- ✓ **Corticosteroids** are usually considered where use of an NSAID or colchicine is contraindicated or in refractory cases.

- ✓ They may be given intravenously, intramuscularly or direct into a joint (intra-articular) when only one or two joints are affected.

- ✓ In patients with a monoarthritis, an intra-articular corticosteroid injection is highly effective in treating an attack.

- ✓ Two different dosing strategies for oral corticosteroid therapy (prednisone or prednisolone) in the treatment of acute gout:
  - 0.5 mg/kg daily for 5 to 10 days followed by abrupt discontinuation or
  - 0.5 mg/kg daily for 2 to 5 days followed by tapering for 7 to 10 days

- ✓ A hypothetical risk exists for a rebound attack upon steroid withdrawal; therefore, gradual tapering is often employed when discontinuing steroid therapy.

- ✓ The adverse effects of corticosteroids are generally dose and duration dependent.

- ✓ **Interleukin-1 inhibitors:** IL-1β is critically associated with the inflammatory response induced by monosodium urate crystals.

- ✓ Anakinra and canakinumab, have demonstrated efficacy in the treatment of acute gout.

- ✓ The EULAR and ACR guidelines suggest that IL-1 inhibitors can be considered for treatment of severe acute gout attacks refractory to other treatments.

Management of chronic gout:

- ✓ The presence of hyperuricaemia is not an indication to commence prophylactic therapy.

- ✓ Some patients may only experience a single episode and a change in lifestyle, diet or concurrent medication may be sufficient to prevent further attacks.

- ✓ Patients who suffer one or more acute attacks within 12 months of the first attack should normally be prescribed prophylactic urate-lowering therapy.

- ✓ There are, however, some groups of patients where prophylactic therapy should be instigated after a single attack. These include individuals with uric acid stones, the presence of tophi at first presentation and young patients with a family history of renal or cardiac disease.

هدول صابتهم ال attack وعم طول بدي اقرر اعطيه Urate lowering Therapy

هدول بكونوا مرحلة متقدمة من ال gout

- ✓ Prophylactic treatment should not be initiated until an acute attack of gout has completely resolved.

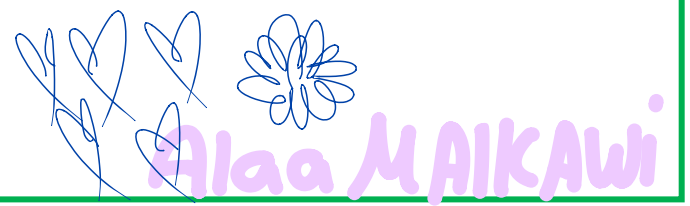
حكيناها قبل — ما بنبلش بال Urate Lowering Therapy — خلال ال attack اما لو كان اصلاً عاش عليهم عادي بكمل

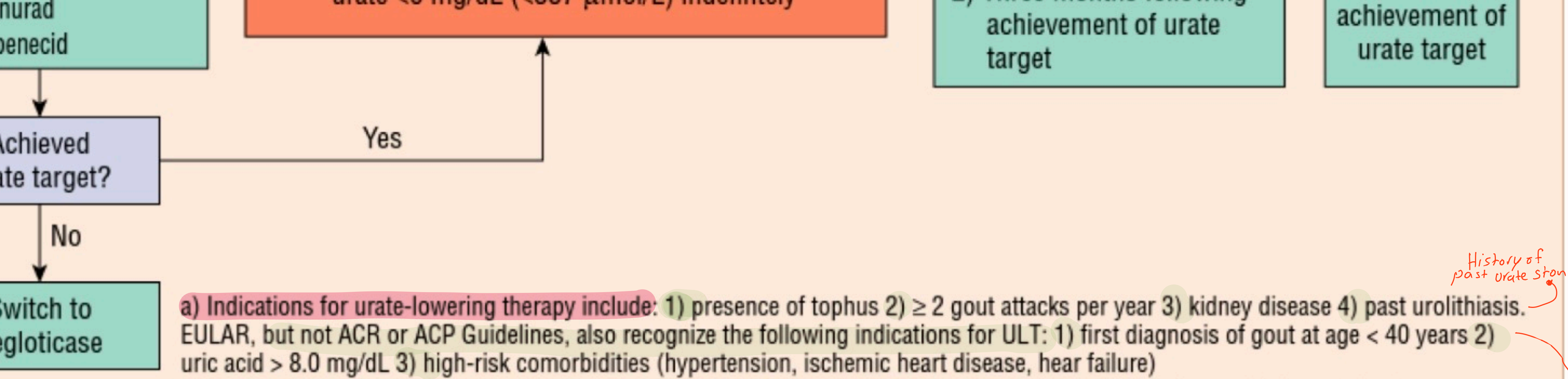
- ✓ Once started, prophylactic treatment should be continued indefinitely even if further acute attacks develop.

