

Geïnccludeerde studies en de effectiviteit bij richtlijn Off-label geneesmiddelen 5-6-2023

Table 1 Efficacy of included studies

Author	Disease	Year of publication	Reference (year of publication)	Efficacy/ effectiveness*	Time to effect, wk	Mean duration of remission [range], mo	Concomitant medication (no. of patients)	AE's (no. of events)	SAE's (no. of events)
Alkeraye	AA	2017	77 (2017)	Responders (\geq 50% regrowth): 9/14 (Pred + MTX), 2/6 (pred)	4	Unk	Pred 500 mg/d; 3 ds/mo	None	None
Anuset	AA	2016	78 (2016)	Total hair regrowth (100%): 15/26 Partial hair regrowth (50-100%): 6/26 Regrowth failure (<50%): 5/26	12	27 [6-72]	Pred 20 mg/d (23), "prophylactic osteoporosis treatment"	Acne (2), elevated liver enzymes (4), pneumocystis pneumonia (1), steroidinduced cataract (1), weight gain (4) [both MTX and Pred] (patients)	None
Chartaux	AA	2010	74 (2010)	Complete hair regrowth: MTX+CST : 12/19 MTX: 8/14	12	Unk	CST 10-20 mg/d (19)	Elevated liver enzymes (4), lymphocytopenia (1), persistent nausea (2) (patients)	None

Droitcourt	AA	2012	59 (2012)	Total or partial regrowth (after 12 mo): 14/20 Total regrowth (after 18 mo): 10/14 Partial regrowth (after 18 mo): 4/14	10 (median)	Unk	IV Pred 500 mg/d, 3 d/mo for 3 mo, FA 5 mg	Nausea (2), neutropenia (1) (patients)	None
Firooz	AA	2013	80 (2013)	Regrowth of terminal hairs: 8/10	7.2	Unk	OCS (10)	Acne (2), amenorrhea (1), anaemia (1), herpes infection (1), hypertension (1), muscle cramp (2), weight gain (1)	None
Hammerschmidt	AA	2014	75 (2014)	>50% regrowth: 21/31	Unk	6.3 mo (3)	IL CST, MNX, SCS	Elevated liver enzymes (2), leukopenia (3), nausea, epigastric pain and diarrhoea (3)	None
Joly	AA	2006	81 (2006)	Complete regrowth: Pred+MTX : 11/16 MTX: 3/6	Unk	Unk	Or Pred 10-20 mg/d (16)	Abdominal pain, nausea, vomiting (1)	Unk
Lim	AA	2017	67 (2017)	Complete response (100% regrowth): 14/29 Partial response	Unk	Unk	FA (29)	Elevated liver enzymes (3), gastrointestinal discomfort (3), lymphopenia (1), reactivation of	Unk

				75-90% regrowth: 12/29 Poor response <50% regrowth: 3/29				pulmonary tuberculosis (1)	
Thi Van	AA	2019	76 (2019)	Good response: 23/38 Medium response: 9/38 Poor response: 6/8	4	Unk	Pred 24 mg/d, 3 ds/week (38)	None	Unk
Vano-Galvan	AA	2017	84 (2017)	Complete response >75% regrowth: MTX: 0/10 MTX+Pred : 3/5 Partial response <75% regrowth: MTX: 5/10 MTX+Pred : 1/5	6.8 - 12	Unk [6.3-6.8]	Pred 0.5-1 mg/kg/d (5)	Elevated liver enzymes (4), weight gain (3)	None
Chong	PedAA	2017	79 (2017)	Good response (≥ 50% hair	8	Unk	OCS 10 mg/kg/d, 3 d/mo for 3 mo	Abdominal discomfort (Unk)	None

				regrowth): 6/14					
Landis	PedAA	2017	82 (2017)	Complete response: 4/11	Unk	Unk	Pred (13)	Unk	Unk
Lucas	PedAA	2016	58 (2016)	Partial response 75-99% regrowth: 2/5 Poor response 25-49% regrowth: 1/5 No change or further loss: 2/5	Unk	Unk	FA (5)	Nausea (1)	None
Royer	PedAA	2011	83 (2011)	Regrowth >50%: 5/14 Regrowth <50%: 9/14	12-27	Unk	SCS (8)	Herpes zoster (1), nausea (1)	None
Anderson	AD	2019	87 (2019)	IGA 0-5: 6-9 months FU: 2.9 12-15 months FU: 2.4 Final visit: 2.7	< 8	Unk	TCS (51), nonsteroidal topicals (29)	Blurry vision (3), cellulitis (2), eczema herpeticum (1), fatigue (14), folliculitis (1), GI discomfort (17), headaches (9), low haematocrit and haemoglobin (2), molluscum (8), mouth sores (3), ocular herpes	Unk

