

### **III. Supplement**

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## 1. PICOs

PICO 1. Should we use NSAIDs over colchicine/corticosteroids in patients experiencing a gout flare to reduce the duration of the flare?

Patients	Patient experiencing a gout flare
Intervention	Using NSAID
Comparator	Using Colchicine/steroid
Outcome	Duration of the flare

PICO 2 Should clinicians initiate ULT during gout flares vs. after gout flares have resolved?

Patients	Patient experiencing a gout flare who did not receive ULT before
Intervention	Start ULT during a gout flare with a concomitant anti-inflammatory drug
Comparator	Use anti-inflammatory drug only
Outcome	Gout flares (duration, pain severity)

PICO 3. Prophylaxis vs. no prophylaxis in patients with gout starting ULT

Patients	Gout patients initiating ULT
Intervention	Use prophylactic anti-inflammatory drugs
Comparator	Initiate ULT without prophylactic anti-inflammatory drugs
Outcome	Gout flares

PICO 4. Should ULT be prescribed to achieve serum urate <6mg/dL in gout in order to prevent gout flares and bone erosion?

Patients	Gout patients
Intervention	prescribing ULT to achieve serum urate <6mg/dL
Comparator	serum urate $\geq$ 6mg/dL
Outcome	Gout flares, bone erosion

PICO 5. Should ULT be stopped vs. continued for patients with gout on ULT?

Patients	Gout patients
Intervention	Stopping ULT
Comparator	Continuing ULT
Outcome	Gout flares

PICO 6. Should xanthine oxidase inhibitors be prescribed over uricosuric agents in chronic tophaceous gout?

Patients	Patients with tophaceous gout
Intervention	Prescription of xanthine oxidase inhibitor
Comparator	Prescription of uricosuric agent
Outcome	Tophi size, bone erosion

PICO 7. Should ULT be used in gout patients vs. no treatment in order to preserve renal function?

Patients	Patients with gout
Intervention	Using ULT (allopurinol, febuxostat, benzbromarone, pegloticase)
Comparator	Not using ULT (allopurinol, febuxostat, benzbromarone, pegloticase)
Outcome	Benefit – renoprotective effect Harm – adverse events of ULT Patients' value and preference

PICO 8. Should prescribing ULT be used to improve cardiovascular outcomes in patients with gout vs. no treatment?

Patients	Patients with gout
Intervention	Prescribing ULT
Comparator	No treatment
Outcome	Cardiovascular outcomes

PICO 9. Should prescribing ULT vs. no treatment be used in CKD 3,4 patients with asymptomatic hyperuricemia in order to protect renal function?

Patients	Asymptomatic hyperuricemia patients with CKD stage 3,4
Intervention	Prescribing ULT
Comparator	Not prescribing ULT
Outcome	Renoprotective effect

## 2. Developers

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	Name	Affiliation
Steering committee	Jeong-Soo Song	Choong-Ang Univ. Division of Rheumatology
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	Shung Chull Chae	Kyungpook Univ. Division of Cardiology
	Bum-Soon Choi	Catholic Univ. Division of Nephrology
	Tae Nyun Kim	Inje Univ. Division of Endocrinology
Developing committee	Hyun Ah Kim	Hallym Univ. Division of Rheumatology
	Jennifer Jooha Lee	Catholic Univ. Division of Rheumatology
	Ji Soo Lee	Ewha Univ. Division of Rheumatology
	Min Kyung Chung	Ewha Univ. Division of Rheumatology
	Joong Kyong Ahn	Sungkyunkwan Univ. Division of Rheumatology

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	Jong-Woo Kim	Inje Univ. Department of Family Medicine
	Bo-Yeon Kim	Soonchunhyang Univ. Division of Endocrinology
	Jin-Ho Shin	Hanyang Univ. Division of Cardiology
	Sang-Gyo Seo	SNU Seoul hospital
	Woo Gyu Kim	Lights and salt Internal Medicine
Methodologist	Soo-Young Kim	Hallym Univ. Department of Family Medicine
	Hyun-Jung Kim	Korea Univ. Department of Preventive Medicine

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### 3. Patient preferences

**Table1. Characteristics of the subjects**

	Total (N=809)	Patients taking ULT (n=755)		P
		ULT adherence≥80% (n=673)	ULT adherence<80% (n=82)	
		Age, mean±SD, years	53.5 ± 13.7	
Male	789 (97.6)	656 (97.6)	81 (98.8)	1.000
BMI, mean±SD, kg/m <sup>2</sup>	26.4 ± 3.7	26.3 ± 3.8	26.6 ± 3.1	0.333
Disease duration, mean±SD, years	8.2 ± 7.9	8.4 ± 7.9	6.1 ± 6.4	<b>0.011</b>
Comorbidities	548 (67.7)	466 (69.2)	49 (59.8)	0.082
Urinary stone	57 (7.0)	48 (7.1)	7 (8.5)	0.644
Diabetes mellitus	97 (12.0)	86 (12.8)	7 (8.5)	0.270
Hypertension	352 (43.5)	305 (45.3)	27 (32.9)	<b>0.033</b>
Dyslipidemia	220 (27.2)	192 (28.5)	16 (19.5)	0.084
Cardiovascular disease*	96 (11.9)	85 (12.6)	6 (7.3)	0.163
Cerebrovascular disease	21 (2.6)	17 (2.5)	1 (1.2)	0.710
Renal dysfunction	87 (10.8)	75 (11.1)	7 (8.5)	0.474
Gout attacks in the past year				
None	342 (42.3)	311 (46.2)	20 (24.4)	<b>&lt;0.001</b>
1-3	359 (44.4)	271 (40.3)	51 (62.2)	
≥4	108 (13.3)	91 (13.5)	11 (13.4)	
Current use of ULT	755 (94.5)	-	-	-
Allopurinol	138 (18.3)	126 (18.7)	12 (14.6)	0.366

Febuxostat	313 (41.5)	283 (42.1)	30 (36.6)	0.343
Benzbromarone	15 (2.0)	15 (2.2)	0 (0)	0.392
Do not know	258 (34.2)	223 (33.1)	35 (42.7)	0.108
Use of alternative treatments	131 (16.4)	112 (16.8)	13 (16.5)	0.940
Natural supplements	117 (14.7)	101 (15.2)	12 (15.4)	0.968
Herbal remedies	15 (1.9)	13 (2.0)	0 (0)	0.381

Data are presented as number (%). ULT, urate lowering therapy; SD, standard deviation; BMD, body mass index

\*includes ischemic heart disease, myocardial infarction, arrhythmia, congestive heart failure

**Table 2. Patients' perspectives and preferences for gout management**

	Total (N=809)	Patients taking ULT (n=755)		P
		ULT adherence>80% (n=673)	ULT adherence<80% (n=82)	
<b>Know management strategies</b>				
Know well	299 (37.0)	258 (38.3)	23 (28.0)	0.063
Know a little	467 (57.8)	387 (57.5)	52 (63.4)	
Do not know	42 (5.2)	28 (4.2)	7 (8.5)	
<b>Perceive gout as a lifelong disease</b>				
Strongly agree	344 (42.5)	297 (44.1)	28 (34.1)	0.322
Agree	394 (48.7)	315 (46.8)	45 (54.9)	
Disagree	16 (2.0)	15 (2.2)	1 (1.2)	
Strongly disagree	27 (3.3)	24 (3.6)	3 (3.7)	
Do not know	28 (3.5)	22 (3.3)	5 (6.1)	



Efforts toward making lifestyle modifications				
Any*	722 (89.2)	606 (90.0)	69 (84.1)	0.101
Regular exercise	449 (55.6)	380 (56.5)	40 (48.8)	0.181
Dietary modification	417 (51.6)	362 (53.8)	34 (41.5)	<b>0.035</b>
Alcohol restriction	614 (75.9)	522 (22.4)	25 (30.5)	0.104
Education preferences about gout management				
During clinic visit	582 (71.9)	492 (73.1)	57 (69.5)	0.490
Health education program	15 (1.9)	13 (1.9)	0 (0)	0.381
TV and radio programs	83 (10.3)	70 (10.4)	6 (7.3)	0.381
Written information (books, magazines, pamphlets)	33 (4.5)	30 (4.3)	1 (1.2)	0.239
Internet searching	283 (35.0)	229 (34.0)	36 (43.9)	0.077
Friends/family members with gout	58 (7.2)	50 (7.4)	5 (6.1)	0.661
Never sought	28 (3.5)	21 (3.1)	1 (1.2)	0.498
Treatment preferences				
ULT only	230 (28.4)	204 (30.3)	13 (15.9)	<b>0.006</b>
Lifestyle modification only	141 (17.4)	104 (15.5)	23 (28.0)	<b>0.004</b>
ULT and lifestyle modification	434 (53.6)	362 (53.8)	45 (54.9)	0.852
Others <sup>†</sup>	8 (1.0)	6 (0.9)	2 (2.4)	0.212

Data are presented as number (%). ULT, urate lowering therapy.

\* Practicing at least one of regular exercise, dietary modification, and alcohol restriction.

<sup>†</sup> Others include natural supplements, herbal remedies, stress management, and joint injection.

**Table 3. Factors affecting adherence to urate lowering therapy**

	Univariable			Multivariable		
	OR	95% CI	P	OR	95% CI	P
Age	1.01	1.001-1.047	<b>0.002</b>	1.03	1.011-1.048	<b>0.002</b>
Disease duration	1.05	1.010-1.089	<b>0.013</b>	-	-	-
Having hypertension	1.52	0.947-2.428	0.083	-	-	-
Acknowledgement of management strategies	2.80	1.105-7.119	<b>0.030</b>	3.56	1.335-9.510	<b>0.011</b>
Practicing dietary modification	1.64	1.032-2.615	<b>0.036</b>	1.50	0.928-2.414	0.098
Preference for taking ULT for treatment	2.17	1.289-3.635	<b>0.003</b>	2.07	1.214-3.516	<b>0.007</b>

OR, odd ratio; CI, confidence interval; ULT, urate lowering therapy

## 4. Review and approval

1) Review – clinical practice guideline committee of Korean College of Rheumatology

Recommendations (10-7-2021)

	<u>Details</u>	
<u>Review</u>	<u>Overall score</u>	<u>81.5%</u>
	<u>Comments</u>	<u>The guidelines were appropriately developed following a sound methodology of evidence-based medicine with participation of the various stakeholders who treat Korean gout patients. The guidelines will be helpful to clinicians, medical students and policymakers. We expect continuous updates of the guidelines incorporating domestic evidences with a proper plan and consensus for the revision.</u>
<u>Decision</u>	<u>Revision</u>	

Recommendations (11-02-2021)

- 1) Revise the recommendation 6 and 8, and change the strength of recommendation accordingly. ('No recommendation' might not be proper).
- 2) It is not clear what recommendation 6 is suggesting.
- 3) Resubmit for review after revision

Recommendations (5-12-2022)

Approved

## **5. Conflict of interests (appendix)**

## 6. Searching terms and strategies

### 1) Urate lowering therapy – KQ2,3,4,5,6,7,8

MEDLINE

1. (("Gout"[Mesh]) OR "Hyperuricemia"[Mesh]) OR "Uric Acid"[Mesh] 31949
2. Gout[TIAB] OR Gouts[TIAB] OR Gouty[TIAB] OR Hyperuricemia[TIAB] OR Urate[TIAB] OR "Uric Acid"[TIAB] OR hyperuricacidaemia[TIAB] OR hyperuricacidemia[TIAB] OR hyperuricaemia[TIAB] 43212
3. 1 OR 2 50601
4. (((("Allopurinol"[Mesh]) OR "Xanthine Oxidase"[Mesh]) OR "Febuxostat"[Mesh]) OR "Benzbromarone"[Mesh]) OR "Uricosuric Agents" [Pharmacological Action]) 20133
5. Probenecid[MeSH Term] OR Apazone[MeSH Term] OR Benzbromarone[MeSH Term] OR benziodarone[Supplementary Concept] OR Halofenate[MeSH Term] OR indacrinone[Supplementary Concept] OR lesinurad[Supplementary Concept] OR Probenecid[MeSH Term] OR Sulfinpyrazone[MeSH Term] OR Ticrynafen[MeSH Term] OR traxanox[Supplementary Concept] OR Zoxazolamine[MeSH Term] 5739
6. allopurinol[TIAB] OR "Xanthine Oxidase"[TIAB] OR Uribenz[TIAB] OR Allopurin[TIAB] OR Allorin[TIAB] OR Allpargin[TIAB] OR Allural[TIAB] OR "Pan Quimica"[TIAB] OR Apulonga[TIAB] OR Apurin[TIAB] OR Atisuril[TIAB] OR Bleminol[TIAB] OR Caplenal[TIAB] OR Capurate[TIAB] OR Cellidrin[TIAB] OR Embarin[TIAB] OR Suspendol[TIAB] OR Foligan[TIAB] OR Hamarin[TIAB] OR Lopurin[TIAB] OR Lysuron[TIAB] OR Jenapurinol[TIAB] OR Milurit[TIAB] OR Milurite[TIAB] OR Novopurol[TIAB] OR Uripurinol[TIAB] OR Urosin[TIAB] OR Urtias[TIAB] OR Xanthomax[TIAB] OR Uridocid[TIAB] OR Xanturic[TIAB] OR Zygout[TIAB] OR Zyloprim[TIAB] OR Zyloric[TIAB] OR Pureduct[TIAB] OR Purinol[TIAB] OR Progout[TIAB] OR Remid[TIAB] OR Rimapurinol[TIAB] OR Antigout[TIAB] OR Antihyperuricemics[TIAB] OR Roucol[TIAB] OR Tipuric[TIAB] OR Allohexal[TIAB] OR Allohexan[TIAB] OR Alloprin[TIAB] OR Uloric[TIAB] OR febuxostat[TIAB] OR benzbromarone[TIAB] 15772

