

**Supplementary file 1:** Details of the search to obtain guidelines on gout.

**1. MEDLINE**

Search strategy for MEDLINE

#1	“Gout”[MeSH]
#2	“Hyperuricemia”[MeSH]
#3	gout*[Title/Abstract]
#4	Hyperuricemia[Title/Abstract]
#5	#1 OR #2 OR #3 OR #4
#6	clinical practice guideline*[tw]
#7	clinical guideline*[tiab]
#8	guideline*[ti]
#9	guidance*[ti]
#10	consensus[ti]
#11	recommendation*[ti]
#12	#6 OR #7 OR #8 OR #9 OR #10 OR #11
#13	#5 AND #12

**2. CBM**

Search strategy for CBM

#1	“痛风” [No weighting and extension]
#2	“高尿酸血症” [No weighting and extension]
#3	“痛风” [Common field: intelligent]
#4	“高尿酸血症” [Common field: intelligent]
#5	#1 OR #2 OR #3 OR #4
#6	“指南” [No weighting and extension]
#7	“指南” [Common field: intelligent]
#8	“指引” [Common field: intelligent]
#9	#6 OR #7 OR #8
#10	#5 AND #9

**3. Guideline databases (NICE, NGC, SIGN, WHO, GIN, DynaMed, UpToDate, Best Practice)**

Combinations of the following key words were searched: “gout”, “hyperuricemia”, “guideline”

**4. Manual search (Google Scholar)**

A search was conducted via the Google Scholar engine using the following terms: ‘(hyperuricemia OR gout) AND (guideline or guidance or consensus or recommendation)’ in English and ‘(痛风 OR 高尿酸血症) AND (指南 OR 指引)’ in Chinese. We screened the first 200 records.

**Supplementary file 2:** Supplementary tables.

**Suppl. Table S1.** Number of recommendations according to topic in the included gout CPGs.

Guideline No.	Diagnosis					Pharmacologic treatment for gout flares					Pharmacologic urate-lowering therapy (ULT) for chronic gouty arthritis					Lifestyle interventions	Prophylaxis	Management of asymptomatic hyperuricemia	Other	Total		
	ultrasound	CT	x-rays	gold standard	other ways	NSAIDs	colchicine	corticosteroids	combination therapy	allopurinol	febuxostat	benzbromarone	probenecid	pegloticase	target of ULT						indications of ULT	combination therapy
1	0	0	0	0	0	1	1	1	0	1	0	0	1	0	1	3	0	6	1	2	5	23
2	0	0	0	0	0	1	1	1	0	0	0	0	0	0	1	0	8	0	0	3	15	
3	0	0	0	0	0	2	0	1	0	1	0	1	0	0	1	0	6	2	5	4	22	
4	0	0	0	0	0	0	0	0	0	3	4	0	3	4	1	2	0	9	4	0	1	31
5	0	0	0	0	0	4	5	9	6	8	2	0	2	4	2	2	15	6	0	17	80	
6	0	0	0	1	0	1	1	1	0	2	2	2	1	1	1	0	1	1	1	2	10	
7	2	1	1	3	3	2	6	5	0	4	2	3	0	0	2	0	3	2	7	1	27	69
8	0	0	0	0	0	2	3	3	0	1	1	0	0	0	1	1	0	1	0	3	12	
9	1	1	0	1	0	1	1	1	0	2	2	1	1	1	1	0	1	1	2	3	12	
10	0	0	1	2	0	1	1	1	1	1	1	1	1	0	1	0	1	1	1	3	11	
11	1	1	0	1	0	1	1	1	0	1	1	1	0	0	0	1	0	1	0	2	12	
12	2	1	1	2	4	2	1	2	1	2	2	1	0	1	2	1	1	1	1	0	4	22
13	0	0	0	1	0	1	2	1	0	0	0	0	0	0	2	0	0	0	0	0	5	
14	0	0	0	0	0	1	1	1	1	1	1	1	1	0	1	1	2	1	0	9	21	
15	0	0	0	1	2	1	1	1	1	1	1	0	0	1	0	0	2	0	1	6	14	
Count		28					58						89				56	26	13	89	359	

The figures in the table represent the amount of recommendations.

Suppl. Table S2. Comparison of recommendations on pharmacologic treatment of gout flares.