								simplex (1), ringworm (1), staphylococcus aureus superinfection (22), transient elevated liver enzymes (5), verruca vulgaris (1) (patients)	
Baum	AD	2019	33 (2019)	Disease severity 6 Months: mild 20; moderate 7; severe 3	Unk	Unk	FA 5 mg/d, CST	GI discomfort (3), alopecia (1)	None
Delcasso	AD	2018	96 (2018)	SCORAD 50: After 3 months: 7/14 After 6 months: 5/8 After 12 months: 9/12	Unk	Unk	EM +/- TCS (20)	GI discomfort (5), headache/weakness (5), hepatic cytolysis (3), infectious (3), lymphopenia (3) (patients)	None
Gerbens+	AD	2018	88 (2018)	MEAN absolute SCORAD reduction: MTX: 32.1 AZA: 32.1	Unk	Unk	AB, TCI, TCS, OCS	Blood and lymphatic system disorders (14), cardiovascular disorders (6), ear and labyrinth disorders (4), gastrointestinal disorders (31), general and	Cholera (1), exacerbation of AD (1), myocardial infarction (2), respiratory problems (2), social reasons after trauma (1)

								administration site conditions (25), hepatobiliary disorders (19), immune system disorders (1), infections (86), injury, poisoning and procedural complications (9), metabolism and nutrition disorders (1), musculoskeletal and connective tissue disorders (21), neoplasms (6), nervous system disorders (22), psychiatric disorders (3), renal and urinary disorders (6), reproductive system and breast disorders (2), respiratory, thoracic and mediastinal disorders (19), skin and subcutaneous tissue disorders (30), surgical and medical procedures (2)	
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Goujon	AD	2006	94 (2006)	>70% improvement: 13/20	2-8	Unk	TCI, TCS	Elevated liver enzymes (2), lymphopenia (1), nausea (4)	Unk
Goujon	AD	2017	28 (2017)	SCORAD 50 after 8 weeks: MTX: 4/50 CSA: 18/43 SCORAD 50 after 24 weeks: MTX: 9/24 CSA: 22/31	Unk	Unk	Em, FA 5mg/d (50), TCI, TCI	Acne/virus papilloma (1), elevated liver enzymes (1), fatigue (6), gastrointestinal disorders (9), headache (1), infections (12), lymphocytopenia (1)	None
Hegazy	AD	2017	85 (2017)	Complete response: 8/37	Unk	Unk	Unk	Unk side effects (3)	Unk
Ho	AD	2018	21 (2018)	Excellent control: >75%	12-24	Unk	Em, TCI, TCS	Unk	Unk
Lyakhovitsky	AD	2010	54 (2010)	Responders: 16/20	9.95 (mean), 2-12 (range)	Unk	FA (20), SAH, TCS	Elevated liver enzymes (5), nausea (5), peripheral neuropathy (1)	None
Mittal	AD	2011	93 (2011)	Excellent response: 7/15 Good response: 3/15 Poor response: 5/15	Unk	Unk	SCS, TCS	None	None

Politeik	AD	2016	98 (2016)	PGA1, good effect: 38/89 PGA2, moderate effect: 28/89 PGA3, failure of treatment: 12/89 Excluded: 11/89	Unk	Unk	Prednisolone 10-30 mg/d (26)	Aggravation of rosacea (1), alopecia (1), concentration problems (1), condylomata acuminata (1), depressive discomfort (1), elevated liver enzymes (2), fatigue (4), folliculitis (1), flu-like discomfort (1), gastrointestinal complaints (6), headache (3), pneumonia (1), shortness of breath (1), vision changes (1)	Unk
Purvis	AD	2019	51 (2019)	A lot better: 23/43 Slightly better: 2/43 No change: 5/43 Excluded: 13/43	Unk	24 (median)	AB, AH, Em, FA 5 mg (43), TCS	Cataracts (1), gastrointestinal upset (4)	None
Rahman	AD	2014	91 (2014)	Good - excellent response: 23/30 No	12	Unk	Unk	Unk	Unk

				response: 7/30					
Roekevisch+	AD	2018	42 (2018)	SCORAD reduction (ITT) MTX: 37.8 AZA: 32.6	Unk	Unk	FA, weekly 5 mg (17)	Blood and lymphatic system disorders (11), eye disorders (4), gastrointestinal disorders (26), general disorders and administration site conditions (22), hepatobiliary disorders (11), infections (52), injury, poisoning, and precdural complications (4), musculoskeletal and connective tissue disorders (16), neoplasms benign, malignant, and unspecified (3), nervous system disorders (2), renal and urinary disorders (6), reproductive system and breast disorders (2), respiratory, thoracic, and medistinal disorders (1), skin and	Exacerbations AD (1), hospitalizatio n because of psychiatric comorbidity (1)