- ✓ Drugs that lower serum uric acid can be classified into three groups according to their pharmacological mode of action.

1) production of uric
2) excretion of uric
3) Move ← uric acid تحول ال Soluble subs

بال guidlines الجديد ال gout تاعت ال 2020 عيزوها صارت ! العكس انه بنبلش ال Urate lowering Therapy خلال ال acute attack





History of past urate stones

a) Indications for urate-lowering therapy include: 1) presence of tophus 2) ≥ 2 gout attacks per year 3) kidney disease 4) past urolithiasis. EULAR, but not ACR or ACP Guidelines, also recognize the following indications for ULT: 1) first diagnosis of gout at age < 40 years 2) uric acid > 8.0 mg/dL 3) high-risk comorbidities (hypertension, ischemic heart disease, hear failure)
b) Recognized as first line by ACR Guidelines but cardiovascular safety concerns have been reported since guideline publication
c) EULAR Guidelines also recognize calcium channel blockers and statins as add-on therapy for uric acid lowering when indicated for treatment of comorbidities
d) The effectiveness of dietary intervention in improving clinical outcomes is noted as an area of inconclusive evidence by 2017 ACP guidelines
e) Targeting and maintaining a specific urate level is noted as an area of inconclusive evidence by 2017 ACP guidelines

ال gout صره عند البشر اما عند الحيوانات
و موجود, لانه عندهم enzyme اسمه Uricase
الجين تبعه موعنا . هوه بحول ال Uric acid لل allantoin ← هاد اله مشاكل بال Solubility و بال excretion فا بتجمع بالجسم وما بصير ترسب بالجسم

* في دوا زي ال Uricase بنعطى IV بشتغل نفس شغله رح نحكي عنه لقدام

حكينا ال gout ← associated with many diseases
هاي ال diseases الي بتيجي مع ال gout
ال Risk تبعها بتزيد بعد عمر ال ٤٠
* اذا حد صابه gout قبل ٤٠ بنحاول نحميه

اول شي نروح على الalgorithim [record 17/12]

١

- ✓ Xanthine oxidase inhibitors (allopurinol and febuxostat): xanthine oxidase catalyses the oxidation of hypoxanthine to xanthine and subsequently xanthine to uric acid.

- ✓ **Allopurinol** is the prophylactic agent of choice in the management of recurrent gout.

- ✓ In order to become pharmacologically active, allopurinol must be metabolised by the liver to oxypurinol. Oxypurinol has a much longer half-life than allopurinol, 14–16 h compared to 2 h.

- ✓ In patients with normal renal function, the starting dose is 100 mg/day; this is gradually increased in 100-mg increments every 2–5 weeks until the optimal serum urate level or the maximum dose is reached(maximum dose is 800 mg/day).

مع Monitoring للSerum uric acid
Target ازا ليسا هو على ال
يرفع 100mg بتصير جرعتة 200mg ولا MAX = 800mg

- ✓ A decrease in serum urate will occur within a couple of days of introducing allopurinol therapy with a peak effect at 7–10 days.

- ✓ The dissolution of tophi may take up to 6–12 months with effective therapy.