No.	1	2	3	5	6	7	8	9	10	11	12	13	14	15
<b>NSAIDs</b>														
<i>Target population</i>	NR	NR	untreated cases	Patients with mild/moderate gout severity <sup>††</sup> particularly those involving one or a few small joints, or 1-2 large joints	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
<i>Line of treatment</i>	NR	1 <sup>st</sup> -line (B)	NR	NR	NR	NR	1 <sup>st</sup> -line	NR	NR	NR	1 <sup>st</sup> -line(A, C)	NR	NR	NR
<i>Dosage</i>	full therapeutic doses (C)	Naproxen 500 mg BID, Indocin 50 mg PO, TID, or comparable dose of other NSAID (B)	relatively high dose (B)	full dosing according to either FDA- or EMA-approved anti-inflammatory/ analgesic doses	NR	maximum dosage(D)	NR	NR	NR	NR	NR	NR	maximum dosage	NR
<b>Colchicine</b>														
<i>Target population</i>	NR	NR	-	Patients with mild/moderate gout severity <sup>††</sup> particularly those involving one or a few small joints, or 1-2 large joints	NR	Patients with CKD and diabetes	NR	NR	NR	Patients with contraindications to NSAIDs	NR	NR	NR	NR
<i>Line of treatment</i>	As an alternative drug (C)	2 <sup>nd</sup> -line(B)	-	NR	NR	NR	1 <sup>st</sup> -line	NR	NR	NR	1 <sup>st</sup> -line(A, C)	NR	NR	NR
<i>Dosage</i>	0.5mg-0.6mg BD-QDS (C)	1-1.2 mg PO x one dose followed by 0.5-0.6 mg every 2-3 h (B)	-	A loading dose of 1.2 mg followed by 0.6 mg 1 h later	low-dose (D)	low-dose (A)	low-dose	low-dose (D)	low-dose (D)	low-dose (1.5-1.8 mg/d)(2)	A loading dose of 1 mg followed 1 h later by 0.5 mg (A,C)	low-dose (strong)	0.5mg BD-QDS	0.5 mg hourly in the first 3 h, with a total of 3-6 tablets (B)
<b>Corticosteroids</b>														
<i>Target population</i>	Elderly people and those with renal insufficiency, hepatic dysfunction, cardiac failure, peptic ulcer disease and hypersensitivity to NSALDs or COX-2 inhibitors	NR	Patients for whom NSAIDs cannot be administered, NSAID administration is ineffective, or polyarthritis occurs	Patients with mild/moderate gout severity <sup>††</sup> particularly those involving one or a few small joints, or 1-2 large joints	NR	Patients with contraindications to NSAID/ COXIBs; kidney transplant patients	NR	Patients with inefficacy, contraindication or intolerance to colchicine or NSAIDs	NR	NR	NR	NR	patients who are unable to tolerate NSAIDs or colchicine	patients who are ineligible for NSAIDs and colchicine
<i>Line of treatment</i>	NR	3 <sup>rd</sup> -line (B)	NR	NR	NR	NR	NR	NR	NR	NR	1 <sup>st</sup> -line (A, C)	1 <sup>st</sup> -line (strong)	NR	NR
<i>Administration pathway</i>	oral, i.m. or intra-articular injections	Patients with polyarticular disease: Prednisolone (PO) or triamcinolone acetonide (i.m.); if only 1-2 joints are involved: triamcinolone acetonide (intra-articular injections)	oral	Involvement of 1-2 joints: oral corticosteroids; Acute gout of 1-2 large joints: intra-articular corticosteroids; Each case scenario: intramuscular triamcinolone acetonide	intra-articular, oral or intramuscular	In case of monoarthritis: intra-articular injections; With more extensive joint involvement: systemically	intra-articular injections	systemically or intra-articular injections	oral, i.m. or intra-articular injections	NR	oral or intra-articular injections	NR	oral, i.m. or intra-articular injections	oral, i.v. or intra-articular injections

<sup>††</sup>: ≤6 of 10 on a 0–10 pain visual analogue score (VAS); NR: not reported; -: not included in the guideline; FDA: Food and Drug Administration; EMA: European Medical Agency; BID/BD: twice daily; TID: three times a day; QDS: four times a day; PO: by mouth or orally; i.m.: intramuscular (with respect to injections); i.v.: intravenous.