								subcutaneous tissue disorders (26), surgical and medical procedures (2)	
Schram	AD	2011	43 (2011)	MEAN absolute SCORAD reduction: MTX: 22.8 AZA: 21.7	Unk	Unk	FA 5 mg (20)	Abnormalities in blood count (6), exacerbation of their eczema (3), gastrointestinal complaints (11), infections (14), increased liver enzymes (7)	None
Shah	AD	2018	30 (2018)	Excellent improvement: >75% 38/41 Good improvement: 50-75% 2/41 Partial improvement: 25-50% 1/41	4-6	Unk	AB (14), CSA 150mg (1), FA 5mg/d, 6ds/week (41), IM TCA (17), tapering doses of Pred (2), valacyclovir (1)	Decreased haemoglobin (1), transient decrease in platelets (1), elevated liver enzymes (8), fatigue (3), nausea (5)	None
Syed	AD	2009	92 (2009)	EASI50: MTX: 30/30 Placebo: 0/30	Unk	Unk	Unk	None	Unk
Vedie	AD	2016	95 (2016)	Responders: 15/28 Non-responders: 12/28	Unk	Unk	AZA (7)	Asthenia (3), digestive disorders (4), hepatic dysfunction (7), infections (4), lymphopenia (2)	Folliculitis (1), herpetic recurrences (1)

				Lost to follow-up: 1/28					
Weatherhead	AD	2007	89 (2007)	MEAN SASSAD reduction: 19 units	3	Unk	Em, TCI, TCS	Elevated liver enzymes (2), herpes simplex (1), nausea (2)	None
Zoller	AD	2008	69 (2008)	Complete remission: 6/9 Significant improvement: 3/9	4-8	Unk	Em, FA (9)	Numbness (1)	Unk
Deo	PedAD	2014	61 (2014)	>50% persistent improvement: 75% (patients) SCORAD reduction (n=9): 16 points	8	Unk	FA 5 mg, 2d/wk, TCS, SAB or SCS (3)	Elevated liver enzymes (4), nausea (4)	Serious pyelonephritis needing hospitalisation (1), viral-induced exacerbation of asthma needing hospitalisation (1)
Dvorakova*	PedAD	2017	86 (2017)	Reduction disease severity: IGA decrease 2.35	11.3	Unk	AB (3), AZA (1), CSA (1), OCS (7)	Anaemia, elevated liver enzymes, fatigue (17), hyperbilirubinemia, lymphocytopenia, nausea/vomiting/abdominal pain (14), neutropeania	Bullous impetigo (1), chest tightness/wheezing (1), hospitalisation for community acquired pneumonia (1), poststreptococcal

									glomerulonephritis (1)
EI-Khalawany	PedAD	2013	63 (2013)	MEAN absolute SCORAD reduction: MTX: 26.3 (12 wks), 24.9 (24 wks) CSA: 25.0 (12 wks), 21.0 (24 wks)	3-5	5	FA (20)	Abnormal renal function test (1), anaemia (6), abnormal liver enzymes (5), fatigue (6), fever (1), flu-like symptoms (1), GI discomfort (9), headache (3), leukopenia (2), nausea and vomiting (4), Oral ulceration (4), pancytopenia (1) (patients)	Unk
Knopfel	PedAD	2018	56 (2018)	Complete/almost complete clearance: 10/28 Marked improvement: 13/28 Mild improvement: 4/28 No improvement: 1/28	Unk	Unk	FA (28), OCS (1), TCS (28),	Elevated liver enzymes (5), headache (1), nausea (6), vomiting (1)	None
Roberts	PedAD, NE	2010	45 (2010)	Clear: 16/25 Almost clear: 3/25	42	Unk	FA, weekly 5 mg (25)	Generalized exanthema (1), lethargy (1), mild lethargy (2),	None

				Ongoing: 3/25 Failed: 1/25 Lost to follow-up: 2/25				nausea (4), transient mouth ulceration (1)	
Taieb	PedAD	2019	90 (2019)	IGA decrease at least 2 points: 14/26	Unk	Unk	SCS, TCS	Gastrointestinal discomfort (1), elevated liver enzymes (1), bone marrow suppression (3), mild fatigue (1)	Unk
Kalyoncu	AO SD	2016	154 (2016)	Remission with treatment: CST+MTX : 85/97 CST+MTX +HCQ: 68/81	Unk	18 (medi an)	CST 43.9 mg/d	Unk	Unk
Bakker	BP	2013	47 (2013)	Clinical remission: 5/6	16	Unk	FA 5mg/week (6)	Unk	None
Bara	BP	2003	100 (2003)	Complete remission: 14/16	Unk	3 (in 1 pt)	0.5% clobetasol, max 20 g/d (10)	Anaemia, thrombopenia, colon ulcerations, pancytopenia (events)	None
Dereure	BP	2002	101 (2002)	Maintenance of complete clinical response: 17/18	Unk	7.8	TCS	Decrease in haemoglobin (6), weary (5) (patients)	None
Du-Thanh	BP	2011	99 (2011)	Complete clinical	Unk	2.5 [0.5-7]	Superpotent TCS (70)	Anaemia (7), asthenia (1), depression	Death (6, 1 MTX related due to