7. 4-6/OR 26482
8. 7 AND 3 6073
9. 8 NOT "review"[Publication Type] OR "review literature as topic"[MeSH Terms] 5268
10. 9 NOT "animals"[MeSH Terms] NOT ("humans"[MeSH Terms] AND "animals"[MeSH Terms]) 4286

#### Embase

1. 'gout'/exp OR 'hyperuricemia'/exp OR 'urate'/exp OR 'uric acid'/exp 68654
2. hyperuricacidaemia:ab,ti OR hyperuricacidemia:ab,ti OR hyperuricaemia:ab,ti OR Gout:ab,ti OR Gouts:ab,ti OR Gouty:ab,ti OR Hyperuricemia:ab,ti OR Urate:ab,ti OR 'Uric Acid':ab,ti 59267
3. 1 or 2 80850
4. 'uricosuric agent'/exp OR 'xanthine oxidase'/exp OR 'allopurinol'/exp OR 'febuxostat'/exp 47326
5. allopurinol:ab,ti OR 'xanthine oxidase':ab,ti OR uribenz:ab,ti OR allopurin:ab,ti OR allorin:ab,ti OR allpargin:ab,ti OR allural:ab,ti OR 'pan quimica':ab,ti OR apulonga:ab,ti OR apurin:ab,ti OR atisuril:ab,ti OR bleminol:ab,ti OR caplenal:ab,ti OR capurate:ab,ti OR cellidrin:ab,ti OR embarin:ab,ti OR suspendol:ab,ti OR foligan:ab,ti OR hamarin:ab,ti OR lopurin:ab,ti OR lysuron:ab,ti OR jenapurinol:ab,ti OR milurit:ab,ti OR milurite:ab,ti OR novopurol:ab,ti OR uripurinol:ab,ti OR urosin:ab,ti OR urtias:ab,ti OR xanthomax:ab,ti OR uridocid:ab,ti OR xanturic:ab,ti OR zygout:ab,ti OR zyloprim:ab,ti OR zyloric:ab,ti OR pureduct:ab,ti OR purinol:ab,ti OR progout:ab,ti OR remid:ab,ti OR rimapurinol:ab,ti OR antigout:ab,ti OR antihyperuricemics:ab,ti OR roucol:ab,ti OR tipuric:ab,ti OR allohexal:ab,ti OR allohexan:ab,ti OR alloprin:ab,ti OR uloric:ab,ti OR febuxostat:ab,ti OR benzbromarone:ab,ti 20407
6. 4 OR 5 50988
7. 3 AND 6 12039
8. 7 NOT ('conference review'/it OR 'review'/it) 10414

9. 8 NOT ('animal cell'/de OR 'animal experiment'/de OR 'animal model'/de OR 'animal tissue'/de OR 'human cell'/de OR 'human tissue'/de OR 'in vitro study'/de OR 'nonhuman'/de) 7763

KMbase

1. (((((((((((([ALL=Gout] OR [ALL=Gouty]) OR [ALL=Gouts]) OR [ALL=통풍]) OR [ALL=고요산혈증]) OR [ALL=Hyperuricemia]) OR [ALL=Uric Acid]) OR [ALL=요산]) OR [ALL=Urate]) OR [ALL=hyperuricacidaemiay]) OR [ALL=hyperuricacidemia]) OR [ALL=hyperuricaemia]) OR [ALL=고요산 혈증]) 1359

2. (((([ALL=allopurinol] OR [ALL=febuxostat]) OR [ALL=Xanthine Oxidase]) OR [ALL=알로푸리놀]) OR [ALL=페부소스타즈])

3. 1 AND 2 139

COCHRANE

1. (Gout OR Gouts OR Gouty OR Hyperuricemia OR Urate OR “Uric Acid” OR hyperuricacidaemia OR hyperuricacidemia OR hyperuricaemia):ab,ti,kw 5148

2. MeSH descriptor:[gout] explode all trees 305

3. MeSH descriptor:[Uric Acid] explode all trees 1070

4. MeSH descriptor:[Hyperuricemia] explode all trees 206

5. 1-4/OR 5148

6. allopurinol OR “Xanthine Oxidase” OR Uribez OR Allopurin OR Allorin OR Allparin OR Allural OR “Pan Quimica” OR Apurong OR Apurin OR Atisuril OR Bleminol OR Caplenal OR Capurate OR Cellidrin OR Embarin OR Suspendol OR Foligan OR Hamarin OR Lopurin OR Lysuron OR



Jenapurinol OR Milurit OR Milurite OR Novopurol OR Uripurinol OR Urosin OR Urtias OR Xanthomax OR Uridocid OR Xanturic OR Zygout OR Zylprim OR Zyloric OR Pureduct OR Purinol OR Progout OR Remid OR Rimapurinol OR Antigout OR Antihyperuricemics OR Roucol OR Tipuric OR Allohexal OR Allohexan OR Alloprin OR Uloric OR febuxostat OR benzbromarone 1564

7. MeSH descriptor:[allopurinol] explode all trees 524

8. MeSH descriptor:[Xanthine Oxidase] explode all trees 134

9. MeSH descriptor:[febuxostat] explode all trees 106

10. MeSH descriptor:[benzbromarone] explode all trees 44

11. 6-10/OR 1564

12. 5 AND 11 891

13. 12/TRIAL 878

## **2) anti-inflammatory drugs – KQ1,2,3**

MEDLINE

1. "Gout"[Mesh] 11876

2. Gout[TIAB] OR Gouts[TIAB] OR Gouty[TIAB] 13578

3. 1 OR 2 16416

4. aceclofenac[Supplementary Concept] OR acemetacin[Supplementary Concept] OR “acetaminophen, aspirin, caffeine drug combination”[Supplementary Concept] OR “acetaminophen, butalbital, caffeine drug combination”[Supplementary Concept] OR “acetaminophen, hydrocodone drug

combination”[Supplementary Concept] OR acetosyringone[Supplementary Concept] OR acetovanillone[Supplementary Concept] OR “acetylsalicylic acid lysinate”[Supplementary Concept] OR Adapalene[Mesh] OR “Adapalene, Benzoyl Peroxide Drug Combination”[Mesh] OR alclofenac[Supplementary Concept] OR alminoprofen[Supplementary Concept] OR amiprilose[Supplementary Concept] OR Ampyrone[Mesh] OR “amylase, phosphates, proteases drug combinations”[Supplementary Concept] OR andrographolide[Supplementary Concept] OR anisodamine[Supplementary Concept] OR anisodine[Supplementary Concept] OR “antiflammin P2”[Supplementary Concept] OR Antipyrine[Mesh] OR Apazone[Mesh] OR apremilast[Supplementary Concept] OR Arteparon[Supplementary Concept] OR Arthrotec[Supplementary Concept] OR Aspirin[Mesh] OR “aspirin, aluminum hydroxide, magnesium hydroxide drug combination”[Supplementary Concept] OR “aspirin, butalbital and caffeine drug combination”[Supplementary Concept] OR “aspirin, meprobamate drug combination”[Supplementary Concept] OR atrinositol[Supplementary Concept] OR azulene[Supplementary Concept] OR baicalin[Supplementary Concept] OR balsalazide[Supplementary Concept] OR bendazac[Supplementary Concept] OR “bendazac lysine”[Supplementary Concept] OR benorilate[Supplementary Concept] OR benoxaprofen[Supplementary Concept] OR benzobarbital[Supplementary Concept] OR berbamine[Supplementary Concept] OR “betulinic acid”[Supplementary Concept] OR bevonium[Supplementary Concept] OR “biphenylacetic acid”[Supplementary Concept] OR boldine[Supplementary Concept] OR “boswellic acid”[Supplementary Concept] OR bromfenac[Supplementary Concept] OR bucillamine[Supplementary Concept] OR Bufexamac[Mesh] OR bumadizone[Supplementary Concept] OR butibufen[Supplementary Concept] OR “carbaspirin calcium”[Supplementary Concept] OR carprofen[Supplementary Concept] OR caryophyllene[Supplementary Concept] OR castanospermine[Supplementary Concept] OR Celecoxib[Mesh] OR cepharanthine[Supplementary Concept] OR “chloroquine diphosphate”[Supplementary Concept] OR “choline magnesium trisalicylate”[Supplementary Concept] OR chrysarobin[Supplementary Concept] OR Clonixin[Mesh] OR Curcumin[Mesh] OR dauricine[Supplementary Concept] OR “dexketoprofen trometamol”[Supplementary Concept] OR Diclofenac[Mesh] OR “diclofenac hydroxyethylpyrrolidine”[Supplementary Concept] OR difenpiramide[Supplementary Concept] OR Diflunisal[Mesh] OR dimephosphon[Supplementary Concept] OR Dipyrone[Mesh] OR diucifon[Supplementary Concept] OR droxicam[Supplementary Concept] OR ebselen[Supplementary Concept] OR ecallantide[Supplementary Concept] OR eltenac[Supplementary Concept] OR “enfenamic acid”[Supplementary Concept] OR Epirizole[Mesh] OR Etanercept[Mesh] OR

ethenzamide[Supplementary Concept] OR Ethonium[Supplementary Concept] OR Etodolac[Mesh] OR etofenamate[Supplementary Concept] OR Etoricoxib[Mesh] OR “evening primrose oil”[Supplementary Concept] OR “fenamic acid”[Supplementary Concept] OR fenbufen[Supplementary Concept] OR fenclofenac[Supplementary Concept] OR fenflumizole[Supplementary Concept] OR Fenoprofen[Mesh] OR fentiazac[Supplementary Concept] OR fepradinol[Supplementary Concept] OR Feprazone[Mesh] OR “ferulic acid”[Supplementary Concept] OR floctafenine[Supplementary Concept] OR flosulide[Supplementary Concept] OR flunixin[Supplementary Concept] OR “flunixin meglumine”[Supplementary Concept] OR flunoxaprofen[Supplementary Concept] OR fluproquazone[Supplementary Concept] OR Flurbiprofen[Mesh] OR “flurbiprofen axetil”[Supplementary Concept] OR glucametacin[Supplementary Concept] OR guacetisal[Supplementary Concept] OR helenalin[Supplementary Concept] OR heliodermin[Supplementary Concept] OR hemodes[Supplementary Concept] OR higenamine[Supplementary Concept] OR Ibuprofen[Mesh] OR ibuproxam[Supplementary Concept] OR icatibant[Supplementary Concept] OR indobufen[Supplementary Concept] OR Indomethacin[Mesh] OR Indoprofen[Mesh] OR iodoantipyrine[Supplementary Concept] OR isoxicam[Supplementary Concept] OR kebuzone[Supplementary Concept] OR Ketoprofen[Mesh] OR “ketoprofen lysine”[Supplementary Concept] OR Ketorolac[Mesh] OR “Ketorolac Tromethamine”[Mesh] OR licofelone[Supplementary Concept] OR lisofylline[Supplementary Concept] OR obenzarit[Supplementary Concept] OR Ionazolac[Supplementary Concept] OR lornoxicam[Supplementary Concept] OR loxoprofen[Supplementary Concept] OR lumiracoxib[Supplementary Concept] OR “Magnesium Salicylate”[Supplementary Concept] OR magnolol[Supplementary Concept] OR manoalide[Supplementary Concept] OR Masoprocol[Mesh] OR “Meclofenamic Acid”[Mesh] OR “Mefenamic Acid”[Mesh] OR Meloxicam[Mesh] OR Mesalamine[Mesh] OR mizoribine[Supplementary Concept] OR mofebutazone[Supplementary Concept] OR mofezolac[Supplementary Concept] OR leucine[Supplementary Concept] OR Nabumetone[Mesh] OR nafamostat[Supplementary Concept] OR Naproxen[Mesh] OR Nebacetin[Supplementary Concept] OR nepafenac[Supplementary Concept] OR nifenazone[Supplementary Concept] OR “Niflumic Acid”[Mesh] OR nimesulide[Supplementary Concept] OR nitroaspirin[Supplementary Concept] OR “Olopatadine Hydrochloride”[Mesh] OR olsalazine[Supplementary Concept] OR olvanil[Supplementary Concept] OR “oren gedoku to”[Supplementary Concept] OR orgotein[Supplementary Concept] OR Oxaprozin[Mesh] OR Oxyphenbutazone[Mesh] OR almidrol[Supplementary Concept] OR parecoxib[Supplementary Concept] OR parthenolide[Supplementary Concept] OR peoniflorin[Supplementary Concept] OR phenidone[Supplementary

