

Supplementary data S1 : Search Algorithm

Algorithm number	Algorithm	Number of hits
Dermatology – specific psoriasis (PSO)		
#1	(((((((((dermatology[MeSH Terms]) OR (dermatology[Title/Abstract])) OR (skin diseases[Title/Abstract])) OR (skin disease[Title/Abstract])) OR (psoriasis[MeSH Terms])) OR (psoriasis[Title/Abstract])) OR (Psoriases[Title/Abstract])) OR (Pustulosis of Palms[Title/Abstract] AND Soles[Title/Abstract])) OR (Pustulosis Palmaris et Plantaris[Title/Abstract])) OR (Palmoplantar Pustulosis[Title/Abstract])) OR (Pustular Psoriasis of Palms[Title/Abstract] AND Soles[Title/Abstract]))	126 973
Methotrexate		
#2	((methotrexate[MeSH Terms]) OR (methotrexate[Title/Abstract])) OR (nordimet[Title/Abstract])	59 530
Liver toxicity		
#3	((((((((((((((((((((((((((((((((((((((Chemical and Drug Induced Liver Injury[MeSH Terms]) OR (Chemically-Induced Liver Toxicity[Title/Abstract])) OR (Chemically Induced Liver Toxicity[Title/Abstract])) OR (Chemically-Induced Liver Toxicities[Title/Abstract])) OR (Liver Toxicities, Chemically-Induced[Title/Abstract])) OR (Liver Toxicity, Chemically-Induced[Title/Abstract])) OR (Toxicities, Chemically-Induced Liver[Title/Abstract])) OR (Toxicity, Chemically-Induced Liver[Title/Abstract])) OR (Drug-Induced Acute Liver Injury[Title/Abstract])) OR (Drug Induced Acute Liver Injury[Title/Abstract])) OR (Liver Injury, Drug-Induced, Acute[Title/Abstract])) OR (Acute Liver Injury, Drug-Induced[Title/Abstract])) OR (Acute Liver Injury, Drug Induced[Title/Abstract])) OR (Hepatitis, Toxic[Title/Abstract])) OR (Toxic Hepatitis[Title/Abstract])) OR (Hepatitis, Toxic[Title/Abstract])) OR (Toxic Hepatitis[Title/Abstract])) OR (Drug-Induced Liver Disease[Title/Abstract])) OR (Disease, Drug-Induced Liver[Title/Abstract])) OR (Diseases, Drug-Induced Liver[Title/Abstract])) OR (Drug Induced Liver Disease[Title/Abstract])) OR (Drug-Induced Liver Diseases[Title/Abstract])) OR (Liver Disease, Drug-	36 880

Algorithm number	Algorithm	Number of hits
	Induced[Title/Abstract])) OR (Liver Diseases, Drug- Induced[Title/Abstract])) OR (Drug-Induced Liver Injury[Title/Abstract])) OR (Drug Induced Liver Injury[Title/Abstract])) OR (Drug-Induced Liver Injuries[Title/Abstract])) OR (Injuries, Drug-Induced Liver[Title/Abstract])) OR (Injury, Drug-Induced Liver[Title/Abstract])) OR (Liver Injuries, Drug- Induced[Title/Abstract])) OR (Liver Injury, Drug- Induced[Title/Abstract])) OR (Liver Injury, Drug Induced[Title/Abstract])) OR (Hepatitis, Drug- Induced[Title/Abstract])) OR (Drug-Induced Hepatitis[Title/Abstract])) OR (Drug-Induced Hepatitis[Title/Abstract])) OR (Hepatitis, Drug- Induced[Title/Abstract])) OR (Hepatitis, Drug Induced[Title/Abstract])) OR (Chemical[Title/Abstract] AND Drug Induced Liver Injury[Title/Abstract])	
Safety		
#4	(((Safety[MeSH Terms]) OR (Safety[Title/Abstract])) OR (Safety issues[Title/Abstract])) OR (Safety issue[Title/Abstract])	699 035
Guidelines		
#5	((((((Guidelines as Topic[MeSH Terms]) OR (Guidelines as Topic[Title/Abstract])) OR (Practice Guidelines as Topic[MeSH Terms])) OR (Practice Guidelines as Topic[Title/Abstract])) OR (Guideline [Publication Type])) OR (Guideline[Title/Abstract])) OR (Guidelines[Title/Abstract])	568 357
Discontinuation therapy		
#6	((Drug Tapering[MeSH Terms]) OR (Drug Tapering[Title/Abstract])) OR (Drug discontinuation[Title/Abstract])	2 923
Management		
#7	((((((((((((Disease Management[MeSH Terms]) OR (Disease Management[Title/Abstract])) OR (Disease Managements[Title/Abstract])) OR (guidelines[Title/Abstract])) OR (guideline[Title/Abstract])) OR (practice guidelines[Title/Abstract])) OR (practice	11 031 747