				remission: TCS+MTX : 70/70 Maintenan ce of complete clinical remission: MTX: 53/70				(1), GD ulceration (3), interstitial pneumopathy (1), leukopenia (2), liver cytolysis (2), Or ulceration (2), pancytopenia (1), pulmonary embolism (1), respiratory tract infection (1), thrombocytopenia (2)	respiratory tract infection in a setting of MTX related pancytopenia) . Other: Unk.
Heilborn	BP	1999	62 (1999)	Marked and rapid decrease in disease activity: 11/11	<1	>24	FA (3), TCS	Anaemia (1), nausea and anorexia (1), pyoderma (2)	Unk
Kjellman	BP	2008	102 (2008)	Remission rate: MTX: 26/31 MTX+pred : 13/37	44-80	Unk	Pred (37)	Anaemia (1), alveolitis (1), elevated liver enzymes (1) GI discomfort (2)	Unk
Kremer	BP	2017	103 (2017)	Disease control: 6/6	Unk	Unk	CST (6)	Unk	Unk
Kwatra	BP	2013	35 (2013)	Complete remission: 15/16	15.2	Unk	FA 1 mg/d, tapered pred 20-60 mg/d	GI intolerance (1), mild nausea and dyspepsia (2), worsening of anaemia (1)	None
Paul	BP	1994	104 (1994)	Clearance and significant decrease in the need for	4-88	Unk	OCS (8)	Anaemia (1), nausea (1), thrombocytopenia (1)	None

				systemic corticosteroids: 5/8					
Click	DM	2013	106 (2013)	Substantial clearing/ near response: 3/8	Unk	Unk	TCS (8)	Alopecia (1), leukopenia (1)	None
Hornung	DM	2012	27 (2012)	CDASI decrease: 8.6	Unk	Unk	FA 5mg/d (11), Pred 5-20 mg/d (9)	Abcess on injection place (1)	Herpes encephalitis (1), pancytopenia (1), urothelial carcinoma (1)
Kasteler	DM	1997	25 (1997)	CST sparing effect: 10/13	Unk	Unk	Or Pred (10)	Mild malaise (2), transient nausea (6)	Unk
Ramanan	DM	2005	73 (2005)	Median time to discontinuation prednisone: MTX: 10 mo Control: 27 mo	Unk	Unk	AZA (1), CSA (1), Cyclophosphamide (1), HCQ (6), IVIg (15), Pred 2m/g/kg/d (31)	Cellulitis of the metacarpophalangeal joint (1), elevated liver enzymes (6), fungal vaginitis (1), herpes zoster (1)	Unk
Ruperto	DM	2016	105 (2016)	PRINTO20 Pred: 51% Pred+CSA : 70% Pred+MTX : 72%	Unk	Unk	Pred 2 mg/kg, after induction phase tapered to 0.25 mg/kg (46)	Cardiac disorders (1), endocrine disorders (9), eye disorders (3), gastrointestinal disorders (9), general disorders and administration site conditions (2), infections and	Dermohypodermatitis (1), paronychia (1)

								infestations (14), investigations (6), metabolism and nutrition disorders (4), musculoskeletal and connective tissue disorders (4), nervous system disorders (2), psychiatric disorders (4), skin and subcutaneous disorders (9), vascular disorders (1)	
Zieglschmid	DM	1995	107 (1995)	Improvement of cutaneous disease: 9/10	Unk	Unk	OCS, Pred, sunscreens, TCS	Alopecia (1), gastrointestinal distress (2), abnormal liver biopsy (2), lung disease (1), leukopenia (1), mild hepatic fibrosis (2), stomatitis (3)	Unk
Chen	E	2016	108 (2016)	Control of disease: 15/41	Unk	Unk	Unk	Elevated liver enzymes (3), elevated creatinine (3), increased procollagen type III aminoterminal peptide (3), nausea (4) (patients)	None

Shaffrali	E	2003	109 (2003)	Successful response: 4/5 No successful response: 1/5	Unk	Unk	Prednisolone 5 mg/d (1)	Abdominal pain (1), flu-like illness (1), liver enzyme elevation (1)	Unk
Tétart	E	2011	48 (2011)	Complete response: no skin-lesions: 11/15 Partial response: still skin-lesions 4/15	Unk	Unk	FA 10 mg/week (12)	Malaise (1), renal insufficiency (1), stomach aches (2), transient lymphopenia (1)	Unk
Patel	All CE	2018	155 (2018)	Complete clearance: 6/32 Partial clearance: 19/32 Failure: 6/32	Unk	Unk	Unk	Anaemia (5), elevated creatinine (3), elevated liver enzymes (10), fatigue (5), gastrointestinal discomfort (7), leukopenia (2), thrombocytopenia (1)	None
Politiek	HE	2016	157 (2016)	PGA1, good effect: 14/42 PGA2, moderate effect: 14/42 PGA3, failure of treatment:	Unk	Unk	OCS (7)	Fatigue (1), gastrointestinal complaints (3), headache (2), hematoma (1), suspicion of an allergic reaction to folic acid or MTX (1), urinary tract infection (1)	Unk