Concept] OR Phenylbutazone[Mesh] OR pimecrolimus[Supplementary Concept] OR pirfenidone[Supplementary Concept] OR Piroxicam[Mesh] OR “piroxicam-beta-cyclodextrin”[Supplementary Concept] OR pirprofen[Supplementary Concept] OR proglumetacin[Supplementary Concept] OR propacetamol[Supplementary Concept] OR propionylcarnitine[Supplementary Concept] OR propyphenazone[Supplementary Concept] OR proquazone[Supplementary Concept] OR pyranoprofen[Supplementary Concept] OR pyrazolone[Supplementary Concept] OR pyrogenal[Supplementary Concept] OR Resveratrol[Mesh] OR RNS60[Supplementary Concept] OR rofecoxib[Supplementary Concept] OR “rosmarinic acid”[Supplementary Concept] OR Rumalon[Supplementary Concept] OR “saiko-keishi-to”[Supplementary Concept] OR saikosaponin[Supplementary Concept] OR salicin[Supplementary Concept] OR salicylamide[Supplementary Concept] OR Salicylates[Mesh] OR “salicylsalicylic acid”[Supplementary Concept] OR semapimod[Supplementary Concept] OR seratrovast[Supplementary Concept] OR serratiopeptidase[Supplementary Concept] OR shikonin[Supplementary Concept] OR sinapaldehyde[Supplementary Concept] OR “Sodium Salicylate”[Mesh] OR Sulfasalazine[Mesh] OR Sulindac[Mesh] OR “sulindac sulfide”[Supplementary Concept] OR “sulindac sulfone”[Supplementary Concept] OR Suprofen[Mesh] OR suxibuzone[Supplementary Concept] OR tanshinone[Supplementary Concept] OR taxifolin[Supplementary Concept] OR tenidap[Supplementary Concept] OR tenoxicam[Supplementary Concept] OR tepoxalin[Supplementary Concept] OR “tiaprofenic acid”[Supplementary Concept] OR tiaramide[Supplementary Concept] OR tinoridine[Supplementary Concept] OR “tolfenamic acid”[Supplementary Concept] OR Tolmetin[Mesh] OR “tramadol, dexketoprofen drug combination”[Supplementary Concept] OR tranilast[Supplementary Concept] OR tribenoside[Supplementary Concept] OR “ursolic acid”[Supplementary Concept] OR valdecoxib[Supplementary Concept] OR zileuton[Supplementary Concept] OR zomepirac[Supplementary Concept] OR deflazacort [Supplementary Concept] OR “alclometasone dipropionate”[Supplementary Concept] OR amcinonide[Supplementary Concept] OR Beclomethasone[Mesh] OR Betamethasone[Mesh] OR “betamethasone acetate”[Supplementary Concept] OR “betamethasone benzoate”[Supplementary Concept] OR “betamethasone dipropionate, betamethasone sodium phosphate drug combination”[Supplementary Concept] OR “betamethasone sodium phosphate”[Supplementary Concept] OR “Betamethasone Valerate”[Mesh] OR Budesonide[Mesh] OR ciclesonide[Supplementary Concept] OR Clobetasol[Mesh] OR “clobetasone butyrate”[Supplementary Concept] OR clocortolone[Supplementary Concept] OR “clocortolone pivalate”[Supplementary Concept] OR Desoximetasone[Mesh] OR Dexamethasone[Mesh] OR “Dexamethasone Isonicotinate”[Mesh] OR “dichlorisone

acetate"[Supplementary Concept] OR diflorasone[Supplementary Concept] OR Diflucortolone[Mesh] OR difluprednate[Supplementary Concept] OR "drocinonide phosphate potassium"[Supplementary Concept] OR Flumethasone[Mesh] OR "flumethasone pivalate"[Supplementary Concept] OR "Fluocinolone Acetonide"[Mesh] OR Fluocinonide[Mesh] OR "fluocortin butyl ester"[Supplementary Concept] OR Fluocortolone[Mesh] OR Fluorometholone[Mesh] OR "fluperolone acetate"[Supplementary Concept] OR "fluprednidene acetate"[Supplementary Concept] OR Fluprednisolone[Mesh] OR Flurandrenolone[Mesh] OR "Fluticasone-Salmeterol Drug Combination"[Mesh] OR halometasone[Supplementary Concept] OR medrysone[Supplementary Concept] OR "Melengestrol Acetate"[Mesh] OR Methylprednisolone[Mesh] OR "Methylprednisolone Hemisuccinate"[Mesh] OR "Methylprednisolone Acetate"[Mesh] OR Paramethasone[Mesh] OR prednicarbate[Supplementary Concept] OR Prednisolone[Mesh] OR "prednisolone hemisuccinate"[Supplementary Concept] OR "prednisolone phosphate"[Supplementary Concept] OR Prednisone[Mesh] OR rimexolone[Supplementary Concept] OR terofenamate[Supplementary Concept] OR "Tobramycin, Dexamethasone Drug Combination"[Mesh] OR Triamcinolone[Mesh] OR "Triamcinolone Acetonide"[Mesh] OR "triamcinolone benetonide"[Supplementary Concept] 371387

5. "Colchicine"[Mesh] OR "Anti-Inflammatory Agents, Non-Steroidal"[Pharmacological Action] OR "Glucocorticoids"[Mesh] OR "Glucocorticoids"[Pharmacological Action] 415968

6. colchicine[TIAB] OR Demecolcine[TIAB] OR Colchamine[TIAB] OR Colcemide[TIAB] OR Colcemid[TIAB] OR Lumicolchicines[TIAB] OR NSAID[TIAB] OR aceclofenac[TIAB] OR Falcol[TIAB] OR "Falcol Difucem"[TIAB] OR "Clanza CR"[TIAB] OR Preservex[TIAB] OR Biofenac[TIAB] OR Sanein[TIAB] OR Beofenac[TIAB] OR Aital[TIAB] OR Bristaflam[TIAB] OR Gerbin[TIAB] OR Diclofenac[TIAB] OR diclofenac[TIAB] OR naproxen[TIAB] OR ibuprofen[TIAB] OR zaltoprofen[TIAB] OR indomethacin[TIAB] OR celecoxib[TIAB] OR nabumeton[TIAB] 89591

7. aceclofenac[TIAB] OR acemetacin[TIAB] OR "acetaminophen"[TIAB] OR acetosyringone[TIAB] OR acetovanillone[TIAB] OR "acetylsalicylic acid lysinate"[TIAB] OR Adapalene[TIAB] OR alclofenac[TIAB] OR alminoprofen[TIAB] OR amiprilose[TIAB] OR Ampyrone[TIAB] OR "amylase,

phosphates, proteases drug combinations”[TIAB] OR andrographolide[TIAB] OR anisodamine[TIAB] OR anisodine[TIAB] OR “antiflammin P2”[TIAB] OR Antipyrine[TIAB] OR Apazone[TIAB] OR apremilast[TIAB] OR Arteparon[TIAB] OR Arthrotec[TIAB] OR Aspirin[TIAB] OR atrinositol[TIAB] OR azulene[TIAB] OR baicalin[TIAB] OR balsalazide[TIAB] OR bendazac[TIAB] OR benorilate[TIAB] OR benoxaprofen[TIAB] OR benzobarbital[TIAB] OR berbamine[TIAB] OR “betulinic acid”[TIAB] OR bevonium[TIAB] OR “biphenylacetic acid”[TIAB] OR boldine[TIAB] OR “boswellic acid”[TIAB] OR bromfenac[TIAB] OR bucillamine[TIAB] OR Bufexamac[TIAB] OR bumadizone[TIAB] OR butibufen[TIAB] OR “carbaspirin calcium”[TIAB] OR carprofen[TIAB] OR caryophyllene[TIAB] OR castanospermine[TIAB] OR Celecoxib[TIAB] OR cepharanthine[TIAB] OR “chloroquine diphosphate”[TIAB] OR “choline magnesium trisalicylate”[TIAB] OR chrysarobin[TIAB] OR Clonixin[TIAB] OR Curcumin[TIAB] OR dauricine[TIAB] OR “dexketoprofen trometamol”[TIAB] OR Diclofenac[TIAB] OR “diclofenac hydroxyethylpyrrolidine”[TIAB] OR difenpiramide[TIAB] OR Diflunisal[TIAB] OR dimephosphon[TIAB] OR Dipyrone[TIAB] OR diucifon[TIAB] OR droxicam[TIAB] OR ebselen[TIAB] OR ecallantide[TIAB] OR eltenac[TIAB] OR “enfenamic acid”[TIAB] OR Epirizole[TIAB] OR Etanercept[TIAB] OR ethenzamide[TIAB] OR Ethonium[TIAB] OR Etodolac[TIAB] OR etofenamate[TIAB] OR Etoricoxib[TIAB] OR “evening primrose oil”[TIAB] OR “fenamic acid”[TIAB] OR fenbufen[TIAB] OR fenclofenac[TIAB] OR fenflumizole[TIAB] OR Fenoprofen[TIAB] OR fentiazac[TIAB] OR fepradinol[TIAB] OR Feprazone[TIAB] OR “ferulic acid”[TIAB] OR floctafenine[TIAB] OR flosulide[TIAB] OR flunixin[TIAB] OR “flunixin meglumine”[TIAB] OR flunoxaprofen[TIAB] OR fluproquazone[TIAB] OR Flurbiprofen[TIAB] OR “flurbiprofen axetil”[TIAB] OR glucametacin[TIAB] OR guacetisal[TIAB] OR helenalin[TIAB] OR heliodermin[TIAB] OR hemodes[TIAB] OR higenamine[TIAB] OR Ibuprofen[TIAB] OR ibuproxam[TIAB] OR icatibant[TIAB] OR indobufen[TIAB] OR Indomethacin[TIAB] OR Indoprofen[TIAB] OR iodoantipyrine[TIAB] OR isoxicam[TIAB] OR kebuzone[TIAB] OR Ketoprofen[TIAB] OR “ketoprofen lysine”[TIAB] OR Ketorolac[TIAB] OR licofelone[TIAB] OR lisofylline[TIAB] OR obenzarit[TIAB] OR lonazolac[TIAB] OR lornoxicam[TIAB] OR loxoprofen[TIAB] OR lumiracoxib[TIAB] OR “Magnesium Salicylate”[TIAB] OR magnolol[TIAB] OR manoalide[TIAB] OR Masoprocol[TIAB] OR “Meclofenamic Acid”[TIAB] OR “Mefenamic Acid”[TIAB] OR Meloxicam[TIAB] OR Mesalamine[TIAB] OR mizoribine[TIAB] OR mofebutazone[TIAB] OR mofezolac[TIAB] OR leucine[TIAB] OR Nabumetone[TIAB] OR nafamostat[TIAB] OR Naproxen[TIAB] OR Nebacetin[TIAB] OR nepafenac[TIAB] OR nifenazone[TIAB] OR “Niflumic Acid”[TIAB] OR nimesulide[TIAB] OR nitroaspirin[TIAB] OR

“Olopatadine Hydrochloride”[TIAB] OR olsalazine[TIAB] OR olvanil[TIAB] OR “oren gedoku to”[TIAB] OR orgotein[TIAB] OR Oxaprozin[TIAB] OR Oxyphenbutazone[TIAB] OR almidrol[TIAB] OR parecoxib[TIAB] OR parthenolide[TIAB] OR peoniflorin[TIAB] OR phenidone[TIAB] OR Phenylbutazone[TIAB] OR pimecrolimus[TIAB] OR pirfenidone[TIAB] OR Piroxicam[TIAB] OR pirprofen[TIAB] OR proglumetacin[TIAB] OR propacetamol[TIAB] OR propionylcarnitine[TIAB] OR propyphenazone[TIAB] OR proquazone[TIAB] OR pyranoprofen[TIAB] OR pyrazolone[TIAB] OR pyrogenal[TIAB] OR Resveratrol[TIAB] OR RNS60[TIAB] OR rofecoxib[TIAB] OR “rosmarinic acid”[TIAB] OR Rumalon[TIAB] OR “saiko-keishi-to”[TIAB] OR saikosaponin[TIAB] OR salicin[TIAB] OR salicylamide[TIAB] OR Salicylates[TIAB] OR “salicylsalicylic acid”[TIAB] OR semapimod[TIAB] OR seratrodist[TIAB] OR serratiopeptidase[TIAB] OR shikonin[TIAB] OR sinapaldehyde[TIAB] OR “Sodium Salicylate”[TIAB] OR Sulfasalazine[TIAB] OR Sulindac[TIAB] OR “sulindac sulfide”[TIAB] OR “sulindac sulfone”[TIAB] OR Suprofen[TIAB] OR suxibuzone[TIAB] OR tanshinone[TIAB] OR taxifolin[TIAB] OR tenidap[TIAB] OR tenoxicam[TIAB] OR tepoxalin[TIAB] OR “tiaprofenic acid”[TIAB] OR tiaramide[TIAB] OR tinoridine[TIAB] OR “tolfenamic acid”[TIAB] OR Tolmetin[TIAB] OR “tramadol, dexketoprofen drug combination”[TIAB] OR tranilast[TIAB] OR tribenoside[TIAB] OR “ursolic acid”[TIAB] OR valdecocixib[TIAB] OR zileuton[TIAB] OR zomepirac[TIAB] OR deflazacort[TIAB] OR “alclometasone dipropionate”[TIAB] OR amcinonide[TIAB] OR Beclomethasone[TIAB] OR Betamethasone[TIAB] OR Budesonide[TIAB] OR ciclesonide[TIAB] OR Clobetasol[TIAB] OR “clobetasone butyrate”[TIAB] OR clocortolone[TIAB] OR Desoximetasone[TIAB] OR Dexamethasone[TIAB] OR “dichlorisone acetate”[TIAB] OR diflorasone[TIAB] OR Diflucortolone[TIAB] OR difluprednate[TIAB] OR “drocinonide phosphate potassium”[TIAB] OR Flumethasone[TIAB] OR “Fluocinolone Acetonide”[TIAB] OR Fluocinonide[TIAB] OR “fluocortin butyl ester”[TIAB] OR Fluocortolone[TIAB] OR Fluorometholone[TIAB] OR “fluperolone acetate”[TIAB] OR “fluprednidene acetate”[TIAB] OR Fluprednisolone[TIAB] OR Flurandrenolone[TIAB] OR “Fluticasone-Salmeterol Drug Combination”[TIAB] OR halometasone[TIAB] OR medrysone[TIAB] OR “Melengestrol Acetate”[TIAB] OR Methylprednisolone[TIAB] OR Paramethasone[TIAB] OR prednicarbate[TIAB] OR Prednisolone[TIAB] OR Prednisone[TIAB] OR rimexolone[TIAB] OR terofenamate[TIAB] OR “Tobramycin, Dexamethasone Drug Combination”[TIAB] OR Triamcinolone[TIAB] 403472