Interpretation of the strength of the recommendations:

1) Names of the grading systems used by each guideline: guideline 1, no name (modified version of the criteria used by the Catalonia Agency for Health Technology Assessment and Research (CAHTAR) Spain and modified from the Intercollegiate Guidelines Network (SIGN)); guidelines 2,4, U.S. Preventive Services Task Force [USPSTF] Ratings; guideline 3, no name; guideline 5, no name (based on previous methods used by the American College of Cardiology); guidelines 6,7,9,10,12,15, Oxford Centre for Evidence-based Medicine – Levels of Evidence; guideline 8, no name; guideline 11, GRADE; guideline 13, ACP grading system; guideline 14, no name

2) Meaning of the symbols: the symbols used in different guidelines varied because of the use of inconsistent grading systems; the same symbol may indicate a different strength of recommendations. The details are presented in a currently published article (WANG D, YU Y, CHEN Y *et al.*: Assessing the Quality of Global Clinical Practice Guidelines on Gout Using AGREE II Instrument. *J Clin Rheumatol* 2018.).

**Suppl. Table S3.** Comparison of recommendations on pharmacologic ULT for chronic gouty arthritis.

No.	1	3	4	5	6	7	8	9	10	11	12	13	14	15
<b>Allopurinol</b>														
<i>Target population</i>	Patients with normal renal function	NR	NR	NR	NR	Patients with CKD	NR	NR	NR	NR	Patients with normal kidney function	NR	NR	NR
<i>Line of treatment</i>	NR	NR	1 <sup>st</sup> -line	1 <sup>st</sup> -line	1 <sup>st</sup> -line (C)	NR	NR	1 <sup>st</sup> -line(C)	1 <sup>st</sup> -line(C)	NR	1 <sup>st</sup> -line (A, B)	NR	1 <sup>st</sup> -line	NR
<i>Dosage</i>	Start at 100-150mg/d, increasing by 100-150mg steps every 4 weeks to a dose of 300 mg/d (A)	Start at 50 mg/d(B)	Start at 100 mg/d, increasing 100 mg/d every 2 to 4 weeks until a target SUA level is reached (max dose, 800 mg) (B)	Start at no greater than 100 mg/d, gradually titrate maintenance dose upward every 2-5 weeks to appropriate maximum dose until SUA target is reached (can be above 300 mg/d)	Started at a low dose and escalated to achieve a target serum urate (D)	Appropriate dose (D)	Started at 100 mg/d, increasing by 100 mg every two to four weeks if required until reaching the therapeutic goal (max. dose 800 mg)	NR	NR	Start at 100 mg/d, increasing gradually (2)	Start at 100 mg/d, increasing by 100 mg increments every 2-4 weeks if required, to reach the uricaemia target (A,B)	NR	Started at a low dose (50-100 mg/d) and increased in 100 mg increments approximately every 4 weeks (max. dose 900 mg)	Start at 100 mg/d, and dose escalation can be considered after 1 month of treatment (B)
<b>Febuxostat</b>														
<i>Target population</i>	-	-	Patients with allopurinol intolerance, contraindication, lack of efficacy or impaired renal function serum creatinine level >1.5	NR	Patients with presence of intolerance or nonresponsiveness to allopurinol	Patients with CKD	NR	NR	If allopurinol is not tolerated or the response inadequate despite appropriate dosing	NR	If the SUA target cannot be reached by an appropriate dose of allopurinol; or if allopurinol cannot be tolerated; except in patients with estimated glomerular filtration rate <30 mL/min	NR	Patients in whom allopurinol is not tolerated or whose renal impairment prevents allopurinol dose escalation sufficient to achieve the therapeutic target.	NR
<i>Line of treatment</i>	-	-	1 <sup>st</sup> -line	1 <sup>st</sup> -line	alternative drug (C)	NR	alternative drug	NR	2 <sup>nd</sup> -line (C)	NR	NR	NR	2 <sup>nd</sup> -line	NR
<i>Dosage</i>	-	-	40mg/d, may be increased after 2 weeks to 80 mg/d (B)	NR	Start with a low dose and escalate to achieve a target serum urate (D)	40 mg/d(A)	80 mg/d or more	NR	NR	NR	NR	NR	Start with a dose of 80 mg/d and increase after 4 weeks to 120 mg/d if necessary	Start with 40 mg/d, and increased to 80 mg/d after 2 weeks (B)
<b>Benzbromarone</b>														
<i>Target population</i>	-	NR	-	-	Patients with presence of intolerance or non-responsiveness to allopurinol	Patients with mild/moderate CKD	-	NR	If allopurinol is not tolerated or the response inadequate despite appropriate dosing	NR	If the SUA target cannot be reached by an appropriate dose of allopurinol	-	Patients who are resistant to, or intolerant of, xanthine oxidase inhibitors	NR
<i>Line of treatment</i>	-	NR	-	-	alternative drug (C)	NR	-	NR	2 <sup>nd</sup> -line(C)	NR	NR	-	NR	NR
<i>Dosage</i>	-	start at 12.5mg/d (B)	-	-	start with a low dose and escalate to achieve a target serum urate (D)	50-200 mg/d(A)	-	NR	NR	start with a low dose (2)	NR	-	50-200 mg/d	50-100 mg/d (B)

