

Anexo 1.

Tabla 1.- Estrategia de búsqueda en Medline vía Ovid

#	Términos de la búsqueda
1	arthritis/ or arthritis, psoriatic/ or arthritis, rheumatoid/ or gout/ or osteoarthritis/ or spondylarthritis/ or exp arthritis, infectious/
2	arthr*.mp.
3	osteoarthr*.mp. or exp osteoarthritis/
4	systemic lupus erythematosus.mp. or Lupus Erythematosus, Systemic/
5	lupus.mp.
6	Spondylarthropathies/ or Spondylitis, Ankylosing/ or spondyloarthropathies.mp. or Spondylitis/ or exp spondylarthritis/
7	ankyl*.mp.
8	spondy*.mp.
9	reiter*.mp.
10	scleroderma.mp. or Scleroderma, Systemic/
11	sclerod*.mp.
12	Chondrocalcinosis/
13	Hyperostosis, Sternocostoclavicular/
14	sacroiliitis/
15	exp Arthralgia/
16	Arthropathy, Neurogenic/
17	exp bursitis/
18	Chondromatosis, Synovial/
19	Hydrarthrosis/
20	Joint Loose Bodies/
21	Metatarsalgia/
22	Shoulder Impingement Syndrome/
23	exp Synovitis/
24	exp Temporomandibular Joint Disorders/
25	Fibromyalgia/
26	Arthropathy, Neurogenic/
27	exp Compartment Syndromes/
28	Polymyalgia Rheumatica/
29	exp tendinopathy/
30	Tennis Elbow/
31	exp Carpal Tunnel Syndrome/
32	exp Ulnar Neuropathies/
33	exp Cartilage Diseases/
34	exp Ligaments, Articular/
35	Fasciitis, Plantar/
36	ankle/ and pain/
37	ankle joint/ and pain/
38	wrist joint/ and pain/
39	wrist/ and pain/
40	elbow/ and pain/
41	elbow joint/ and pain/
42	(knee/ or knee joint/) and pain/

43	antiphospholipid syndrome/
44	dermatomyositis/
45	eosinophilia-myalgia syndrome/
46	polymyositis/
47	connective tissue diseases/
48	autoimmune diseases/
49	rheumatic fever/
50	tuberculosis, osteoarticular/
51	rheuma*.mp.
52	rheuma*.mp.
53	rheuma*.mp.
54	gout*.mp.
55	polyarthr*.mp.
56	oligoarthr*.mp.
57	Sjogren's Syndrome/ or sjogren*.mp.
58	sjoegren*.mp.
59	Still's Disease, Adult- Onset/ or still* disease*.mp.
60	bechterew*.mp.
61	joint disease/ or joint disease*.mp.
62	coxarth*.mp.
63	spinal osteophytosis.mp. or Spinal Osteophytosis/
64	spinal osteophyt*.mp.
65	Arthritis, Gouty.mp. or Arthritis, Gouty/
66	osteoarthritis, hip/ or osteoarthritis, spine/ or osteoarthritis, knee.mp.
67	musculoskeletal diseases/ or bone diseases/ or cartilage diseases/ or fasciitis/ or foot deformities/ or foot diseases/ or hand deformities/ or joint diseases/ or muscular diseases/ or musculoskeletal abnormalities/ or rheumatic diseases/ or tennis elbow/
68	musculoskeletal disease*.mp.
69	msk.mp.
70	musculoskeletal injur*.mp.
71	musculoskeletal condition*.mp.
72	musculoskeletal disorder*.mp.
73	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72
74	Methotrexate/
75	Methotrexate.tw.
76	amet?opterine.tw.
77	mexate.tw.
78	Abitrexate.tw.
79	A Met?opterine\$.tw.
80	Antifolan.tw.
81	Emt?exate.tw.
82	Enthexate.tw.
83	Farmitrexate.tw.
84	Folex.tw.
85	Ledertrexate.tw.