8. 4-7/OR 630033

9. 3 AND 8 2385

10. 9 NOT ("review"[Publication Type] OR "review literature as topic"[MeSH Terms]) 1893

11. 10 NOT ("animals"[MeSH Terms] NOT ("humans"[MeSH Terms] AND "animals"[MeSH Terms])) 1765

EMBASE

1. 'gout'/exp 23415

2. Gout:ab,ti OR Gouts:ab,ti OR Gouty:ab,ti 19126

3. 1 or 2 26480

4. 'colchicine'/exp OR 'nonsteroid antiinflammatory agent'/exp OR 'glucocorticoid'/exp 1372595

5. colchicine:ab,ti OR demecolcine:ab,ti OR colchamine:ab,ti OR colcemide:ab,ti OR colcemid:ab,ti OR lumicolchicines:ab,ti OR nsaid:ab,ti OR aceclofenac:ab,ti OR falcol:ab,ti OR 'falcol difucrem':ab,ti OR 'clanza cr':ab,ti OR preservex:ab,ti OR biofenac:ab,ti OR sanein:ab,ti OR beofenac:ab,ti OR aital:ab,ti OR bristaflam:ab,ti OR gerbin:ab,ti OR diclofenac:ab,ti OR naproxen:ab,ti OR ibuprofen:ab,ti OR zaltoprofen:ab,ti OR indomethacin:ab,ti OR celecoxib:ab,ti OR nabumeton:ab,ti 119309

6. aceclofenac:ab,ti OR acemetacin:ab,ti OR 'acetaminophen':ab,ti OR acetosyringone:ab,ti OR acetovanillone:ab,ti OR 'acetylsalicylic acid lysinate':ab,ti OR adapalene:ab,ti OR alclofenac:ab,ti OR alminoprofen:ab,ti OR amiprilose:ab,ti OR ampyrone:ab,ti OR 'amylase, phosphates, proteases drug combinations':ab,ti OR andrographolide:ab,ti OR anisodamine:ab,ti OR anisodine:ab,ti OR 'antiflammin p2':ab,ti OR antipyrine:ab,ti OR apazone:ab,ti OR apremilast:ab,ti OR arteparon:ab,ti OR arthrotec:ab,ti OR aspirin:ab,ti OR atrinositol:ab,ti OR azulene:ab,ti OR baicalin:ab,ti OR balsalazide:ab,ti OR bendazac:ab,ti OR benorilate:ab,ti OR benoxaprofen:ab,ti OR benzobarbital:ab,ti OR berbamine:ab,ti OR 'betulinic acid':ab,ti OR bevonium:ab,ti OR



'biphenylacetic acid':ab,ti OR boldine:ab,ti OR 'boswellic acid':ab,ti OR bromfenac:ab,ti OR bucillamine:ab,ti OR bufexamac:ab,ti OR bumadizone:ab,ti OR butibufen:ab,ti OR 'carbaspirin calcium':ab,ti OR carprofen:ab,ti OR caryophyllene:ab,ti OR castanospermine:ab,ti OR celecoxib:ab,ti OR cepharanthine:ab,ti OR 'chloroquine diphosphate':ab,ti OR 'choline magnesium trisalicylate':ab,ti OR chrysarobin:ab,ti OR clonixin:ab,ti OR curcumin:ab,ti OR dauricine:ab,ti OR 'dexketoprofen trometamol':ab,ti OR diclofenac:ab,ti OR 'diclofenac hydroxyethylpyrrolidine':ab,ti OR difenpiramide:ab,ti OR diflunisal:ab,ti OR dimephosphon:ab,ti OR dipyrone:ab,ti OR diucifon:ab,ti OR droxicam:ab,ti OR ebselen:ab,ti OR ecallantide:ab,ti OR eltenac:ab,ti OR 'enfenamic acid':ab,ti OR epirizole:ab,ti OR etanercept:ab,ti OR ethenzamide:ab,ti OR ethonium:ab,ti OR etodolac:ab,ti OR etofenamate:ab,ti OR etoricoxib:ab,ti OR 'evening primrose oil':ab,ti OR 'fenamic acid':ab,ti OR fenbufen:ab,ti OR fenclofenac:ab,ti OR fenflumizole:ab,ti OR fenoprofen:ab,ti OR fentiazac:ab,ti OR fepradinol:ab,ti OR feprazone:ab,ti OR 'ferulic acid':ab,ti OR floctafenine:ab,ti OR flosulide:ab,ti OR flunixin:ab,ti OR 'flunixin meglumine':ab,ti OR flunoxaprofen:ab,ti OR fluproquazone:ab,ti OR flurbiprofen:ab,ti OR 'flurbiprofen axetil':ab,ti OR glucametacin:ab,ti OR guacetisal:ab,ti OR helenalin:ab,ti OR heliodermin:ab,ti OR hemodes:ab,ti OR higenamine:ab,ti OR ibuprofen:ab,ti OR ibuproxam:ab,ti OR icatibant:ab,ti OR indobufen:ab,ti OR indomethacin:ab,ti OR indoprofen:ab,ti OR iodoantipyrine:ab,ti OR isoxicam:ab,ti OR kebuzone:ab,ti OR ketoprofen:ab,ti OR 'ketoprofen lysine':ab,ti OR ketorolac:ab,ti OR licofelone:ab,ti OR lisofylline:ab,ti OR obenzarit:ab,ti OR lonazolac:ab,ti OR lornoxicam:ab,ti OR loxoprofen:ab,ti OR lumiracoxib:ab,ti OR 'magnesium salicylate':ab,ti OR magnolol:ab,ti OR manoalide:ab,ti OR masoprocol:ab,ti OR 'meclofenamic acid':ab,ti OR 'mefenamic acid':ab,ti OR meloxicam:ab,ti OR mesalamine:ab,ti OR mizoribine:ab,ti OR mofebutazone:ab,ti OR mofezolac:ab,ti OR leucine:ab,ti OR nabumetone:ab,ti OR nafamostat:ab,ti OR naproxen:ab,ti OR nebacetin:ab,ti OR nepafenac:ab,ti OR nifenazone:ab,ti OR 'niflumic acid':ab,ti OR nimesulide:ab,ti OR nitroaspirin:ab,ti OR 'olopatadine hydrochloride':ab,ti OR olsalazine:ab,ti OR olvanil:ab,ti OR 'oren gedoku to':ab,ti OR orgotein:ab,ti OR oxaprozin:ab,ti OR oxyphenbutazone:ab,ti OR almidrol:ab,ti OR parecoxib:ab,ti OR parthenolide:ab,ti OR peoniflorin:ab,ti OR phenidone:ab,ti OR phenylbutazone:ab,ti OR pimecrolimus:ab,ti OR pirfenidone:ab,ti OR piroxicam:ab,ti OR pirprofen:ab,ti OR proglumetacin:ab,ti OR propacetamol:ab,ti OR propionylcarnitine:ab,ti OR propyphenazone:ab,ti OR proquazone:ab,ti OR pyranoprofen:ab,ti OR pyrazolone:ab,ti OR pyrogenal:ab,ti OR resveratrol:ab,ti OR rns60:ab,ti OR rofecoxib:ab,ti OR 'rosmarinic acid':ab,ti OR rumalon:ab,ti OR 'saiko-keishi-to':ab,ti OR saikosaponin:ab,ti OR salicin:ab,ti OR salicylamide:ab,ti OR salicylates:ab,ti OR 'salicylsalicylic

acid':ab,ti OR semapimod:ab,ti OR seratrodist:ab,ti OR serratiopeptidase:ab,ti OR shikonin:ab,ti OR sinapaldehyde:ab,ti OR 'sodium salicylate':ab,ti OR sulfasalazine:ab,ti OR sulindac:ab,ti OR 'sulindac sulfide':ab,ti OR 'sulindac sulfone':ab,ti OR suprofen:ab,ti OR suxibuzone:ab,ti OR tanshinone:ab,ti OR taxifolin:ab,ti OR tenidap:ab,ti OR tenoxicam:ab,ti OR tepoxalin:ab,ti OR 'tiapropenic acid':ab,ti OR tiaramide:ab,ti OR tinoridine:ab,ti OR 'tolfenamic acid':ab,ti OR tolmetin:ab,ti OR 'tramadol, dexketoprofen drug combination':ab,ti OR tranilast:ab,ti OR tribenoside:ab,ti OR 'ursolic acid':ab,ti OR valdecoxib:ab,ti OR zileuton:ab,ti OR zomepirac:ab,ti OR deflazacort:ab,ti OR 'alclometasone dipropionate':ab,ti OR amcinonide:ab,ti OR beclomethasone:ab,ti OR betamethasone:ab,ti OR budesonide:ab,ti OR ciclesonide:ab,ti OR clobetasol:ab,ti OR 'clobetasone butyrate':ab,ti OR clocortolone:ab,ti OR desoximetasone:ab,ti OR dexamethasone:ab,ti OR 'dichlorisone acetate':ab,ti OR diflorasone:ab,ti OR diflucortolone:ab,ti OR difluprednate:ab,ti OR 'drocinonide phosphate potassium':ab,ti OR flumethasone:ab,ti OR 'fluocinolone acetonide':ab,ti OR fluocinonide:ab,ti OR 'fluocortin butyl ester':ab,ti OR fluocortolone:ab,ti OR fluorometholone:ab,ti OR 'fluperolone acetate':ab,ti OR 'fluprednidene acetate':ab,ti OR fluprednisolone:ab,ti OR flurandrenolone:ab,ti OR 'fluticasone-salmeterol drug combination':ab,ti OR halometasone:ab,ti OR medrysone:ab,ti OR 'melengestrol acetate':ab,ti OR methylprednisolone:ab,ti OR paramethasone:ab,ti OR prednicarbate:ab,ti OR prednisolone:ab,ti OR prednisone:ab,ti OR rimexolone:ab,ti OR terofenamate:ab,ti OR 'tobramycin, dexamethasone drug combination':ab,ti OR triamcinolone:ab,ti 554702

7. 4-6/OR 1561242

8. 3 AND 7 6830

9. 8 NOT ('animal cell'/de OR 'animal experiment'/de OR 'animal model'/de OR 'animal tissue'/de OR 'human cell'/de OR 'human tissue'/de OR 'in vitro study'/de OR 'nonhuman'/de) 5537

10. 9 NOT ('conference review'/it OR 'review'/it) 4545

## KMbase

1. ([ALL=Gout] OR [ALL=Gouty] OR [ALL=Gouts] OR [ALL=통풍]) 494

2. (((((((((((([ALL=항염증] OR [ALL=colchicine]) OR [ALL=NSAID]) OR [ALL=acefenac]) OR [ALL=diclofenac]) OR [ALL=naproxen]) OR [ALL=ibuprofen]) OR [ALL=zaltoprofen]) OR [ALL=indomethacin]) OR [ALL=celecoxib]) OR [ALL=nabumeton]) OR [ALL=glucocorticoid]) OR [ALL=hydrocortisone]) OR [ALL=triamcinolone]) OR [ALL=prednisolone]) OR [ALL=methylprednisolone]) 6426

3. 1 AND 2 44

## COCHRANE

1. (Gout OR Gouts OR Gouty):ab,ti,kw 1448

2. MeSH descriptor:[gout] explode all trees 315

3. 1 OR 2 1487

5. (colchicine OR Demecolcine OR Colchamine OR Colcemide OR Colcemid OR Lumicolchicines OR NSAID OR aceclofenac OR Falcol OR “Falcol Difucrem” OR “Clanza CR” OR Preservex OR Biofenac OR Sanein OR Beofenac OR Aital OR Bristaflam OR Gerbin OR Diclofenac OR diclofenac OR naproxen OR ibuprofen OR zaltoprofen OR indomethacin OR celecoxib OR nabumeton OR aceclofenac OR acetaminophen OR acetaminophen OR acetosyringone OR acetovanillone OR “acetylsalicylic acid lysinate” OR Adapalene OR alclofenac OR alminoprofen OR amiprilose OR Ampyrone OR “amylase, phosphates, proteases drug combinations” OR andrographolide OR anisodamine OR anisodine OR “antiflammin P2” OR Antipyrine OR

