><li>• Citric acid monohydrate</li><li>• Sodium citrate</li><li>• Disodium hydrogen phosphate dehydrate</li><li>• Sodium dihydrogen phosphate dehydrate</li><li>• Sodium chloride</li><li>• Sodium hydroxide added as necessary to adjust pH</li></ul>	<ul style="list-style-type: none"><li>• Adalimumab</li><li>• Mannitol</li><li>• Polysorbate 80</li><li>• Water for injection</li></ul>

**Supplementary Table 2. Frequency of Needle Pain Immediately After Injection in Patients Who Were Able to Tell the Difference**

	<b>Needle Entry</b>	<b>Solution</b>
<b>Most Pain Caused by:</b>	<b>n (%)</b>	<b>n (%)</b>
<i>Study 1</i>		
40 mg/0.8 mL formulation	14 (25.5)	36 (65.5)
40 mg/0.4 mL formulation	24 (43.6)	10 (18.2)
<i>Study 2</i>		
40 mg/0.8 mL formulation	12 (21.8)	43 (78.2)
40 mg/0.4 mL formulation	21 (38.2)	8 (14.5)

N=55 for the analysis in both Study 1 and Study 2, based on all patients who were able to tell the difference between needle entry and the solution for  $\geq 1$  of the injections.

**Supplementary Table 3. Draize Scale Ratings 10 and 30 Minutes After Injection in Study 1 (cITT Population)**

Time after injection	Frequency of Hemorrhage/Petechiae					
	None n (%)	≤5 Petechiae n (%)	>5 Petechiae n (%)	Many petechiae n (%)	Spots of blood n (%)	Bleeding n (%)
10 minutes						
40 mg/0.8 mL formulation	57 (91.9)	5 (8.1)	0	0	0	0
40 mg/0.4 mL formulation	60 (96.8)	2 (3.2)	0	0	0	
30 minutes						
40 mg/0.8 mL formulation	61 (98.4)	1 (1.6)	0	0	0	0
40 mg/0.4 mL formulation	61 (98.4)	1 (1.6)	0	0	0	0
Time after injection	Frequency of Erythema					
	None n (%)	Very slight n (%)	Well defined n (%)	Moderate/severe n (%)	Severe n (%)	
10 minutes						
40 mg/0.8 mL formulation	43 (69.4)	16 (25.8)	3 (4.8)	0	0	
40 mg/0.4 mL formulation	40 (64.5)	21 (33.9)	1 (1.6)	0	0	
30 minutes						
40 mg/0.8 mL formulation	47 (75.8)	11 (17.7)	4 (6.5)	0	0	
40 mg/0.4 mL formulation	45 (72.6)	14 (22.6)	3 (4.8)	0	0	
Time after injection	Frequency of Edema					
	None n (%)	Very slight n (%)	Slight n (%)	Moderate n (%)	Severe n (%)	
10 minutes						
40 mg/0.8 mL formulation	50 (80.6)	10 (16.1)	2 (3.2)	0	0	
40 mg/0.4 mL formulation	52 (83.9)	8 (12.9)	2 (3.2)	0	0	
30 minutes						
40 mg/0.8 mL formulation	53 (85.5)	6 (9.7)	3 (4.8)	0	0	
40 mg/0.4 mL formulation	53 (85.5)	8 (12.9)	1 (1.6)	0	0	

Time after injection	Frequency of Pruritus		
	None n (%)	Occasional pruritus n (%)	Constant pruritus n (%)
10 minutes			
40 mg/0.8 mL formulation	62 (100)	0	0
40 mg/0.4 mL formulation	61 (98.4)	1 (1.6)	0
30 minutes			
40 mg/0.8 mL formulation	61 (98.4)	1 (1.6)	0
40 mg/0.4 mL formulation	61 (98.4)	1 (1.6)	0

cITT=crossover intent to treat.

**Supplementary Table 4. Draize Scale Ratings 10 and 30 Minutes After Injection in Study 2 (cITT Population)**

<b>Frequency of Hemorrhage/Petechiae</b>						
<b>Time after injection</b>	<b>None n (%)</b>	<b>≤5 Petechiae n (%)</b>	<b>&gt;5 Petechiae n (%)</b>	<b>Many petechiae n (%)</b>	<b>Spots of blood n (%)</b>	<b>Bleeding n (%)</b>
10 minutes						
40 mg/0.8 mL formulation	48 (80.0)	12 (20.0)	0	0	0	0
40 mg/0.4 mL formulation	54 (90.0)	6 (10.0)	0	0	0	0
30 minutes						
40 mg/0.8 mL formulation	49 (81.7)	11 (18.3)	0	0	0	0
40 mg/0.4 mL formulation	55 (91.7)	5 (8.3)	0	0	0	0
<b>Frequency of Erythema</b>						
<b>Time after injection</b>	<b>None n (%)</b>	<b>Very slight n (%)</b>	<b>Well defined n (%)</b>	<b>Moderate/severe n (%)</b>	<b>Severe n (%)</b>	
10 minutes						
40 mg/0.8 mL formulation	30 (50.0)	26 (43.3)	4 (6.7)	0	0	
40 mg/0.4 mL formulation	38 (63.3)	15 (25.0)	6 (10.0)	1 (1.7)	0	
30 minutes						
40 mg/0.8 mL formulation	36 (60.0)	20 (33.3)	4 (6.7)	0	0	
40 mg/0.4 mL formulation	45 (75.0)	9 (15.0)	5 (8.3)	1 (1.7)	0	
<b>Frequency of Edema</b>						
<b>Time after injection</b>	<b>None n (%)</b>	<b>Very slight n (%)</b>	<b>Slight n (%)</b>	<b>Moderate n (%)</b>	<b>Severe n (%)</b>	
10 minutes						
40 mg/0.8 mL formulation	54 (90.0)	5 (8.3)	1 (1.7)	0	0	
40 mg/0.4 mL formulation	56 (93.3)	3 (5.0)	1 (1.7)	0	0	
30 minutes						
40 mg/0.8 mL formulation	55 (91.7)	4 (6.7)	1 (1.7)	0	0	
40 mg/0.4 mL formulation	57 (95.0)	2 (3.3)	1 (1.7)	0	0	

<b>Time after injection</b>	<b>Frequency of Pruritus</b>		
	<b>None n (%)</b>	<b>Occasional pruritus n (%)</b>	<b>Constant pruritus n (%)</b>
10 minutes			
40 mg/0.8 mL formulation	59 (98.3)	0	1 (1.7)
40 mg/0.4 mL formulation	57 (95.0)	2 (3.3)	1 (1.7)
30 minutes			
40 mg/0.8 mL formulation	58 (96.7)	1 (1.7)	1 (1.7)
40 mg/0.4 mL formulation	58 (96.7)	0	2 (3.3)

cITT=crossover intent to treat.