Algorithm number	Algorithm	Number of hits
	guideline[Title/Abstract])) OR (Management[Title/Abstract])) OR (therapy[Title/Abstract])) OR (therapy[MeSH Terms])) OR (therapies[Title/Abstract])) OR (treatment[Title/Abstract])) OR (treatments[Title/Abstract])) OR (therapeutics[Title/Abstract])) OR (therapeutic[Title/Abstract])) OR (therapeutics[MeSH Terms]))	
Filters		
#8	Language: English/French	
#9	Period: 2015-2022	
#10	Species: Human	
Total		
#11	#1 AND #2 AND #3 AND #8 AND #9 AND # 10 <i>Dermatology PSO AND MTX AND liver toxicity</i>	23
#12	#1 AND #2 AND #3 AND #5 AND #8 AND #9 AND # 10 <i>Dermatology PSO AND MTX AND liver toxicity AND guidelines</i>	4
#13	#1 AND #2 AND #3 AND #6 AND #8 AND #9 AND # 10 <i>Dermatology PSO AND MTX AND liver toxicity AND discontinuation therapy</i>	0
#14	#1 AND #2 AND #5 AND #7 AND #8 AND #9 AND # 10 <i>Dermatology PSO AND MTX AND guidelines AND management</i>	93
#15	#1 AND #2 AND #3 AND #7 AND #8 AND #9 AND # 10 <i>Dermatology PSO AND MTX AND liver toxicity AND management</i>	18
#16	#1 AND #2 AND #4 AND #8 AND #9 AND # 10 <i>Dermatology PSO AND MTX AND safety</i>	216
#17	#1 AND #2 AND #3 AND #4 AND #8 AND #9 AND # 10 <i>Dermatology PSO AND MTX AND liver toxicity AND safety</i>	5
Total number of hits: 359		

Supplementary data S2 : Flow chart



Supplementary data S3: Characteristics of the studies included

First author	Year	Country	Type of study	Number of centers or Registry	Number of patients	MTX dosage (mg/week)	MTX administration route	Liver enzyme levels	fibrosis or cirrhosis development	discontinuation
Conway ²⁶	2015	Ireland	Meta-analysis	N.R.	13 177	6 to 25	Oral, IM, SC	yes	yes	N.R.
West ¹⁰	2016	United Kingdom	Meta-analysis	N.R.	5 995	7 to 25	N.R.	yes	N.R.	N.R.
Van Winden ⁴⁵	2020	The Netherlands	Meta-analysis	N.R.	39 561	2.5 to 30	N.R.	yes	N.R.	N.R.
Lajevardi ⁴⁷	2015	Iran	RCT	1	44	7.5 to 15	N.R.	yes	N.R.	yes
Abidi ⁴⁶	2020	India	RCT	N.R.	90	7.5	N.R.	yes	N.R.	yes
Mahajan ²⁴	2020	India	RCT	1	134	Total cumulative dose: 0-5.2 g	N.R.	N.R.	yes	N.R.
Reich ²⁹	2020	Germany	RCT	28	162	5 to 30	Oral	yes	N.R.	yes
Kt ³⁰	2021	India	RCT	1	84	Up to 25	Oral	yes	N.R.	N.R.
Singh ⁴⁸	2021	India	RCT	1	66	Up to 25	IM	yes	N.R.	N.R.
Choonhakarn ³⁹	2022	Thailand	RCT	1	77	10 to 25	Oral, SC	yes	N.R.	N.R.
Dogra ³⁸	2022	India	RCT	1	100	Up to 25	Oral, SC	yes	N.R.	N.R.
Wilsmann-Theis ⁴⁹	2015	Germany	Retrospective	6	17	5 to 10	Oral	yes	N.R.	yes
Klufas ⁴⁴	2016	Canada	Retrospective	N.R.	51	3.8 to 21.4	Oral, SC	yes	N.R.	N.R.
Cabello Zurita ³³	2017	Spain	Retrospective	1	218	12	Oral, SC	yes	N.R.	yes
Rongngernn ⁵¹	2017	Thailand	Retrospective	N.R.	41	N.R.	N.R.	N.R.	yes	N.R.
Tula ³⁵	2017	Turkey	Retrospective	1	393	2.5 to 25	N.R.	yes	yes	N.R.
Tang ²⁵	2018	Taiwan	Retrospective	National Health Insurance Research Database	3 544	N.R.	N.R.	N.R.	yes	N.R.
Drach ³⁴	2019	Swiss	Retrospective	SDNTT	66	7.5 to 15	SC	yes	N.R.	N.R.
Gelfand ³⁶	2021	Danmark	Retrospective	Registry of Medicinal Products Statistics	40 237	1 to 25	N.R.	N.R.	yes	yes