Apazone OR apremilast OR Arteparon OR Arthrotec OR Aspirin OR atrinositol OR azulene OR baicalin OR balsalazide OR bendazac OR benorilate OR benoxaprofen OR benzobarbital OR berbamine OR “betulinic acid” OR bevonium OR “biphenylacetic acid” OR boldine OR “boswellic acid” OR bromfenac OR bucillamine OR Bufexamac OR bumadizone OR butibufen OR “carbaspirin calcium” OR carprofen OR caryophyllene OR castanospermine OR Celecoxib OR cepharanthine OR “chloroquine diphosphate” OR “choline magnesium trisalicylate” OR chrysarobin OR Clonixin OR Curcumin OR dauricine OR “dexketoprofen trometamol” OR Diclofenac OR “diclofenac hydroxyethylpyrrolidine” OR difenpiramide OR Diflunisal OR dimephosphon OR Dipyrone OR diucifon OR droxicam OR ebselen OR ecallantide OR eltenac OR “enfenamic acid” OR Epirizole OR Etanercept OR ethenzamide OR Ethonium OR Etodolac OR etofenamate OR Etoricoxib OR “evening primrose oil” OR “fenamic acid” OR fenbufen OR fenclofenac OR fenflumizole OR Fenoprofen OR fentiazac OR fepradinol OR Feprazone OR “ferulic acid” OR floctafenine OR flosulide OR flunixin OR “flunixin meglumine” OR flunoxaprofen OR fluproquazone OR Flurbiprofen OR “flurbiprofen axetil” OR glucametacin OR guacetisal OR helenalin OR heliodermin OR hemodes OR higenamine OR Ibuprofen OR ibuproxam OR icatibant OR indobufen OR Indomethacin OR Indoprofen OR iodoantipyrine OR isoxicam OR kebuzone OR Ketoprofen OR “ketoprofen lysine” OR Ketorolac OR licofelone OR lisofylline OR obenzarit OR lonazolac OR lornoxicam OR loxoprofen OR lumiracoxib OR “Magnesium Salicylate” OR magnolol OR manoalide OR Masoprocol OR “Meclofenamic Acid” OR “Mefenamic Acid” OR Meloxicam OR Mesalamine OR mizoribine OR mofebutazone OR mofezolac OR leucine OR Nabumetone OR nafamostat OR Naproxen OR Nebacetin OR nepafenac OR nifenazone OR “Niflumic Acid” OR nimesulide OR nitroaspirin OR “Olopatadine Hydrochloride” OR olsalazine OR olvanil OR “oren gedoku to” OR orgotein OR Oxaprozin OR Oxyphenbutazone OR almidrol OR parecoxib OR parthenolide OR peoniflorin OR phenidone OR Phenylbutazone OR pimecrolimus OR pirfenidone OR Piroxicam OR pirprofen OR proglumetacin OR propacetamol OR propionylcarnitine OR propyphenazone OR proquazone OR pyranoprofen OR pyrazolone OR pyrogenal OR Resveratrol OR RNS60 OR rofecoxib OR “rosmarinic acid” OR Rumalon OR “saiko-keishi-to” OR saikosaponin OR salicin OR salicylamide OR Salicylates OR “salicylsalicylic acid” OR semapimod OR seratrodist OR serratiopeptidase OR shikonin OR sinapaldehyde OR “Sodium Salicylate” OR Sulfasalazine OR Sulindac OR “sulindac sulfide” OR “sulindac sulfone” OR Suprofen OR suxibuzone OR tanshinone OR taxifolin OR tenidap OR tenoxicam OR tepoxalin OR “tiaprofenic acid” OR tiaramide OR tinoridine OR “tolfenamic acid” OR Tolmetin OR “tramadol, dexketoprofen drug combination” OR tranilast OR tribenoside OR “ursolic

acid" OR valdecoxib OR zileuton OR zomepirac OR deflazacort OR "alclometasone dipropionate" OR amcinonide OR Beclomethasone OR Betamethasone OR Budesonide OR ciclesonide OR Clobetasol OR "clobetasone butyrate" OR clocortolone OR Desoximetasone OR Dexamethasone OR "dichlorisone acetate" OR diflorasone OR Diflucortolone OR difluprednate OR "drocinonide phosphate potassium" OR Flumethasone OR "Fluocinolone Acetonide" OR Fluocinonide OR "fluocortin butyl ester" OR Fluocortolone OR Fluorometholone OR "fluperolone acetate" OR "fluprednidene acetate" OR Fluprednisolone OR Flurandrenolone OR "Fluticasone-Salmeterol Drug Combination" OR halometasone OR medrysone OR "Melengestrol Acetate" OR Methylprednisolone OR Paramethasone OR prednicarbate OR Prednisolone OR Prednisone OR rimexolone OR terofenamate OR "Tobramycin, Dexamethasone Drug Combination" OR Triamcinolone):ab,ti,kw 89344

6. 4 AND 5 393

7. 6/trials 377

### 3) 만성콩팥병 – KQ9

MEDLINE

1. "Hyperuricemia"[Mesh] 3319
2. "Hyperuricemia"[TW] 7617
3. ("Hyperuricemia"[Mesh]) OR "Hyperuricemia"[TW] 7617
4. "Renal Insufficiency, Chronic"[Mesh] 110421
5. "Renal Insufficiency, Chronic"[TIAB] OR "Chronic Renal Insufficiencies"[TIAB] OR "Renal Insufficiencies, Chronic"[TIAB] OR "Chronic Renal Insufficiency"[TIAB] OR "Kidney Insufficiency, Chronic"[TIAB] OR "Chronic Kidney Insufficiency"[TIAB] OR "Chronic Kidney Insufficiencies"[TIAB]

OR "Kidney Insufficiencies, Chronic"[TIAB] OR "Chronic Kidney Diseases"[TIAB] OR "Chronic Kidney Disease"[TIAB] OR "Disease, Chronic Kidney"[TIAB] OR "Diseases, Chronic Kidney"[TIAB] OR "Kidney Disease, Chronic"[TIAB] OR "Kidney Diseases, Chronic"[TIAB] OR "Chronic Renal Diseases"[TIAB] OR "Chronic Renal Disease"[TIAB] OR "Disease, Chronic Renal"[TIAB] OR "Diseases, Chronic Renal"[TIAB] OR "Renal Disease, Chronic"[TIAB] OR "Renal Diseases, Chronic"[TIAB] OR "CKD"[TIAB] OR "CKD stage 3"[TIAB] OR "CKD stage 4"[TIAB] 56909

6. ("Renal Insufficiency, Chronic"[Mesh]) OR (("Renal Insufficiency, Chronic"[TIAB] OR "Chronic Renal Insufficiencies"[TIAB] OR "Renal Insufficiencies, Chronic"[TIAB] OR "Chronic Renal Insufficiency"[TIAB] OR "Kidney Insufficiency, Chronic"[TIAB] OR "Chronic Kidney Insufficiency"[TIAB] OR "Chronic Kidney Insufficiencies"[TIAB] OR "Kidney Insufficiencies, Chronic"[TIAB] OR "Chronic Kidney Diseases"[TIAB] OR "Chronic Kidney Disease"[TIAB] OR "Disease, Chronic Kidney"[TIAB] OR "Diseases, Chronic Kidney"[TIAB] OR "Kidney Disease, Chronic"[TIAB] OR "Kidney Diseases, Chronic"[TIAB] OR "Chronic Renal Diseases"[TIAB] OR "Chronic Renal Disease"[TIAB] OR "Disease, Chronic Renal"[TIAB] OR "Diseases, Chronic Renal"[TIAB] OR "Renal Disease, Chronic"[TIAB] OR "Renal Diseases, Chronic"[TIAB] OR "CKD"[TIAB] OR "CKD stage 3"[TIAB] OR "CKD stage 4"[TIAB])) 138471

7. #3 AND #6 823

8. "Uric Acid"[Mesh] 23911

9. "Uric Acid"[TIAB] OR "Acid, Uric"[TIAB] OR "2,6,8-Trihydroxypurine"[TIAB] OR "Trioxopurine"[TIAB] OR "Potassium Urate"[TIAB] OR "Urate, Potassium"[TIAB] OR "Urate"[TIAB] OR "Ammonium Acid Urate"[TIAB] OR "Acid Urate, Ammonium"[TIAB] OR "Urate, Ammonium Acid"[TIAB] OR "Sodium Urate Monohydrate"[TIAB] OR "Monohydrate, Sodium Urate"[TIAB] OR "Urate Monohydrate, Sodium"[TIAB] OR "Monosodium Urate Monohydrate"[TIAB] OR "Monohydrate, Monosodium Urate"[TIAB] OR "Urate Monohydrate, Monosodium"[TIAB] OR "Sodium Acid Urate Monohydrate"[TIAB] OR "Sodium Urate"[TIAB] OR "Urate, Sodium"[TIAB] OR "Monosodium Urate"[TIAB] OR "Urate, Monosodium"[TIAB] OR "Sodium Acid Urate"[TIAB] OR "Acid Urate, Sodium"[TIAB] OR "Urate, Sodium Acid"[TIAB] OR "Uric Acid Lowering Agents"[TIAB] OR "Urate lowering therapy"[TIAB] OR "ULT"[TIAB] 32549

10. "Uricosuric Agents"[Mesh] 1211

11. "Uricosuric Agents"[TIAB] OR "Agents, Uricosuric"[TIAB] 198
12. "Uricosuric Agents" [Pharmacological Action] 6655
13. "Allopurinol"[Mesh] OR "Xanthine Oxidase"[Mesh] OR "Febuxostat"[Mesh] OR "Benzbromarone"[Mesh] OR "Uricosuric Agents" [Pharmacological Action] 20257
14. "Probenecid"[MeSH] OR "Apazone"[MeSH] OR "Benzbromarone"[MeSH] OR "benziodarone"[Supplementary Concept] OR "Halofenate"[MeSH] OR "indacrinone"[Supplementary Concept] OR "lesinurad"[Supplementary Concept] OR "Probenecid"[MeSH] OR "Sulfinpyrazone"[MeSH] OR "Ticrynafen"[MeSH] OR "traxanox"[Supplementary Concept] OR "Zoxazolamine"[MeSH] 5769
15. "allopurinol"[TIAB] OR "Xanthine Oxidase"[TIAB] OR "Uribenz"[TIAB] OR "Allopurin"[TIAB] OR "Allorin"[TIAB] OR "Allpargin"[TIAB] OR "Allural"[TIAB] OR "Pan Quimica"[TIAB] OR "Apulonga"[TIAB] OR "Apurin"[TIAB] OR "Atisuril"[TIAB] OR "Bleminol"[TIAB] OR "Caplenal"[TIAB] OR "Capurate"[TIAB] OR "Cellidrin"[TIAB] OR "Embarin"[TIAB] OR "Suspendol"[TIAB] OR "Foligan"[TIAB] OR "Hamarin"[TIAB] OR "Lopurin"[TIAB] OR "Lysuron"[TIAB] OR "Jenapurinol"[TIAB] OR "Milurit"[TIAB] OR "Milurite"[TIAB] OR "Novopurol"[TIAB] OR "Uripurinol"[TIAB] OR "Urosin"[TIAB] OR "Urtias"[TIAB] OR "Xanthomax"[TIAB] OR "Uridocid"[TIAB] OR "Xanturic"[TIAB] OR "Zygout"[TIAB] OR "Zyloprim"[TIAB] OR "Zyloric"[TIAB] OR "Pureduct"[TIAB] OR "Purinol"[TIAB] OR "Progout"[TIAB] OR "Remid"[TIAB] OR "Rimapurinol"[TIAB] OR "Antigout"[TIAB] OR "Antihyperuricemics"[TIAB] OR "Roucol"[TIAB] OR "Tipuric"[TIAB] OR "Allohexal"[TIAB] OR "Allohexan"[TIAB] OR "Alloprin"[TIAB] OR "Uloric"[TIAB] OR "febuxostat"[TIAB] OR "benzbromarone"[TIAB] 15941
16. (((((((("Uric Acid"[Mesh]) OR ("Uric Acid"[TIAB] OR "Acid, Uric"[TIAB] OR "2,6,8-Trihydroxypurine"[TIAB] OR "Trioxopurine"[TIAB] OR "Potassium Urate"[TIAB] OR "Urate, Potassium"[TIAB] OR "Urate"[TIAB] OR "Ammonium Acid Urate"[TIAB] OR "Acid Urate, Ammonium"[TIAB] OR "Urate, Ammonium Acid"[TIAB] OR "Sodium Urate Monohydrate"[TIAB] OR "Monohydrate, Sodium Urate"[TIAB] OR "Urate Monohydrate, Sodium"[TIAB] OR "Monosodium Urate Monohydrate"[TIAB] OR "Monohydrate, Monosodium Urate"[TIAB] OR "Urate Monohydrate, Monosodium"[TIAB] OR "Sodium Acid Urate Monohydrate"[TIAB] OR "Sodium Urate"[TIAB] OR "Urate, Sodium"[TIAB] OR "Monosodium Urate"[TIAB] OR "Urate, Monosodium"[TIAB] OR "Sodium Acid Urate"[TIAB] OR "Acid Urate, Sodium"[TIAB] OR "Urate, Sodium Acid"[TIAB] OR

"Uric Acid Lowering Agents"[TIAB] OR "Urate lowering therapy"[TIAB] OR "ULT"[TIAB])) OR "Uricosuric Agents"[Mesh]) OR (("Uricosuric Agents"[TIAB] OR "Agents, Uricosuric"[TIAB])) OR "Uricosuric Agents" [Pharmacological Action]) OR (("Allopurinol"[Mesh] OR "Xanthine Oxidase"[Mesh] OR "Febuxostat"[Mesh] OR "Benzbromarone"[Mesh] OR "Uricosuric Agents" [Pharmacological Action])) OR (("Probenecid"[MeSH] OR "Apazone"[MeSH] OR "Benzbromarone"[MeSH] OR "benziodarone"[Supplementary Concept] OR "Halofenate"[MeSH] OR "indacrinone"[Supplementary Concept] OR "Ilesinurad"[Supplementary Concept] OR "Probenecid"[MeSH] OR "Sulfinpyrazone"[MeSH] OR "Ticrynafen"[MeSH] OR "traxanox"[Supplementary Concept] OR "Zoxazolamine"[MeSH])) OR (("allopurinol"[TIAB] OR "Xanthine Oxidase"[TIAB] OR "Uribenz"[TIAB] OR "Allopurin"[TIAB] OR "Allorin"[TIAB] OR "Allpargin"[TIAB] OR "Allural"[TIAB] OR "Pan Quimica"[TIAB] OR "Apulonga"[TIAB] OR "Apurin"[TIAB] OR "Atisuril"[TIAB] OR "Bleminol"[TIAB] OR "Caplenal"[TIAB] OR "Capurate"[TIAB] OR "Cellidrin"[TIAB] OR "Embarin"[TIAB] OR "Suspendol"[TIAB] OR "Foligan"[TIAB] OR "Hamarin"[TIAB] OR "Lopurin"[TIAB] OR "Lysuron"[TIAB] OR "Jenapurinol"[TIAB] OR "Milurit"[TIAB] OR "Milurite"[TIAB] OR "Novopurol"[TIAB] OR "Uripurinol"[TIAB] OR "Urosin"[TIAB] OR "Urtias"[TIAB] OR "Xanthomax"[TIAB] OR "Uridocid"[TIAB] OR "Xanturic"[TIAB] OR "Zygout"[TIAB] OR "Zyloprim"[TIAB] OR "Zyloric"[TIAB] OR "Pureduct"[TIAB] OR "Purinol"[TIAB] OR "Progout"[TIAB] OR "Remid"[TIAB] OR "Rimapurinol"[TIAB] OR "Antigout"[TIAB] OR "Antihyperuricemics"[TIAB] OR "Roucol"[TIAB] OR "Tipuric"[TIAB] OR "Allohexal"[TIAB] OR "Allohexan"[TIAB] OR "Alloprin"[TIAB] OR "Uloric"[TIAB] OR "febuxostat"[TIAB] OR "benzbromarone"[TIAB])) 61804