86	Methoblastin.tw.
87	Methohexate.tw.
88	Methotrate.tw.
89	Methylaminopterin.tw.
90	Metotrexat\$.tw.
91	Mtx.tw.
92	Novatrex.tw.
93	Rheumatrex.tw.
94	74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93
95	Drug Administration Routes/ or Infusions, Parenteral/ or Infusions, Subcutaneous/ or Infusions, Intravenous/ or Injections, Intramuscular/ or Injections, Intravenous/ or Injections, Subcutaneous/
96	(subcutaneous or intravenous or intramuscular or enteral or parenteral or injection or injected).tw.
97	95 or 96
98	73 and 94 and 97
99	Epidemiologic studies/
100	exp case control studies/
101	exp cohort studies/
102	Case control.tw.
103	(cohort adj (study or studies)).tw.
104	Cohort analy\$.tw.
105	(Follow up adj (study or studies)).tw.
106	(observational adj (study or studies)).tw.
107	Longitudinal.tw.
108	Retrospective.tw.
109	Cross sectional.tw.
110	Cross-sectional studies/
111	99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110
112	98 and 111
113	Randomized Controlled Trials as Topic/
114	randomized controlled trial/
115	Random Allocation/
116	Double Blind Method/
117	Single Blind Method/
118	clinical trial/
119	clinical trial, phase i.pt.
120	clinical trial, phase ii.pt.
121	clinical trial, phase iii.pt.
122	clinical trial, phase iv.pt.
123	controlled clinical trial.pt.
124	randomized controlled trial.pt.
125	multicenter study.pt.
126	clinical trial.pt.
127	exp Clinical Trials as topic/
128	(clinical adj trial\$).tw.
129	((singl\$ or doubl\$ or treb\$ or tripl\$) adj (blind\$3 or mask\$3)).tw.
130	placebos/

131	placebo\$.tw.
132	randomly allocated.tw.
133	(allocated adj2 random\$.tw.
134	113 or 114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 131 or 132 or 133
135	case report.tw.
136	letter/
137	historical article/
138	135 or 136 or 137
139	134 not 138
140	98 and 139
141	meta-analysis.pt.
142	meta-analysis/ or systematic review/ or meta-analysis as topic/ or "meta analysis (topic)"/ or "systematic review (topic)"/ or exp technology assessment, biomedical/
143	((systematic* adj3 (review* or overview*)) or (methodologic* adj3 (review* or overview*))).ti,ab.
144	((quantitative adj3 (review* or overview* or syntheses*) or (research adj3 (integrati* or overview*))).ti,ab.
145	((integrative adj3 (review* or overview*)) or (collaborative adj3 (review* or overview*)) or (pool* adj3 analy*))).ti,ab.
146	(data syntheses* or data extraction* or data abstraction*).ti,ab.
147	(handsearch* or hand search*).ti,ab.
148	(mantel haenszel or peto or der simonian or dersimonian or fixed effect* or latin square*).ti,ab.
149	(met analy* or metanaly* or technology assessment* or HTA or HTAs or technology overview* or technology appraisal*).ti,ab.
150	(meta regression* or metaregression*).ti,ab.
151	(meta-analy* or metaanaly* or systematic review* or biomedical technology assessment* or bio-medical technology assessment*).mp,hw.
152	(medline or cochrane or pubmed or medlars or embase or cinahl).ti,ab,hw.
153	(cochrane or (health adj2 technology assessment) or evidence report).jw.
154	(meta-analysis or systematic review).tw.
155	(comparative adj3 (efficacy or effectiveness)).ti,ab.
156	(outcomes research or relative effectiveness).ti,ab.
157	((indirect or indirect treatment or mixed-treatment) adj comparison*).ti,ab.
158	141 or 142 or 143 or 144 or 145 or 146 or 147 or 148 or 149 or 150 or 151 or 152 or 153 or 154 or 155 or 156 or 157
159	98 and 158

Tabla 2.- Estrategia de búsqueda en Embase

#	Términos de la búsqueda
#139	#137 AND [embase]/lim NOT [medline]/lim AND ([english]/lim OR [french]/lim OR [spanish]/lim)
#138	#137 AND [embase]/lim NOT [medline]/lim
#137	#52 AND #136
#136	#135 NOT #134
#135	#103 OR #104 OR #105 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #116 OR #117 OR #119 OR #120 OR #121 OR #127
#134	#128 OR #129 OR #133
#133	#130 NOT #132
#132	#130 AND #131
#131	'human'/exp
#130	'animal'/exp
#129	editorial:pt
#128	letter:pt
#127	#125 AND #126
#126	review:pt
#125	#123 OR #124
#124	'selection criteria':ab
#123	'data extraction':ab
#121	'relevant journals':ab
#120	'manual search?'
#119	'hand search?'
#117	bibliograph?
#116	'reference lists':ab
#114	bids.ab
#113	cinahl:ab OR cinhal:ab
#112	cinahl:ab OR cinhal:ab
#111	psychinfo:ab OR psycinfo:ab
#110	psychlit:ab OR psyclit:ab
#109	embase:ab
#108	cochrane:ab
#107	cancerlit:ab
#106	#103 OR #104 OR #105
#105	(systematic NEAR/1 (review? OR overvie?)):ab,ti
#104	meta NEAR/3 analy? OR metaanalys?
#103	'meta analysis'/exp
#102	#100 AND [embase]/lim NOT [medline]/lim AND ([english]/lim OR [french]/lim OR [spanish]/lim)
#101	#100 AND [embase]/lim NOT [medline]/lim
#100	#99 NOT #75
#99	#52 AND #98
#98	#93 NOT #97
#97	#94 OR #95 OR #96
#96	'abstract report'/exp OR 'letter'/exp
#95	'case report':ab,ti
#94	'case study'/exp