				9/42 Excluded: 5/42					
Berianu	EF	2015	110 (2015)	Complete remission: 9/16	26	27.1 [7-36]	Pred (15)	Unk	Unk
Lebeaux	EF	2012	111 (2012)	Complete remission: 4/12	Unk	Unk	Pred (12)	Unk	Unk
Mertens	EF	2016	44 (2016)	MEDIAN difference modified skin score: 9	Unk	Unk	Analgesics, antiemetics, FA 5-25 mg/week, SCS ≤15 mg/d	Alopecia (4), gastrointestinal discomfort (9), mild stomatitis (5)	None
Hossain	ENL	2013	156 (2013)	Persistent remission: 9/9	4-8	Unk	Pred tapered from 30-40 mg/d (9)	Crusted scabies (1), extensive pityriasis versicolor (1), facial swelling (1), multiple folliculitis (2), weight gain (1)	None
Naka	GA	2018	52 (2018)	Complete resolution: 3/11 Partial resolution: 4/11 No improvement: 4/11	≥4	Unk	FA (11)	Diarrhoea (2), gastrointestinal upset (2), hair loss (2)	None
Arfi	LE	1995	114 (1995)	Improvement: 16/16	Unk	Unk	Pred 5-30 mg	Elevated liver enzymes (2) (patients)	None

Böhm	LE	1998	32 (1998)	Improvement: 10/12 Complete response: 6/12 Partial response: 4/12	2-6	5-24 (in 5 pts)	GCS systemic (6), TCS (3)	Elevated liver enzymes (3) (patients)	None
Böhm	LE	2003	115 (2003)	Complete response: 15/22 Clinical improvement: 21/22	8 [2-22]	Unk	FA 5 mg/d (Unk)	Elevated liver enzymes and vomitus (10)	None
Carneiro	LE	1999	112 (1999)	Presence of cutaneous lesions: MTX: 3/20 Placebo: 16/21	Unk	Unk	SCS <0.5 mg/kg/d	Diarrhoea (5), dyspepsia (9), elevated liver enzymes (31), infection (4), nausea (6), oral ulcer (6), urticaria (1), weakness (5)	Unk
Fruchter§	LE	2017	116 (2017)	≥50% improvement: 10/19	Unk	Unk	Unk	Adverse events, details unknown (6)	Unk
Gansauge	LE	1997	53 (1997)	Resolve of cutaneous lesions: 8/10	Unk	Unk	Pred, FA	Elevated liver enzymes (2), general malaise (4) (patients)	None
Islam	LE	2012	113 (2012)	Number of patients with skin rash: MTX: 0/13 CQ: 3/19	24	Unk	Unk	Anorexia and nausea (7), elevated liver enzymes (2)	None
Kan	LE	2016	117 (2016)	Both the MTX and AZA	Unk	Unk	HCQ (Unk), OCS (Unk)	Unk	Unk

				clusters appeared to have better clinical outcomes and lower total medical costs relative to CST monotherapy.					
Wenzel	LE	2005	118 (2005)	Significant clinical improvement in CLAI: 42/43	0.5-2	Unk	Antimalarials (19), low dose prednisolone (18)	Elevated liver enzymes (23), fatigue (11), GI discomfort (22), infections (2), minor hair loss (2)	None
Chauhan	LP	2018	119 (2018)	Mean CSS reduction (%): MTX: 53.31 MTX + TCA: 83.53 Mean VAS reduction (%): MTX: 65.31 MTX + TCA: 93.29 Mean	16	Unk	TCA 0.1% oral paste 3 times/d	Anaemia (1), nausea (1)	None

				QLIQ reduction (%) MTX: 80.26 MTX + TCA: 96.00					
Ilyas	LP	2016	38 (2016)	>50% clearance of cutaneous lesions: 35/55	Unk	Unk	FA 1mg/d (55)	Elevated liver enzymes (Unk), leukopenia (Unk), nausea (4)	Unk
Kanwar	LP	2013	37 (2013)	Complete remission: 14/24	2	Unk [3- Unk]	FA 5 mg/d, 2 D/Wk	Deranged liver function abnormality (4), marginal decrease in haemoglobin (6), reduced appetite (2)	Unk
Lajevardi	LP	2016	26 (2016)	TS score reduction: 2.06	Unk	Unk	FA 1mg/d (18)	Epigastric pain (1), nausea (1), pityriasis rosea (1)	Elevation of liver enzymes (1)
Malekzad	LP	2012	31 (2012)	Excellent improvement >75%: 12/15 Mild improvement <75%: 3/15 Unresponsive: 1/15	2	6	Em, FA 1 mg/d (18), SAH	Elevated liver enzymes (1), anaemia (1)	None