17. #7 AND #16 612

18. #17 NOT "review"[Publication Type] OR "review literature as topic"[MeSH] 476

19. #18 NOT ("animals"[MeSH] NOT "humans"[MeSH]) 453

EMBASE

1. hyperuricemia/exp 15020



2. hyperuricemia':ab,ti,kw,de OR 'hyperuricacidaemia':ab,ti OR 'hyperuricacidemia':ab,ti OR 'hyperuricaemia':ab,ti OR 'senile hyperuricaemia':ab,ti OR 'senile hyperuricemia':ab,ti 18335
3. 'hyperuricemia'/exp OR ('hyperuricemia':ab,ti,kw,de OR 'hyperuricacidaemia':ab,ti OR 'hyperuricacidemia':ab,ti OR 'hyperuricaemia':ab,ti OR 'senile hyperuricaemia':ab,ti OR 'senile hyperuricemia':ab,ti) 18335
4. 'chronic kidney failure'/exp 142125
5. 'renal insufficiency, chronic':ab,ti OR 'chronic renal insufficiencies':ab,ti OR 'renal insufficiencies, chronic':ab,ti OR 'chronic renal insufficiency':ab,ti OR 'kidney insufficiency, chronic':ab,ti OR 'chronic kidney insufficiency':ab,ti OR 'chronic kidney insufficiencies':ab,ti OR 'kidney insufficiencies, chronic':ab,ti OR 'chronic kidney diseases':ab,ti OR 'chronic kidney disease':ab,ti OR 'disease, chronic kidney':ab,ti OR 'diseases, chronic kidney':ab,ti OR 'kidney disease, chronic':ab,ti OR 'kidney diseases, chronic':ab,ti OR 'chronic renal diseases':ab,ti OR 'chronic renal disease':ab,ti OR 'disease, chronic renal':ab,ti OR 'diseases, chronic renal':ab,ti OR 'renal disease, chronic':ab,ti OR 'renal diseases, chronic':ab,ti OR 'ckd':ab,ti OR 'ckd stage 3':ab,ti OR 'ckd stage 4':ab,ti 89653
6. 'chronic kidney failure'/exp OR ('renal insufficiency, chronic':ab,ti OR 'chronic renal insufficiencies':ab,ti OR 'renal insufficiencies, chronic':ab,ti OR 'chronic renal insufficiency':ab,ti OR 'kidney insufficiency, chronic':ab,ti OR 'chronic kidney insufficiency':ab,ti OR 'chronic kidney insufficiencies':ab,ti OR 'kidney insufficiencies, chronic':ab,ti OR 'chronic kidney diseases':ab,ti OR 'chronic kidney disease':ab,ti OR 'disease, chronic kidney':ab,ti OR 'diseases, chronic kidney':ab,ti OR 'kidney disease, chronic':ab,ti OR 'kidney diseases, chronic':ab,ti OR 'chronic renal diseases':ab,ti OR 'chronic renal disease':ab,ti OR 'disease, chronic renal':ab,ti OR 'diseases, chronic renal':ab,ti OR 'renal disease, chronic':ab,ti OR 'renal diseases, chronic':ab,ti OR 'ckd':ab,ti OR 'ckd stage 3':ab,ti OR 'ckd stage 4':ab,ti) 163445
7. #3 AND #6 1759
8. 'uric acid'/exp 43125
9. 'uric acid':ab,ti OR 'acid, uric':ab,ti OR '2,6,8-trihydroxypurine':ab,ti OR 'trioxopurine':ab,ti OR 'potassium urate':ab,ti OR 'urate, potassium':ab,ti OR 'urate':ab,ti OR 'ammonium acid urate':ab,ti OR 'acid urate, ammonium':ab,ti OR 'urate, ammonium acid':ab,ti OR 'sodium urate monohydrate':ab,ti OR

'monohydrate, sodium urate':ab,ti OR 'urate monohydrate, sodium':ab,ti OR 'monosodium urate monohydrate':ab,ti OR 'monohydrate, monosodium urate':ab,ti OR 'urate monohydrate, monosodium':ab,ti OR 'sodium acid urate monohydrate':ab,ti OR 'sodium urate':ab,ti OR 'urate, sodium':ab,ti OR 'monosodium urate':ab,ti OR 'urate, monosodium':ab,ti OR 'sodium acid urate':ab,ti OR 'acid urate, sodium':ab,ti OR 'urate, sodium acid':ab,ti OR 'uric acid lowering agents':ab,ti OR 'urate lowering therapy':ab,ti OR 'ult':ab,ti 45315

10. 'uricosuric agent'/exp 16917

11. 'uricosuric agents':ab,ti OR 'agents, uricosuric':ab,ti 174

12. 'allopurinol'/exp OR 'xanthine oxidase'/exp OR 'febuxostat'/exp OR 'benzbromarone'/exp 34051

13. 'azapropazone'/exp OR 'benzbromarone'/exp OR 'benziodarone'/exp OR 'halofenate'/exp OR 'indacrinone'/exp OR 'lesinurad'/exp OR 'probenecid'/exp OR 'sulfipyrazone'/exp OR 'tienilic acid'/exp OR 'traxanox'/exp OR 'zoxazolamine'/exp 17266

14. 'allopurinol':ab,ti OR 'xanthine oxidase':ab,ti OR 'uribenz':ab,ti OR 'allopurin':ab,ti OR 'allorin':ab,ti OR 'allpargin':ab,ti OR 'allural':ab,ti OR 'pan quimica':ab,ti OR 'apulonga':ab,ti OR 'apurin':ab,ti OR 'atisuril':ab,ti OR 'bleminol':ab,ti OR 'caplenal':ab,ti OR 'capurate':ab,ti OR 'cellidrin':ab,ti OR 'embarin':ab,ti OR 'suspendol':ab,ti OR 'foligan':ab,ti OR 'hamarin':ab,ti OR 'lopurin':ab,ti OR 'lysuron':ab,ti OR 'jenapurinol':ab,ti OR 'milurit':ab,ti OR 'milurite':ab,ti OR 'novopurol':ab,ti OR 'uripurinol':ab,ti OR 'urosin':ab,ti OR 'urtias':ab,ti OR 'xanthomax':ab,ti OR 'uridocid':ab,ti OR 'xanturic':ab,ti OR 'zygout':ab,ti OR 'zyloprim':ab,ti OR 'zyloric':ab,ti OR 'pureduct':ab,ti OR 'purinol':ab,ti OR 'progout':ab,ti OR 'remid':ab,ti OR 'rimapurinol':ab,ti OR 'antigout':ab,ti OR 'antihyperuricemics':ab,ti OR 'roucol':ab,ti OR 'tipuric':ab,ti OR 'allohexal':ab,ti OR 'allohexan':ab,ti OR 'alloprin':ab,ti OR 'uloric':ab,ti OR 'febuxostat':ab,ti OR 'benzbromarone':ab,ti 20747

15. 'uric acid'/exp OR ('uric acid':ab,ti OR 'acid, uric':ab,ti OR '2,6,8-trihydroxypurine':ab,ti OR 'trioxopurine':ab,ti OR 'potassium urate':ab,ti OR 'urate, potassium':ab,ti OR 'urate':ab,ti OR 'ammonium acid urate':ab,ti OR 'acid urate, ammonium':ab,ti OR 'urate, ammonium acid':ab,ti OR 'sodium urate monohydrate':ab,ti OR 'monohydrate, sodium urate':ab,ti OR 'urate monohydrate, sodium':ab,ti OR 'monosodium urate monohydrate':ab,ti OR 'monohydrate, monosodium urate':ab,ti OR 'urate monohydrate, monosodium':ab,ti OR 'sodium acid urate monohydrate':ab,ti OR 'sodium urate':ab,ti OR 'urate, sodium':ab,ti OR 'monosodium urate':ab,ti OR 'urate, monosodium':ab,ti OR 'sodium acid urate':ab,ti OR 'acid urate, sodium':ab,ti OR 'urate, sodium

acid':ab,ti OR 'uric acid lowering agents':ab,ti OR 'urate lowering therapy':ab,ti OR 'ult':ab,ti) OR 'uricosuric agent'/exp OR ('uricosuric agents':ab,ti OR 'agents, uricosuric':ab,ti) OR ('allopurinol'/exp OR 'xanthine oxidase'/exp OR 'febuxostat'/exp OR 'benzbromarone'/exp) OR ('azapropazone'/exp OR 'benzbromarone'/exp OR 'benziodarone'/exp OR 'halofenate'/exp OR 'indacrinone'/exp OR 'lesinurad'/exp OR 'probenecid'/exp OR 'sulfipyrazone'/exp OR 'tienilic acid'/exp OR 'traxanox'/exp OR 'zoxazolamine'/exp) OR ('allopurinol':ab,ti OR 'xanthine oxidase':ab,ti OR 'uribenz':ab,ti OR 'allopurin':ab,ti OR 'allorin':ab,ti OR 'allpargin':ab,ti OR 'allural':ab,ti OR 'pan quimica':ab,ti OR 'apulonga':ab,ti OR 'apurin':ab,ti OR 'atisuril':ab,ti OR 'bleminol':ab,ti OR 'caplrenal':ab,ti OR 'capurate':ab,ti OR 'cellidrin':ab,ti OR 'embarin':ab,ti OR 'suspendol':ab,ti OR 'foligan':ab,ti OR 'hamarin':ab,ti OR 'lopurin':ab,ti OR 'lysuron':ab,ti OR 'jenapurinol':ab,ti OR 'milurit':ab,ti OR 'milurite':ab,ti OR 'novopurol':ab,ti OR 'uripurinol':ab,ti OR 'urosin':ab,ti OR 'urtias':ab,ti OR 'xanthomax':ab,ti OR 'uridocid':ab,ti OR 'xanturic':ab,ti OR 'zygout':ab,ti OR 'zyloprim':ab,ti OR 'zyloric':ab,ti OR 'pureduct':ab,ti OR 'purinol':ab,ti OR 'progout':ab,ti OR 'remid':ab,ti OR 'rimapurinol':ab,ti OR 'antigout':ab,ti OR 'antihyperuricemics':ab,ti OR 'roucol':ab,ti OR 'tipuric':ab,ti OR 'allohexal':ab,ti OR 'allohexan':ab,ti OR 'alloprin':ab,ti OR 'uloric':ab,ti OR 'febuxostat':ab,ti OR 'benzbromarone':ab,ti) 104078

16. #7 AND #15 1222

17. #16 NOT ('conference review'/it OR 'review'/it) 1022

18. #17 NOT ('animal cell'/de OR 'animal experiment'/de OR 'animal model'/de OR 'animal tissue'/de OR 'human cell'/de OR 'human tissue'/de OR 'in vitro study'/de OR 'nonhuman'/de) 775

#### KMBASE

1. [ALL=고요산혈증] OR [ALL=Hyperuricemia] OR [ALL=hyperuricacidaemiay] OR [ALL=hyperuricacidemia] OR [ALL=hyperuricaemia] OR

[ALL=고요산 혈증] 263

2. [ALL=Chronic Kidney Disease] OR [ALL=Chronic Renal Disease] OR [ALL=만성 신질환] OR [ALL=만성신질환] 803

3. (([ALL=allopurinol] OR [ALL=febuxostat] OR [ALL=Xanthine Oxidase] OR [ALL=Benzbromarone] OR [ALL=알로푸리놀] OR [ALL=페부소스타즈] OR [ALL=Uric Acid] OR [ALL=요산] OR [ALL=Urate] OR [ALL=Uricosuric Agents]) OR [ALL=Uric Acid Lowering Agents] OR [ALL=Urate lowering therapy] OR [ALL=요산저하제]) 1720
4. #1 AND #2 AND #3 17

#### COCHRANE

1. [mh Hyperuricemia] 213
2. "Hyperuricemia":ti,ab,kw 1011
3. #1 OR #2 1011
4. [mh "Renal Insufficiency, Chronic"] 6088
5. "Renal Insufficiency, Chronic":ti,ab,kw OR "Chronic Renal Insufficiencies":ti,ab,kw OR "Renal Insufficiencies, Chronic":ti,ab,kw OR "Chronic Renal Insufficiency":ti,ab,kw OR "Kidney Insufficiency, Chronic":ti,ab,kw OR "Chronic Kidney Insufficiency":ti,ab,kw OR "Chronic Kidney Insufficiencies":ti,ab,kw OR "Kidney Insufficiencies, Chronic":ti,ab,kw OR "Chronic Kidney Diseases":ti,ab,kw OR "Chronic Kidney Disease":ti,ab,kw OR "Disease, Chronic Kidney":ti,ab,kw OR "Diseases, Chronic Kidney":ti,ab,kw OR "Kidney Disease, Chronic":ti,ab,kw OR "Kidney Diseases, Chronic":ti,ab,kw OR "Chronic Renal Diseases":ti,ab,kw OR "Chronic Renal Disease":ti,ab,kw OR "Disease, Chronic Renal":ti,ab,kw OR "Diseases, Chronic Renal":ti,ab,kw OR "Renal Disease, Chronic":ti,ab,kw OR "Renal Diseases, Chronic":ti,ab,kw OR "CKD":ti,ab,kw OR "CKD stage 3":ti,ab,kw OR "CKD stage 4":ti,ab,kw 8768
6. #4 OR #5 12166
7. #3 AND #6 115