#93	#79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92
#92	'prospective study'/exp
#91	placebo?
#90	((treble OR triple) NEAR/1 blind?):ab,ti
#89	'double blind?'
#88	'single blind?'
#87	(allocated NEAR/2 random):ab,ti
#86	'allocated randomly':ab,ti
#85	'randomly allocated':ab,ti
#84	'random allocation':ab,ti
#83	random AND allocation:ab,ti
#82	rct:ab,ti
#81	'randomi?ed controlled trial?'
#80	'clinical trial'/exp OR 'randomized controlled trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp
#79	'clinical trial'/exp
#78	#76 AND [embase]/lim NOT [medline]/lim AND ([english]/lim OR [french]/lim OR [spanish]/lim)
#77	#76 AND [embase]/lim NOT [medline]/lim
#76	#74 NOT #75
#75	'conference abstract'/it OR 'conference paper'/it OR 'note'/it OR 'short survey'/it
#74	#52 AND #73
#73	#53 OR #54 OR #55 OR #56 OR #60 OR #61 OR #63 OR #64 OR #68 OR #69 OR #70 OR #71 OR #72
#72	('cross sectional' NEAR/1 (study OR studies)):ab,ti
#71	(epidemiologic? NEAR/1 (study OR studies)):ab,ti
#70	(observational NEAR/1 (study OR studies)):ab,ti
#69	(observational NEAR/1 (study OR studies)):ab,ti
#68	('follow up' NEAR/1 (study OR studies)):ab,ti
#64	case:ab,ti AND (control NEAR/1 (study OR studies)):ab,ti
#63	(cohort NEAR/1 (study OR studies)):ab,ti
#61	'cohort analysis'/exp
#60	#58 NOT #59
#59	'randomized controlled trial (topic)'/exp
#58	'prospective study'/exp
#56	'clinical study'/exp OR 'case control study'/exp OR 'family study'/exp OR 'longitudinal study'/exp OR 'retrospective study'/exp
#55	'case control study'/exp
#54	'case control study'/exp
#53	'clinical study'/exp
#52	#48 AND #51
#51	#49 OR #50
#50	subcutaneous:ab,ti OR intravenous:ab,ti OR intramuscular:ab,ti OR enteral:ab,ti OR parenteral:ab,ti OR injection:ab,ti OR injected:ab,ti
#49	'drug administration route'/exp OR 'infusion'/exp OR 'subcutaneous drug administration'/exp OR 'intramuscular drug administration'/exp OR 'intravenous drug administration'/exp
#48	#28 AND #47
#47	#29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46