Torti	LP	2007	120 (2007)	Substantial improvement: >75% clear 10/18 Moderate improvement 25-75% clear: 6/18 No response <25% clear: 2/18	Unk	Unk	Systemic antifungals, TCS, TAC	Unk	Unk
Turan	LP	2009	121 (2009)	Complete response: 10/11	4	Unk	Unk	Fatigue (1), nausea (1)	Unk
Kortekangas-Savolainen	LP, vulvovaginal	2007	122 (2007)	Long-term symptom relief: 6/6	Unk	6	TCS (3)	Hair loss (1), herpes simplex (1)	Unk
Babahosseini	LPP	2019	123 (2019)	Complete responders: 10/26 Partial responders: 12/26 Non-responders: 4/26	9	Unk	TCS (26)	Anaemia (1), dizziness (1), ecchymosis (1), oedema (1), erythema (2), fatigue (1), headache (1), hypertension (1), LFT rising (7), stupor (1)	Unk
Bakhtiar	LPP	2018	126 (2018)	Effective: 63/79	Unk	Unk	Unk	None	None
Bulbul baskan	LPP	2017	124 (2017)	Clinical response: MTX: 10/10 CSA 6/6	Unk	Unk	Unk	None	None

Kerkemeyer	LPP	2018	125 (2018)	Partial improvement: 1/7	Unk	Unk	Unk	Unk	Unk
Naeini	LPP	2017	127 (2017)	LPP Activity Index points decrease: MTX: 2.46 HCQ: 0.67	Unk	Unk	None	Elevated liver enzymes (1)	None
Karadag	LS	2018	164 (2018)	Median total clinical score reduction: 11.5	Unk	Unk	IV MP 1000mg/d, for 3 D	None	None
Kreuter	LS	2009	165 (2009)	Softening of sclerotic skin and elimination of signs of active disease: 14/15	Unk	>6	MP (15), Pred 5 mg/d (Unk)	Diabetes Mellitus (2), increase of glucose level (2), mild nausea and headache (3), weight gain (1)	None
Fernandez-de-Misa	LyP	2018	158 (2018)	Complete response: 25/51	Unk	Unk	Unk	Unk	Unk
Bulur	M/PedM	2017	128 (2017)	Clinical improvement: 14/14	Unk	Unk	Unk	None	None
Christen-Zaech	M/PedM	2008	129 (2008)	Less induration, violaceous coloration: 38/39	Unk	6 (in 3 pts)	OCS 0.5 - 1 mg/kg/d (34), FA 1 mg/d (39)	Elevated liver enzymes (1), GI discomfort (5) (patients)	None
Kreuter	M	2005	136 (2005)	Decrease of clinical score: MD 6	12	None	MP (7)	Nausea (3), headache (3), elevation of liver enzymes (1)	None

Kroft	M/EF/SS	2009	70 (2009)	Clinical improvement: MTX: 38/47 MTX+CS: 11/11	Unk	Unk	FA (not routinely and exact dose not indicated), SCS (6)	Unk	Unk
Mertens	M	2016	64 (2016)	Stop due to disease remission: 48/107	Unk	Unk	FA (78), SCS (37)	Depression (1), fatigue (3), GI discomfort (7), haematotoxicity (2), headache (1), hepatotoxicity (5), pulmonary discomfort (3), renal impairment (1)	Unk
Platsidaki	M	2017	49 (2017)	Very good response: 6/20 Good response: 10/20 Fair response: 2/20 Failed treatment 2/20	≤12	Unk	FA (20), TA	Abdominal pain (4), elevated liver enzymes (1), nausea (4)	None
Seyger	M	1998	137 (1998)	Significant improvement on MSS and VAS for tightness, no significant	Unk	Unk	Unk	Elevated liver enzymes (4), fatigue (2), nausea (2), stomatitis (3), weight loss (1)	None

				improvement on durometer and VAS for itching					
Shahidi	M	2018	41 (2018)	mLoSSI, LoSDI and MRI: showed significant improvement	Unk	Unk	FA 1 mg/d, methylprednisolone 20-30 mg/kg/month	Alopecia (6), anorexia (1), fatigue (13), headache (5), hypokalaemia (8), leukopenia (2), nausea (11), striae rubrae (7)	None
Wlodek	M	2018	138 (2018)	Very well response: 4/8	Unk	Unk	Topical imiquimod (1)	Back pain (1), elevated liver enzymes (1), P3NP elevation (1), urinary symptoms (1)	None
Cox	PedM	2008	130 (2008)	Responders: 8/10	3 (median)	6 [2-12]	SCS 30 mg/kg/d, 3 d/mo (9), FA (10)	Hyperglycaemia, nausea, varicella zoster (1) (patients)	None
Fitch	PedM	2006	66 (2006)	Inactive lesions: 16/17	MTX: 24.4 , MTX+ CST: 9.2	Unk	FA (19), OCS (12), TCS	Elevated glucose (1), elevated liver enzymes (1), weight gain (2), weight gain and mild cushingoid features (several)	Unk
Koch	PedM	2013	41 (2013)	Disease inactivity: 17/17	8.4	21	FA 1mg/d (17), Or Pred (9)	Unk	Unk
Li	PedM	2019	131 (2019)	PGA-A, mLoSSI, LSCAM scores decreased	Unk	Unk	Pred (32)	Blurred vision (1), gastro-intestinal problems (11), hair thinning (1), infection (3),	Dehydration/gastroenteritis (1)