8. [mh "Uric Acid"] 1084
9. "Uric Acid":ti,ab,kw OR "Acid, Uric":ti,ab,kw OR "2,6,8-Trihydroxypurine":ti,ab,kw OR "Trioxopurine":ti,ab,kw OR "Potassium Urate":ti,ab,kw OR "Urate, Potassium":ti,ab,kw OR "Urate":ti,ab,kw OR "Ammonium Acid Urate":ti,ab,kw OR "Acid Urate, Ammonium":ti,ab,kw OR "Urate, Ammonium Acid":ti,ab,kw OR "Sodium Urate Monohydrate":ti,ab,kw OR "Monohydrate, Sodium Urate":ti,ab,kw OR "Urate Monohydrate, Sodium":ti,ab,kw OR "Monosodium Urate Monohydrate":ti,ab,kw OR "Monohydrate, Monosodium Urate":ti,ab,kw OR "Urate Monohydrate, Monosodium":ti,ab,kw OR "Sodium Acid Urate Monohydrate":ti,ab,kw OR "Sodium Urate":ti,ab,kw OR "Urate, Sodium":ti,ab,kw OR "Monosodium Urate":ti,ab,kw OR "Urate, Monosodium":ti,ab,kw OR "Sodium Acid Urate":ti,ab,kw OR "Acid Urate, Sodium":ti,ab,kw OR "Urate, Sodium Acid":ti,ab,kw OR "Uric Acid Lowering Agents":ti,ab,kw OR "Urate lowering therapy":ti,ab,kw OR "ULT":ti,ab,kw 4257
10. [mh "Uricosuric Agents"] 70
11. "Uricosuric Agents":ti,ab,kw OR "Agents, Uricosuric":ti,ab,kw 75
12. [mh Allopurinol] OR [mh "Xanthine Oxidase"] OR [mh Febuxostat] OR [mh Benzbromarone] 669
13. [mh Probenecid] OR [mh Apazone] OR [mh Benzbromarone] OR "benziodarone":ti,ab,kw OR [mh Halofenate] OR "indacrinone":ti,ab,kw OR "lesinurad":ti,ab,kw OR [mh Probenecid] OR [mh "Sulfinpyrazone"] OR [mh Ticrynafen] OR "traxanox":ti,ab,kw OR [mh Zoxazolamine] 505
14. "allopurinol":ti,ab,kw OR "Xanthine Oxidase":ti,ab,kw OR "Uribenz":ti,ab,kw OR "Allopurin":ti,ab,kw OR "Allorin":ti,ab,kw OR "Allpargin":ti,ab,kw OR "Allural":ti,ab,kw OR "Pan Quimica":ti,ab,kw OR "Apulonga":ti,ab,kw OR "Apurin":ti,ab,kw OR "Atisuril":ti,ab,kw OR "Bleminol":ti,ab,kw OR "Caplenal":ti,ab,kw OR "Capurate":ti,ab,kw OR "Cellidrin":ti,ab,kw OR "Embarin":ti,ab,kw OR "Suspendol":ti,ab,kw OR "Foligan":ti,ab,kw OR "Hamarin":ti,ab,kw OR "Lopurin":ti,ab,kw OR "Lysuron":ti,ab,kw OR "Jenapurinol":ti,ab,kw OR "Milurit":ti,ab,kw OR "Milurite":ti,ab,kw OR "Novopurol":ti,ab,kw OR "Uripurinol":ti,ab,kw OR "Urosin":ti,ab,kw OR "Urtias":ti,ab,kw OR "Xanthomax":ti,ab,kw OR "Uridocid":ti,ab,kw OR "Xanturic":ti,ab,kw OR "Zygout":ti,ab,kw OR "Zyloprim":ti,ab,kw OR "Zyloric":ti,ab,kw OR "Pureduct":ti,ab,kw OR "Purinol":ti,ab,kw OR "Progout":ti,ab,kw OR "Remid":ti,ab,kw OR "Rimapurinol":ti,ab,kw OR "Antigout":ti,ab,kw OR "Antihyperuricemics":ti,ab,kw OR "Roucol":ti,ab,kw OR

"Tipuric":ti,ab,kw OR "Allohexal":ti,ab,kw OR "Allohexan":ti,ab,kw OR "Alloprin":ti,ab,kw OR "Uloric":ti,ab,kw OR "febuxostat":ti,ab,kw OR "benzbromarone":ti,ab,kw 1603

15. {OR #8-#14} 5376

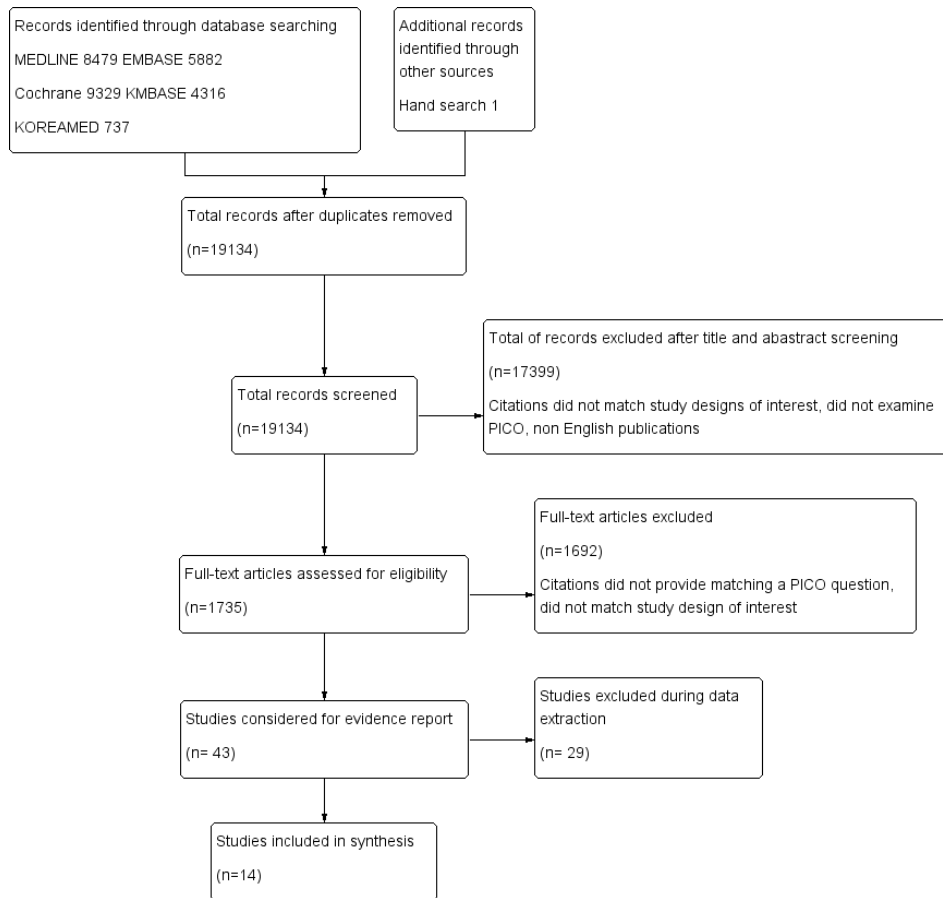
16. #7 AND #15 103

#### **4) KOREAMED**

KoreaMed

(MeSH\_Terms:"Gout" OR MeSH\_Terms:"Hyperuricemia" OR MeSH\_Terms:"Uric Acid" OR All\_Fields:"Gout" OR All\_Fields:"Gouts" OR All\_Fields:"Gouty" OR All\_Fields:"Hyperuricemia" OR All\_Fields:"Urate" OR All\_Fields:"Uric Acid" OR All\_Fields:"hyperuricacidaemia" OR All\_Fields:"hyperuricacidemia" OR All\_Fields:"hyperuricaemia") 737

## 7. Literature selection



## 8. Evidence table

**KQ1**

*Should we use NSAIDs over colchicine/corticosteroids in patients experiencing a gout flare to reduce the duration of the flare?*

### 1) Characteristics of selected studies (Evidence table)

Study	Design	Characteristics	Intervention	Control	Outcome
Billy 2017	Systematic Review	Acute gout patients	NSAIDs	Steroid	Pain, Acute gout duration
Roddy2019	RCT	Acute gout patients	NSAIDs	Colchicine	Pain, Acute gout duration

### 2) Assessment of risk of bias

Billy (Amstar: 8)

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?			o	
2. Was there duplicate study selection and data extraction?	o			
3. Was a comprehensive literature search performed?	o			



4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	o			
5. Was a list of studies (included and excluded) provided?		o		
6. Were the characteristics of the included studies provided?	o			
7. Was the scientific quality of the included studies assessed and documented?	o			
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	o			
9. Were the methods used to combine the findings of studies appropriate?	o			
10. Was the likelihood of publication bias assessed?	o			
11. Was the conflict of interest stated?		o		

Roddy

Roddy et al. (2020)	+	+	-	-		+	
	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias

### 3) GRADE evidence profile

Certainty assessment							N <sup>o</sup> of patients		Effect		Certainty	Importance
N <sup>o</sup> of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAIDs	steroid	Relative (95% CI)	Absolute (95% CI)		

### Pain

2	randomised trials	not serious	not serious	serious	not serious	none	267	267	-	SMD 0.09 SD lower (0.26 lower to 0.08 higher)	⊕⊕⊕○ MODERATE	IMPORTANT
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### Duration of flare

1	randomised trials	serious	not serious	not serious	serious	none	-/10	-/10	not estimable		⊕⊕○○ LOW	critical
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CI: Confidence interval; SMD: Standardised mean difference

## Explanations

- a. short-term pain (7 days)
- b. Time to disease resolution

Certainty assessment	N <sup>o</sup> of patients	Effect	Certainty	Importance
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N <sub>o</sub> of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	NSAID	colchicine	Relative (95% CI)	Absolute (95% CI)		
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**Pain<sup>a</sup>**

1	randomised trials	serious <sup>b</sup>	not serious	not serious	not serious	none	200	199	-	not estimable	⊕⊕⊕○ MODERATE	IMPORTANT
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**Duration (follow up: median 28 days)<sup>c</sup>**

1	randomised trials	serious <sup>b</sup>	not serious	not serious	not serious	none	200	199	-	median 1 days lower (0 to 0)	⊕⊕⊕○ MODERATE	CRITICAL
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CI: Confidence interval

## Explanations

a. mean change in worst pain intensity over days 1–7

b. This is an open label study without blinded outcome assessment or placebo tablets, and collection of solely self-reported outcomes.

c. Days to complete pain resolution

<b><u>KQ2</u></b>	<i>Should we start ULT during a gout flare vs. after a gout flare has resolved when initiating ULT?</i>
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### 1) Characteristics of selected studies (Evidence table)

Study	Design	Characteristics	Intervention	Control	Outcome
Fatma 2016	Systematic Review	Initiation of any ULT in patients with acute gout	Allopurinol	Placebo	Gout attack :Pain severity and Duration of gout attack

## 2) Assessment of risk of bias

AMSTAR: 8

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?			o	
2. Was there duplicate study selection and data extraction?	o			
3. Was a comprehensive literature search performed?	o			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	o			
5. Was a list of studies (included and excluded) provided?		o		
6. Were the characteristics of the included studies provided?	o			
7. Was the scientific quality of the included studies assessed and documented?	o			
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	o			
9. Were the methods used to combine the findings of studies appropriate?	o			

10. Was the likelihood of publication bias assessed?	o			
11. Was the conflict of interest stated?		o		

### 3) GRADE evidence profile

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	With ULT be used during a gout flare	With after a gout flare has resolved	Relative (95% CI)	Absolute (95% CI)		

#### Gout flares

2	randomized trials	not serious	not serious	not serious	very serious <sub>a,b</sub>	none	5/53 (9.4%)	8/49 (16.3%)	not estimable		⊕⊕○○ LOW	
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#### Duration of gout attack

1	randomized trials	serious <sup>c</sup>	not serious	not serious	very serious <sub>a,b</sub>	none	14	17	not estimable		⊕○○○ VERY LOW	
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#### Pain

2	randomized trials	serious <sup>c</sup>	not serious	not serious	serious <sup>a</sup>	none	41	45	not estimable		⊕⊕○○ LOW	
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CI: Confidence interval

## Explanations

- a. wide confidence intervals
- b. small sample sizes in each arm
- c. RCT with two domains with high RoB

<b><u>KQ3</u></b>	<i>Should prophylaxis vs. no prophylaxis be used in patients with gout starting ULT?</i>
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### 1) Characteristics of selected studies (Evidence table)

Study	Design	Characteristics	Intervention	Control	Outcome
Paulus 1974	Placebo controlled trial	Gout	Prophylactic colchicine therapy	placebo	Gout flare
Borstad 2004	Randomised clinical trial	Gout	Prophylactic colchicine therapy	none	Gout flare
Yamanaka 2018	Randomised clinical trial	Gout	Prophylactic colchicine therapy	Step febuxostat increase	wise dose Gout flare