**Recommendations in gout guidelines / Y. Yu et al.**

No.	1	3	4	5	6	7	8	9	10	11	12	13	14	15
<b>Probenecid</b>														
<i>Target population</i>	Patients with contraindications to allopurinol	-	NR	Patients with a creatinine clearance <50 ml/minute	Patients with presence of intolerance or non-responsiveness to allopurinol	-	-	NR	If allopurinol is not tolerated or the response inadequate despite appropriate dosing	-	-	-	Patients who are resistant to or intolerant of xanthine oxidase inhibitors	-
<i>Line of treatment</i>	alternative drug (C)	-	2 <sup>nd</sup> -line (B)	not recommended as 1 <sup>st</sup> -line	alternative drug (C)	-	-	NR	2 <sup>nd</sup> -line (C)	-	-	-	NR	-
<i>Dosage</i>	initial dosage 500-1000mg, increase to 1500-2000mg in divided doses (C)	-	Start at 250 mg/d, may be titrated up monthly to a total of 3 g daily in twice daily divided doses (B)	NR	Start with a low dose and escalate to achieve a target serum urate (D)	-	-	NR	NR	-	-	-	500-2000 mg/d	-
<b>ULT target</b>	<6mg/dL (C)	<6mg/dL (A)	<6mg/dl	<6mg/dL or <5mg/dL (patients with tophi)	<6mg/dL (C)	<6mg/dL (D)	<6mg/dL	<6mg/d(C) or <5mg/dL (patients with tophi) (B)	<6mg/d(C) or <5mg/dL (patients with tophi) (C)	<6mg/dL (1)	<6mg/d(C) or <5mg/dL (patients with tophi) (C)	NR	<5mg/dL (the less stringent target)	<6mg/dL or <5mg/dL (patients with tophi) (B)
<b>Indications for ULT</b>														
<i>Attack frequency</i>	≥3 attacks per year(A)	Recurrent gouty arthritis (A)	>2 attacks per year (B)	≥2 attacks per year	NR	NR	Recurrent acute attacks	NR	-	>2 attacks per year (1)	≥2 attacks per year (A)	≥2 attacks per year (strong)	≥2 attacks per year	NR
<i>Tophi</i>	Yes (A)	Yes (A)	Yes (B)	Yes	-	-	Yes	-	Yes (D)	Yes (1)	Yes (A)	Yes (strong)	Yes	-
<i>Renal stones</i>	Yes	-	Yes (B)	Yes	-	-	-	-	-	-	Yes (A)	Yes (strong)	Yes	-
<i>Radiographic changes</i>	Yes	-	Yes (B)	Yes	-	-	Yes	-	-	-	-	-	-	-
<i>Arthropathy</i>	-	-	Yes (B)	-	-	-	Yes	-	-	Yes (1)	Yes (A)	-	Yes	-
<i>Comorbidities</i>	-	-	-	CKD	-	-	-	-	-	-	renal impairment, hypertension, ischemic heart disease, heart failure (A)	chronic renal disease (strong)	renal impairment	-
<i>Initiation time of ULT</i>	after an acute flare is well-controlled (about two weeks after the flare)	should not be initiated at the time of flare; about 2 weeks after remission of gout flare	at least 2 weeks after resolution of an acute gout flare	could be started during an acute gout flare, provided that effective anti-inflammatory management has been instituted	NR	NR	NR	NR	NR	NR	NR	NR	delayed until inflammation has settled	NR

NR: not reported; -: not involved; \*: on a low purine diet, 24 h excretion of less than 3 mmol urate, or a Uurate/Ucreatinine ratio of <0.35 mmol/mmol in an untimed random urine. Interpretation to the strength of the recommendations: see Table S2.