				in all groups 44/44, no significant differences in treatment failure between groups				laboratory abnormalities (3), lip and nasal ulcer (1), medication intolerance (5), mood problems (5), seizure recurrence (1)	
Mirsky	PedM	2012	132 (2012)	No disease relapses: 31/90	Unk	20.4	Unk	Unk	Unk
Piram	PedM	2013	133 (2013)	Significant disease improvement MTX+CST combined compared to MTX or CST alone: OR 5 (95% CI, 1.2-20.7)	Unk	Unk	Calcipotriene (29), HCQ (20), methylprednisolone 21 mg/kg (20), OCS 0,8 mg/kg (6), tacrolimus (14), TCS (33), UVB (3), vit A or vit E TA (Unk)	Headache, nausea	Unk
Rattanakaemakorn	PedM	2017	68 (2017)	Responders, improvement: 7/7	8	Unk	FA, daily (7)	Mild nausea (1)	Unk
Torok	PedM	2012	29 (2012)	Significant mLosSI improvement after 1.77 mo: 36/36	4.32	Unk	FA 1 mg/d(36), Pred 0.25-2 mg/kg/d (36)	Anticipator emesis (7), cushingoid facies (23), elevated liver enzymes (1), light striae (2), oral candidiasis (1)	None

Uziel	PedM	2000	134 (2000)	Inactive lesions: 9/11	08-52	Unk	D-penicillamine (1), IV MP (8), naproxen (1), Pred (3)	Elevated liver enzymes (1), leukopenia (1), nausea (1)	Unk
Weibel	PedM	2006	135 (2006)	Arrest of disease progression: 32/34	22.8	Unk	IV MP (34), CST	Abdominal discomfort (4), elevated liver enzymes (6), headache (3), lymphopenia (4), mouth ulcers (3), nausea (14)	None
Zulian	PedM	2011	50 (2011)	Decrease in target skin lesion activity MTX: - 44.4% Placebo: - 12.1%	Unk	Unk	FA (46), Pred 1mg/kg	Alopecia (2), fatigue (2), headache (5), hepatotoxicity (3), nausea (8)	None
Zulian±	PedM	2012	55 (2012)	Responders: 48/65 Relapse: 10/65 Lost-to-follow-up: 7/65	Unk	Unk [25.6- Unk]	FA (65)	Elevated liver enzymes (3), headache (7), nausea (16), transitory hair loss and fatigue (2)	None
Torrelo	Pa	2017	159 (2017)	Good control of active symptoms and signs and no reappearance of further attacks: 5/5	Unk	Unk	Pred 1 mg/kg/d (5)	Unk	Unk

Moustafa	PD	2015	160 (2015)	Disease control: 8	Unk	Unk	Unk	Diarrhoea (1), elevated creatinine (9), fatigue (1), hair loss (2), minimally reduces haemoglobin (1), solar purpura (2)	Unk
Rivitti	PF	1973	22 (1973)	Good response: 1/8 Slight improvement: 2/8 No improvement: 5/8	Unk	Unk	SCS, TCA 4-24 mg (8)	None	Death by bronchopneumonia (1)
Spring	PN	2014	161 (2014)	Decrease PNASI/PNRS >75%: 10/13 Tend to improvement: 2/13 Relapse: 1/13	Unk	Unk	Em, TCS	Fatigue (1), liver enzyme elevation (1), nausea (1), typical side effects (Unk)	Unk
Egan	PPP	1999	23 (1999)	CST sparing effect: 5/5	4	Unk	TCS (3), SCS (4)	GI discomfort (1)	None
Klejtman	Pr	2018	163 (2018)	Objective complete response: 16/28 Subjective complete response: 19/28	9.6	19	Unk	Anaemia (1), asthenia (1), cutaneous abscess (1), elevated liver enzymes (4), hair loss (1), hepatocarcinoma (1),	Unk

								gastrointestinal discomfort (2)	
Sharma	PrD	2007	162 (2007)	Mean DASl reduction: 7.9	Unk	Unk	Prednisolone ≤30 mg/d	Dermatophytosis (4), folliculitis (4), furuncles (4)	Unk
Allison	PRP	2002	139 (2002)	Poor response: 5/5	Unk	Unk	Unk	Unk	Unk
Chapalain	PRP	1999	140 (1999)	Significant improvement: 3/5 Complete clearance: 2/5	4	Unk	Unk	Cytolysis (1)	None
Dicken	PRP	1994	141 (1994)	Favourable response (clearing): 8/8	Unk	Unk	TCS	None	None
Knowles	PRP	1970	142 (1970)	Complete clearance: 6/6	4-40	Unk	TA	GI discomfort (1)	Unk
Baum	PV	2012	33 (2012)	Treatment response: 16/19	Unk	Unk	TA	Unk	Unk
Lever	PV	1972	143 (1972)	Freedom of lesions: Pred -> MTX: 7/15 MTX -> pred: 2/9	Unk	Unk [4-121]	Unk	Leukopenia (2)	
Mashkilleys on	PV	1988	144 (1988)	Effective: 42/53 Not effective: 6/53 Further	0.36	Unk	SCS (53)	Gastric ulcer (3), herpes simplex (4), moniliasis (2), necrotizing gingivitis (Unk), pneumonia (8),	0-7 pts (exact number unclear)