### 2) Assessment of risk of bias

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Borstad et al. (2012)	+		+		+	-	+
Paulus et al. (1974)	-		+	+	-	+	
Yamanaka et al. (2018)	+	+	-	-	+	+	

### 3) GRADE evidence profile

Certainty assessment	Nº of patients	Effect	Certainty	Importance
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№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[intervention]	[comparison]	Relative (95% CI)	Absolute (95% CI)		
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**Gout flare**

3	randomised trials	not serious	not serious	not serious	serious ⇩	none	48/143 (33.6%)	90/193 (46.6%)	not estimable		⊕⊕⊕○ MODERATE	
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CI: Confidence interval

<b><u>KQ4</u></b>	<i>Should prescribing ULT to achieve serum urate &lt;6mg/dL be used in gout on ULT in order to prevent gout flares and bone erosion?</i>
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**1) Characteristics of selected studies (Evidence table)**








Study	Design	Characteristics	Intervention	Control	Outcome
Shiozawa 2017	Systematic Review	Individuals with preexisting gout	SUA levels at baseline Stratified by urate-lowering therapy use	none	Gout flare
Dalbeth 2019	Randomised clinical trial	Gout patients with serum uric acid level over 6mg/dL	Dose escalation with serum uric acid target below 6	none	CT erosion score

**2) Assessment of risk of bias**

Shiozawa AMSTAR: 5

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?			o	
2. Was there duplicate study selection and data extraction?	o			
3. Was a comprehensive literature search performed?	o			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	o			
5. Was a list of studies (included and excluded) provided?	o			
6. Were the characteristics of the included studies provided?	o			
7. Was the scientific quality of the included studies assessed and documented?		o		
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?		o		
9. Were the methods used to combine the findings of studies appropriate?		o		
10. Was the likelihood of publication bias assessed?		o		
11. Was the conflict of interest stated?		o		0

Dalbeth

	Random sequence generation (selection bias)
	Allocation concealment (selection bias)
	Blinding of participants and personnel (performance bias)
	Blinding of outcome assessment (detection bias)
	Incomplete outcome data (attrition bias)
	Selective reporting (reporting bias)
	Other bias
Dalbeth et al. (2019)	      

### 3) GRADE evidence profile

Certainty assessment							Nº of patients		Effect		Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[uric acid level below 6]	[uric acid over 6]	Relative (95% CI)	Absolute (95% CI)		

Bone erosion

Certainty assessment							N° of patients		Effect		Certainty	Importance
N° of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	[uric acid level below 6]	[uric acid over 6]	Relative (95% CI)	Absolute (95% CI)		
1	randomised trials	not serious	not serious	serious <sup>a</sup>	serious <sup>b</sup>	none			-		⊕⊕○○ LOW	

### Gout flare

17	observational studies	not serious	not serious	serious <sup>c</sup>	not serious	dose response gradient			not estimable		⊕⊕○○ LOW	
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CI: Confidence interval

### Explanations

- a. not comparing according to the serum uric acid level, but according to the use of treatment serum uric acid target or not
- b. results are based on group using serum uric acid target and group using fixed dose regimen without serum uric acid target
- c. multiple comparators based on serum uric acid category

<b><u>KQ5</u></b>	<i>Should stopping ULT vs. continuing ULT be used for patients with gout on ULT?</i>
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### 1) Characteristics of selected studies

### 1) Characteristics of selected studies (Evidence table)

Study	Design	Characteristics	Intervention	Control	Outcome
Belson 2018	Systematic Review	Gout patients with urate lowering therapy	Discontinuation of urate lowering therapy	none	Relapse

### 2) Assessment of risk of bias

AMSTAR: 7

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?	o			
2. Was there duplicate study selection and data extraction?	o			
3. Was a comprehensive literature search performed?	o			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?	o			
5. Was a list of studies (included and excluded) provided?		o		
6. Were the characteristics of the included studies provided?	o			
7. Was the scientific quality of the included studies assessed and documented?	o			
8. Was the scientific quality of the included studies used appropriately in formulating	o			

conclusions?				
9. Were the methods used to combine the findings of studies appropriate?		o		
10. Was the likelihood of publication bias assessed?		o		
11. Was the conflict of interest stated?		o		0

### 3) GRADE evidence profile

Certainty assessment							Impact	Certainty	Importance
N <sub>e</sub> of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			

relapse (follow up: range 12 months to 96 months)

5	observational studies	serious	not serious	not serious	serious	none	Continuation of urate lowering therapy vs. discontinuation Loebl (1974): RR 0.36(0.20-0.53) Sample size 33 Gast (1986): RR 0.5 (0.19-0.81) Sample size 10 Van Lieshout-Zuidema (1992): RR 0.81 (0.64-0.97) Sample size 21 Darmawan (2002): RR 0.59 (0.52-0.66) Sample size 206 Perez-Ruiz (2011): RR 0.39 (0.32-0.45) Sample size 211 *RR: relative risk	⊕○○○ VERY LOW	
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CI: Confidence interval

**KQ6**

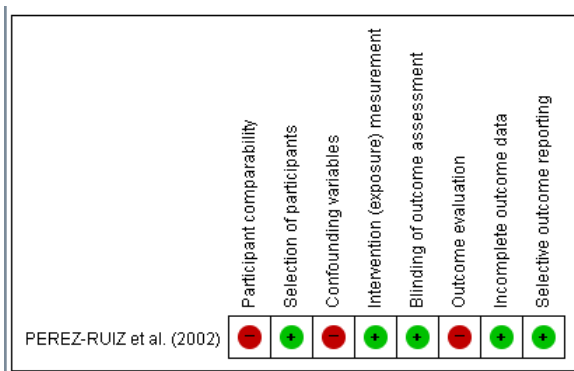
*Should prescription of xanthine oxidase inhibitors over uricosuric agents be used in chronic tophaceous gout?*

**1) Characteristics of selected studies**

Study	Design	Characteristics	Intervention	Control	Outcome
Perez-Ruiz 2002	Observational prospective study	Patients with tophaceous gout	Xathine oxidase inhibitor (allopurinol)	Uricosuric agent (benzbromarone)	Tophi size reduction

**2) Assessment of risk of bias**

Risk of Bias for Nonrandomized studies (RoBANS)



### 3) GRADE evidence profile

Certainty assessment							Impact	Certainty	Importance
N <sub>o</sub> of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			

#### tophi reduction

1	observational studies	serious <sup>a</sup>	not serious	not serious	serious	none	Allopurinol and benzbromarone are equally effective when optimal serum urate levels are achieved during therapy.	⊕○○○ VERY LOW	CRITICAL
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CI: Confidence interval

### Explanations

a. Risk of bias determined by ROBANS is considered to be serious.

<b><u>KQ7</u></b>	<i>Should ULT vs no treatment be used in gout patients in order to preserve renal function?</i>
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### 1) Characteristics of selected studies

Study	Design	Characteristics	Intervention	Control	Outcome
Wang 2013	Systematic Review	Patients with hyperuricemia	ULT drugs 1) Benzbromarone and losartan	Placebo or no URT	Renal function: SCr, eGFR or CCr



- 
- 2) Allopurinol and febuxostat
  - 3) Rasburicase and pegloticase
- 

**2) Assessment of risk of bias**

**AMSTAR 10점**

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?	<input type="radio"/>			
2. Was there duplicate study selection and data extraction?	<input type="radio"/>			
3. Was a comprehensive literature search performed?	<input type="radio"/>			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?			<input type="radio"/>	
5. Was a list of studies (included and excluded) provided?	<input type="radio"/>			
6. Were the characteristics of the included studies provided?	<input type="radio"/>			
7. Was the scientific quality of the included studies assessed and documented?	<input type="radio"/>			
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	<input type="radio"/>			
9. Were the methods used to combine the findings of studies appropriate?	<input type="radio"/>			

10. Was the likelihood of publication bias assessed?	o			
11. Was the conflict of interest stated?	o			

### 3) GRADE evidence profile

Certainty assessment							Impact	Certainty	Importance
Nº of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
<b>Reduction of sCr</b>									
9	randomised trials	serious <sup>a</sup>	not serious	serious <sup>b</sup>	not serious	all plausible residual confounding would reduce the demonstrated effect dose response gradient	The ULT tended to be associated with reduction of SCr (SMD 5 21.253, 95% CI 21.985 to 20.520, I2593.0%; Fig. 3).	⊕⊕⊕⊕ HIGH	CRITICAL
<b>Improvement in renal function (eGFR or CCr)</b>									
3	randomised trials	serious <sup>c</sup>	not serious	serious <sup>b</sup>	not serious	all plausible residual confounding would reduce the demonstrated effect dose response gradient	The hypouricemic treatment was also found to have benefits on eGFR (SMD 5 0.412, 95% CI 0.142-0.682, I2 5 30.6%; Fig. 4).	⊕⊕⊕⊕ HIGH	CRITICAL

CI: Confidence interval

### Explanations

a. Lack of allocation concealment 7/9 studies, lack of blinding 8/9 studies, Description of withdrawals 8/9 studies, Intention to treat analysis 3/9 studies

b. Population different from PICO. Intended population: gout patients. Studied population: hyperuricemia subjects

c. Lack of allocation concealment in 1/3 studies, lack of blinding in 3/3 studies, description of withdrawal in 1/3 studies, Intention to treat analysis in 2/3 studies

<b><u>KQ8</u></b>	<i>Should prescribing ULT vs. no treatment be used to improve cardiovascular outcomes in patients with gout?</i>
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No evidence

<b><u>KQ9</u></b>	<i>Should prescribing ULT vs. no treatment be used in CKD 3,4 patients with asymptomatic hyperuricemia in order to protect renal function?</i>
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**1) Characteristics of selected studies (Evidence table)**

Study	Design	Characteristics	Intervention	Control	Outcome
Kanji, 2015	Systematic Review	CKD patients with urate lowering therapy	Febuxostat	none	Renal protective effect

Xiang Zeng, 2018	Xia Systematic Review	CKD patients with urate lowering therapy	Febuxostat	none	Renal protective effect
Tsu-Chen Lin, 2019	Systematic Review	CKD patients with urate lowering therapy	Febuxostat	none	Renal protective effect

**2) Assessment of risk of bias**

Kanji, 2015, AMSTAR: 6

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?			0	
2. Was there duplicate study selection and data extraction?	0			
3. Was a comprehensive literature search performed?	0			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?		0		
5. Was a list of studies (included and excluded) provided?		0		

6. Were the characteristics of the included studies provided?	0			
7. Was the scientific quality of the included studies assessed and documented?	0			
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	0			
9. Were the methods used to combine the findings of studies appropriate?		0		
10. Was the likelihood of publication bias assessed?	0			
11. Was the conflict of interest stated?		0		

Tsu-Chen Lin, 2019, AMSTAR : 7

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?	<input type="radio"/>			
2. Was there duplicate study selection and data extraction?	<input type="radio"/>			
3. Was a comprehensive literature search performed?	<input type="radio"/>			
4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?		<input type="radio"/>		

5. Was a list of studies (included and excluded) provided?		<input type="radio"/>		
6. Were the characteristics of the included studies provided?	<input type="radio"/>			
7. Was the scientific quality of the included studies assessed and documented?	<input type="radio"/>			
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?	<input type="radio"/>			
9. Were the methods used to combine the findings of studies appropriate?	<input type="radio"/>			
10. Was the likelihood of publication bias assessed?		<input type="radio"/>		
11. Was the conflict of interest stated?		<input type="radio"/>		

Xiang Xia Zeng, 2018, AMSTAR : 6

Questions	Assessment			
	Yes	No	Can't answer	Not applicable
1. Was an 'a priori' design provided?		<input type="radio"/>		
2. Was there duplicate study selection and data extraction?	<input type="radio"/>			
3. Was a comprehensive literature search performed?	<input type="radio"/>			

4. Was the status of publication (i.e. grey literature) used as an inclusion criterion?		o		
5. Was a list of studies (included and excluded) provided?		o		
6. Were the characteristics of the included studies provided?	o			
7. Was the scientific quality of the included studies assessed and documented?	o			
8. Was the scientific quality of the included studies used appropriately in formulating conclusions?		o		
9. Were the methods used to combine the findings of studies appropriate?	o			
10. Was the likelihood of publication bias assessed?	o			
11. Was the conflict of interest stated?		o		

### 3) GRADE evidence profile

Certainty assessment							impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			

Certainty assessment							impact	Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations			
13	randomised trials	serious	not serious	not serious	serious	none	urate lowering therapy vs. Placebo Shankar( 2017): MD 0.21 (-0.17,0.59) Sample size 108 Kenneth( 2016): MD 0.05 (-0.34,0.44) Sample size 106 Kenichi( 2015): MD 0.11 (-0.47,0.69) Sample size 46 Chen( 2016): MD 0.45 (-0.24,1.13) Sample size 34 Andrew( 2013): MD 0.21 (-0.17,0.59) Sample size 320 Kimura( 2018): MD 0.5 (-1.43, 2.43) Sample size 441 Mukri( 2018): MD 0.7 (-4.58, 5.98) Sample size 93 Sircar( 2015): MD 7.6 (1.89, 13.31) Sample size 93 Goicoechea (2010): MD 5.000 (2.725, 7.275) Sample size 113 Kao (2011): MD 0.00 (-3.367, 3.367) Sample size 67 Momeni(2010): MD 1.650 (-8.522, 11.8222) Sample size 44 Shi (2012): MD 1.600 (-9.263, 12.463) Sample size 40 Siu(2006): MD 7.1 (-0.375, 14.575) Sample size 54  *MD: Mean difference	 LOW	

CI: Confidence interval