First author	Year	Country	Type of study	Number of centers or Registry	Number of patients	MTX dosage (mg/week)	MTX administration route	Liver enzyme levels	fibrosis or cirrhosis development	discontinuation
Ozkok Akbulut ³²	2021	Turkey	Retrospective	5	649	15.3±3.8	Oral, SC	yes	yes	yes
Sahin ⁴¹	2021	Turkey	Retrospective	1	195	Up to 15	N.R.	yes	N.R.	yes
Koch ⁵⁰	2021	New Zeland	Retrospective	N.R.	66	5.7±7.1	N.R.	yes	yes	N.R.
Wang ⁴³	2022	China	Retrospective	N.R.	42	0.1 to 10	Oral	yes	N.R.	N.R.
Ergun ⁴²	2017	Turkey	Observational study	6	289	0.3 to 0.7	N.R.	yes	N.R.	yes
Talme ⁵²	2017	Sweden	Observational study	N.R.	201	10 to 20	N.R.	N.R.	yes	N.R.
Yan ³⁷	2019	China	Observational study	1	235	7.5 to 15	Oral	yes	N.R.	yes
Gisondi ²⁸	2020	Italy	Observational study	N.R.	130	15	SC	yes	N.R.	N.R.
Munera-Campos ²³	2021	Spain	Observational study	BIOBADADERM	3 171	N.R.	N.R.	yes	yes	N.R.
Mazhar ³¹	2023	Sweden	Observational study	SCREAM	6 294	N.R.	Oral, SC	yes	yes	yes
Van Geel ⁴⁰	2015	The Netherlands	Systematic review	Child-CAPTURE	52	0.03 to 0.5	N.R.	yes	N.R.	N.R.
Carrascosa ⁶⁴	2016	Spain	Systematic review and Guideline	N.A.	N.A.	N.A.	N.A.	yes	yes	N.R.
Yélamos ²¹	2015	Spain	Systematic review	N.A.	N.A.	N.A.	N.A.	N.R.	yes	N.R.
Menting ⁶⁸	2016	The Netherlands	Systematic review	1 352	N.A.	N.A.	N.A.	yes	N.R.	N.R.
Ighani ⁶¹	2019	Canada	Systematic review	N.A.	N.A.	N.A.	N.A.	yes	N.R.	yes
Ouellette ¹⁴	2022	USA	Systematic review	N.A.	N.A.	N.A.	N.A.	N.R.	yes	
Van Huizen ⁶⁷	2022	The Netherlands	Systematic review and Consensus statement	N.A.	N.A.	N.A.	N.A.	N.R.	N.R.	yes
Guidelines and consensus statement										
First author	Year	Country	Type of study							

Hsu ²²	2012	Canada	Guideline
Warren ⁶³	2016	United Kingdom	Guideline
NICE ⁵⁹	2017	United Kingdom	Guideline
Raaby ⁵⁷	2017	Danmark	Guideline
Busger op Vollenbroek ⁷⁴	2018	The Netherlands	Guideline
Nast ¹⁶	2018	German	Guideline
Amatore ⁵⁸	2019	France	Guideline
Arnone ⁶⁵	2019	Brazil	Guideline
Menter ²⁰	2020	USA	Guideline
Nast ⁵³	2020	International	Guideline
Krantz ⁶⁰	2023	Sweden	Consensus statements
Viswanath ⁵⁶	2015	India	Consensus statements
Rademaker ⁵⁵	2017	Australia	Consensus statements
Kostovic ¹⁸	2018	Croatia	Consensus statement
Abramovits ⁵⁴	2020	USA	Consensus statement
Chat ⁴	2021	USA	Consensus statements
<i>IM: Intramuscular; MTX: Methotrexate; N.A: Not Applicable; N.R: Not Reported; RCT: Randomized Control Trial; SC: Subcutaneous; SCREAM: The Stockholm CREATinine Measurements; SDNTT: Swiss Dermatology Network for Targeted Therapies.</i>			