				exacerbation of the disease: 3/53 Discontinue due to drug induced side effects: 2/53				pyoderma (4), TBC (3)	
Peck	PV	1971	24 (1971)	Lowering antibodies with a correlation with clinical activity: 13/13 Steroid-sparing: 13/13	Unk	Unk	Calcium folinate (10), CST (13)	Gastrointestinal discomfort (1), leukopenia (1), mouth lesions (7), nausea (2)	Unk
Smith	PV	1999	145 (1999)	Pred stopped in 6 months: 6/9	Unk	Unk [7-55 d]	Pred (9)	Liver enzyme elevation (2), nausea (1)	Unk
Tran	PV	2013	39 (2013)	Improvement in clinical symptoms: 21/23	Unk	Unk [0-26]	FA 1 mg/d, TCA injections, TCS	Haematocrit decrease (1), abnormalities on liver ultrasound (1)	Unk
Lower	Sar	1995	146 (1995)	Responders: 16/23 Non-responders: 1/23 Unk: 5	Unk	Unk	Antimalarial agents, nonsteroidals, pred (3)	Cough (1), hepatotoxicity (6), mouth sores, nausea	Leukopenia requiring hospitalization (1)

Veien	Sar	1997	147 (1997)	Clearing skin lesions: 12/16	16 - 104	Unk	Unk	Elevated liver enzymes (2), fatigue (2), nausea (6), stomatitis (1)	None
Schanz	Sci	2013	71 (2013)	Responders: 12/22 Stable disease: 10/22	Unk	Unk	FA 5 mg (22), Prednisolone 1mg/kg after induction phase tapered (22)	Unk	Unk
Breuckmann	SD	2005	72 (2005)	No response: 7/7	NA	NA	FA	Unk	Unk
Herrick	SS	2017	148 (2017)	mRSS reduction: MTX: -4.0 MMF: -3.8 CP: -3.5	Unk	Unk	Unk	Unk	Unk
Pope	SS	2001	151 (2001)	No significant differences in UCLA skin score, modified Rodnan score and MD global assessment	Unk	Unk	Additional MTX 1.25-3.5 mg/week (11)	Oral ulcers (1)	MTX (3), placebo (7)
Sumanth	SS	2007	149 (2007)	Improvement of skin score: Excellent: 1/33 Moderate: 4/33 Mild: 12/33	Unk	Unk	Unk	Nausea/vomiting (3), fever (2), oedema (2), increased bilirubin (2), alopecia (92), anorexia (1), dyspnoea (1), headache (1),	Unk

				None: 3/33 Deterioration: 5/33 Lost-to-follow-up: 8/33				elevated liver enzymes (1), upper respiratory tract infection (1), angioedema (1), fever (1)	
Van den Hoogen	SS	1996	150 (1996)	Significant improvement of TSS and VAS: MTX: 8/17 Placebo: 1/12	Unk	Unk	Pred <10 mg/d	Elevated liver enzymes (6), headache (1), pancytopenia (1)	Renal crisis (1), sudden death (1)
Leducq	Ur	2019	152 (2019)	Complete urticaria remission (ITT): MTX: 3/38 Placebo: 0/32	Unk	Unk	H1-AH (39)	Anaemia (4), asthenia (4), cholestasis (5), elevated liver enzymes (17), gastrointestinal discomfort (17), headache (3), insomnia (1), leukopenia (4), lymphopenia (3), nasopharyngitis (5), neutropenia (1), respiratory tract infection (4), urinary tract infection (1)	Cerebrovascular stroke (1), unstable angina (1)
Perez	Ur	2010	65 (2010)	Responders: 12/16 Steroid-sparing: 2/16	Unk	Unk	FA 5 mg (16), Prednisolone 10-60 mg/d (16)	Dyspnoea (1), fatigue, hair thinning	Unk
Sagi	Ur	2011	57 (2011)	Complete clinical	3-5	Unk [4-15]	AH (5), FA 5 mg (8), Pred (8)	Gastrointestinal discomfort (2),	None

				remission: 7/8 No response: 1/8				liver enzymes elevation (1), subjective fatigue (1)	
Sharma	Ur	2014	153 (2014)	>2/3 of baseline urticaria scores achieved: MTX: 3.5/10 Placebo: 3.67/7	Unk	Unk	Levocetirizine 5 mg/d (Unk)	Liver enzyme elevation (2), uncontrollable nausea (1), vomiting (1)	None
AlGhamdi	Vi	2013	36 (2013)	Clinical improvement: no change (6/6)	Unk	Unk	FA, 5 mg/d	None	None
Singh	Vi	2015	46 (2015)	New vitiliginous lesions: MTX: 6/25 CST 7/25	Unk	Unk	FA 5 mg/week	Nausea (4), severe nausea (1)	None

* - at the end of treatment duration

See also the abbreviation list on page **Fout! Bladwijzer niet gedefinieerd..**