#46	rheumatrex:ab,ti
#45	novatrex:ab,ti
#44	mtx:ab,ti
#43	metotrexat?
#42	methylaminopterin:ab,ti
#41	methotrate:ab,ti
#40	methohexate:ab,ti
#39	methoblastin:ab,ti
#38	ledertrexate:ab,ti
#37	folex:ab,ti
#36	farmitrexate:ab,ti
#35	enthexate:ab,ti
#34	antifolan:ab,ti
#33	'a met?opterine?'
#32	abitrexate:ab,ti
#31	mexate:ab,ti
#30	methotrexate:ab,ti
#29	'methotrexate'/exp
#28	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27
#27	musculoskeletal AND disorder*:ab,ti
#26	musculoskeletal AND condition*:ab,ti
#25	musculoskeletal AND injur*:ab,ti
#24	msk:ab,ti
#23	'musculoskeletal disease':ab,ti
#22	'musculoskeletal disease'/exp OR 'bone disease'/exp OR 'chondropathy'/exp OR 'fasciitis'/exp OR 'foot malformation'/exp OR 'foot disease'/exp OR 'hand malformation'/exp OR 'muscle disease'/exp OR 'musculoskeletal system malformation'/exp OR 'rheumatic disease'/exp OR 'tennis elbow'/exp
#21	'hip osteoarthritis'/exp OR 'knee osteoarthritis'/exp OR 'hand osteoarthritis'/exp
#20	'arthritis, gouty':ab,ti
#19	spinal:ab,ti AND osteophyt*:ab,ti
#18	'spondylosis'/exp OR 'spinal osteophytosis':ab,ti
#17	coxarth*:ab,ti
#16	'arthropathy'/exp OR 'joint disease':ab,ti
#15	bechterew*:ab,ti
#14	'adult onset still disease'/exp OR (still*:ab,ti AND disease*:ab,ti)
#13	'sjoegren syndrome'/exp OR sjoegren*:ab,ti
#12	rheuma*:ab,ti OR gout*:ab,ti OR polyarthr*:ab,ti OR oligoarthr*:ab,ti
#11	'antiphospholipid syndrome'/exp OR 'dermatomyositis'/exp OR 'eosinophilia myalgia syndrome'/exp OR 'polymyositis'/exp OR 'connective tissue disease'/exp OR 'autoimmune disease'/exp OR 'rheumatic fever'/exp OR 'tuberculous arthritis'/exp
#10	'ankle'/exp AND 'pain'/exp OR 'wrist'/exp AND 'pain'/exp OR 'elbow'/exp AND 'pain'/exp OR 'knee'/exp AND 'pain'/exp
#9	'chondrocalcinosis'/exp OR 'hyperostosis'/exp OR 'sacroiliitis'/exp OR 'arthralgia'/exp OR 'neuropathic joint disease'/exp OR 'bursitis'/exp OR 'chondromatosis'/exp OR 'joint effusion'/exp OR 'joint destruction'/exp OR 'metatarsalgia'/exp OR 'shoulder impingement syndrome'/exp OR 'synovitis'/exp OR 'temporomandibular joint disorder'/exp OR 'fibromyalgia'/exp OR 'compartment syndrome'/exp OR 'rheumatic polymyalgia'/exp OR 'tendinitis'/exp OR 'tennis

	elbow'/exp OR 'carpal tunnel syndrome'/exp OR 'cubital tunnel syndrome'/exp OR 'chondropathy'/exp OR 'ligament'/exp
#8	'systemic sclerosis'/exp OR scleroderma:ab,ti OR sclerod*:ab,ti
#7	ankyl*:ab,ti OR spondy*:ab,ti OR reiter*:ab,ti
#6	'spondyloarthropathy'/exp OR 'ankylosing spondylitis'/exp OR 'spondylitis'/exp OR 'spondylarthritis'/exp OR spondyloarthropathies:ab,ti
#5	'systemic lupus erythematosus':ab,ti OR lupus:ab,ti
#4	systemic:ab,ti AND lupus:ab,ti AND erythematosus:ab,ti OR lupus:ab,ti
#3	'systemic lupus erythematosus'/exp
#2	arthr* OR osteoarthr*:ab,ti
#1	'arthritis'/exp OR 'psoriatic arthritis'/exp OR 'gout'/exp OR 'osteoarthritis'/exp OR 'spondylarthritis'/exp OR 'infectious arthritis'/exp

Estudios excluidos y motivos de exclusión.

	Estudio	Motivo de exclusión
1	Arthur_2002 (1)	Solo incluye 8 pacientes
2	Albaqami 2019 (2)	No analiza subcutáneos
3	Beauvais_2017 (3)	No analiza subcutáneos
4	Bengana_2017 (4)	No analiza grupo subcutáneo
5	Blanco-García 2011 (5)	Compara básicamente al grupo al que se le prescribió oral vs parenteral
6	Boulos_2005 (6)	RS, con artículos sin datos de formulación parenteral
7	Cipriani 2014 (7)	RS de moderada calidad (no se busca en Embase, criterios de inclusión y exclusión poco claros). Los artículos sobre MTX parenteral ya están incluidos en la actual RS
8	Chen_2013 (8)	RS, con artículo sobre MTX sc ya incluido en esta revisión
9	Chollet-Janin_2007 (9)	Solo incluye 5 pacientes
10	Collins 2008 (10)	Serie de casos
11	Conway 2015 (11)	No analiza individualmente los resultados de la formulación parenteral.
12	Curtis 2014 (12)	Sin datos concretos de la formulación parenteral
13	Daien_2017 (13)	RS sin datos específicos de la formulación parenteral
14	Dalkilic 2013 (14)	Sin datos concretos de la formulación parenteral
15	Dalrymple 2008 (15)	No hay datos de MTX parenteral
16	De Cuyper 2016 (16)	Adherencia, sin especificar MTX subcutáneo
17	Dervieux_2010 (17)	Solo 10 pacientes pasaron de oral a parenteral
18	Desoky_1997 (18)	Sólo analiza 9 pacientes
19	Fitzpatrick 2013 (19)	Costes, no costo-efectividad
20	Freeman-Narrod 2006 (20)	No incluidas enfermedades reumáticas
21	Gaujoux-Viala 2014 (21)	RS de gran calidad que no aporta datos ya comentados en esta RS
22	Goodman 2015 (22)	RS de moderada calidad (sólo buscan Medline, límites por fechas). Los artículos sobre MTX parenteral ya están incluidos en la actual RS
23	Gottheil 2016 (23)	Póster ACR, con los mismos datos que póster EULAR, ya incluido en la revisión
24	Hasanzhadeh 2012 (24)	Costes MTX sc vs anti-TNF
25	Herman 1989 (25)	Estudio de biodisponibilidad en el que no se pueden extraer datos relevantes de MTX intravenoso
26	Jay 2015 (26)	Revisión literaria
27	Kinder 2005 (27)	Sin datos específicos de la formulación parenteral
28	Kromann 2015 (28)	La mitad de los pacientes proceden del servicio de dermatología con lo que es posible que no tengan enfermedad reumática
29	Li 2016(29)	RS con artículos ya incluidos en esta revisión
30	Lopez-Olivo 2014 (30)	RS de gran calidad. Los artículos sobre MTX parenteral ya están incluidos en la actual RS
31	Mazaud 2017 (31)	Sin datos específicos de la formulación parenteral
32	Mouterde 2011 (32)	RS de gran calidad. Los artículos sobre MTX parenteral ya están incluidos en la actual RS
33	Parker_2004 (33)	Solo evalúan 8 pacientes
34	Pasma 2015 (34)	No se pueden extraer datos completos y relevantes del MTX parenteral
35	Pichlmeier 2014 (35)	Pacientes sanos, estudio de farmacodinámica
36	Poyatos 2016 (36)	Pacientes oncológicos
37	Ramiro 2014 (37)	RS de gran calidad. Sin datos concretos de MTX parenteral
38	Roychowdhury 2002 (38)	MTX oral
39	Rozin 2004 (39)	Serie de casos clínicos

40	Saraux 2018 (40)	Datos de un abstract congreso, incluido artículo original
41	Schiff 2013 (41)	Datos de un abstract congreso, incluido artículo original
42	Schiff 2013_2(42)	Datos de un abstract congreso, incluido artículo original
43	Schiff 2014_1 (43)	Revisión literaria
44	Sifuentes 2016 (44)	Sin datos específicos de la formulación parenteral
45	Steinsson_1982 (45)	Solo 3 pacientes con MTX intramuscular incluidos
46	Swierkot_2008 (46)	Sin datos específicos de la formulación parenteral
47	Tornero 2016 (47)	Metodología no incluida
48	Tornero 2017 (48)	Metodología no incluida
49	Van Roon 2010 (49)	Revisión narrativa
50	Vermaak 2015 (50)	RS sin un análisis específico de MTX
51	Verstappen 2007 (51)	Aporta unos datos de seguridad ya incluidos en el estudio de Bakker 2010 (estudio incluido)
52	Visser 2009 (52)	RS de gran calidad. Los artículos sobre MTX parenteral ya están incluidos en la actual RS
53	Wessels 2008 (53)	Revisión narrativa
54	Williams_1985 (54)	Sin datos específicos de la formulación parenteral
55	Wilsdon 2019 (55)	RS de gran calidad, sin datos específicos de MTX parenteral
56	Yacizi 2013 (56)	Revisión narrativa

Abreviaturas: ACR= American College of Rheumatology; EULAR= European League Against Rheumatism; im= intramuscular; MTX=metrotexato; RS=revisión sistemática; sc= subcutáneo; TNF= Factor de necrosis tumoral