Tophi حكينا بالalgorithim ازا المريض عنده
بنعمل على ال anti-inflamm Mang ment لمدة ٦ اشهر
بعد ما ينزل ال uric acid ٦> (لانها بهها ١٢-٦ شهر للتذوب)

- ✓ Approximately 3–5% of patients treated with allopurinol suffer from an adverse reaction.
- ✓ Mild adverse effects as skin rash, leukopenia, GI problems, headache, and urticaria can occur with allopurinol administration.
- ✓ A more severe adverse reaction known as "allopurinol hypersensitivity syndrome", which includes severe rash (toxic epidermal necrolysis, erythema multiforme, or exfoliative dermatitis), hepatitis, interstitial nephritis, and eosinophilia.
- ✓ Risk factors associated with the development of allopurinol hypersensitivity included female gender, age above 60 years, initial starting dose of allopurinol exceeding 100 mg/day, kidney disease, CV disease, and use of allopurinol for treatment of asymptomatic hyperuricemia.
- ✓ The dose of azathioprine or mercaptopurine should be reduced to approximately a quarter of the normal dose when co-prescribed with allopurinol.
- ✓ In addition, full blood counts should be performed at regular intervals to identify potential toxicity.

- ✓ **Febuxostat** is a more selective and potent inhibitor of xanthine oxidase than allopurinol and has no effect on other enzymes involved in purine or pyrimidine metabolism.
- ✓ It is licensed for the treatment of chronic hyperuricaemia in conditions where urate deposition has already occurred including a history, or presence of, tophus and/or gouty arthritis.
- ✓ It is recommended as a secondline agent in patients who are intolerant of allopurinol or have C/Is
- ✓ The increased potency and good oral bioavailability of febuxostat leads to rapid decreases in serum uric acid levels permitting the testing of levels 2 weeks after starting therapy or adjusting the dose.
- ✓ Febuxostat should not be given to patients with IHD or CHF because of CV side effects.
- ✓ When initiating therapy with febuxostat, gout flare prophylaxis should be prescribed.
- ✓ The most common adverse effects include respiratory infection, diarrhea, headache and liver function abnormalities.

- ✓ The use of febuxostat is not recommended in patients concomitantly treated with mercaptopurine or azathioprine and theophylline, serum levels of theophylline should be monitored.

- ✓ Febuxostat is more effective than fixed-dose allopurinol 300 mg in lowering uric acid concentrations in trials of up to 40 months' duration. However, a reduction in the incidence of episodes of acute gout has not been demonstrated.

(2) [بالاردن هو موجودين]

- ✓ **Uricosuric agents (probenecid & lesinurad)** increase uric acid excretion primarily by inhibiting post-secretory renal proximal tubular reabsorption of uric acid from filtered urate in the kidney.

(US-50) < GFR لازم عشان نعطيهم

- ✓ They are indicated as second-line agents in those who are urate under-excreters and are dependent on the patient having an adequate level of renal function.

- ✓ These agents should be avoided in patients with urate nephropathy or those who are over producers of uric acid due to the high risk of developing renal stones.

- ✓ Patients receiving a uricosuric agent are required to maintain an adequate fluid intake.

- ✓ **Probenecid** is given initially at a dose of 250 mg twice a day for 1 to 2 weeks and then 500 mg twice a day for 2 weeks. Thereafter, the daily dose is increased by 500-mg increments every 1 to 2 weeks until satisfactory control is achieved or a maximum dose of 2 g is reached.

250 → 500 → 1000

- ✓ Probenecid can inhibit tubular secretion of other organic acids; so, increased plasma concentrations of penicillins, cephalosporins, sulfonamides, and indomethacin can occur.

- ✓ **Lesinurad** is approved as combination therapy with a xanthine oxidase inhibitor for treatment of hyperuricemia associated with gout in patients who have not achieved target serum UA concentrations with xanthine oxidase inhibitor monotherapy.

- ✓ Lesinurad carries a black box warning which highlights the increased risk of acute kidney injury when used in the absence of xanthine oxidase inhibitor therapy.

- ✓ The only approved dose of lesinurad is 200 mg daily due to increased risk of renal events when used at higher doses.

Titration جاي

مرجع لـ pb

- ✓ Lesinurad should not be used in patients with creatinine clearance less than 45 mL/ min.

3

- ✓ **Pegloticase (PEG-uricase):** is a pegylated, recombinant form of uricase.

- ✓ It works to reduce serum uric acid by converting uric acid to allantoin, a water-soluble and easily excreted substance.

- ✓ It has demonstrated efficacy in reducing serum UA and resolving tophi in patients with severe gout & hyperuricemia (UA ≥ 8 mg/dL) who have failed or have a contraindication to other ULT.

- ✓ The IV infusions of pegloticase must be given over no less than 2 hours every 2 weeks, a potential inconvenience to many patients.

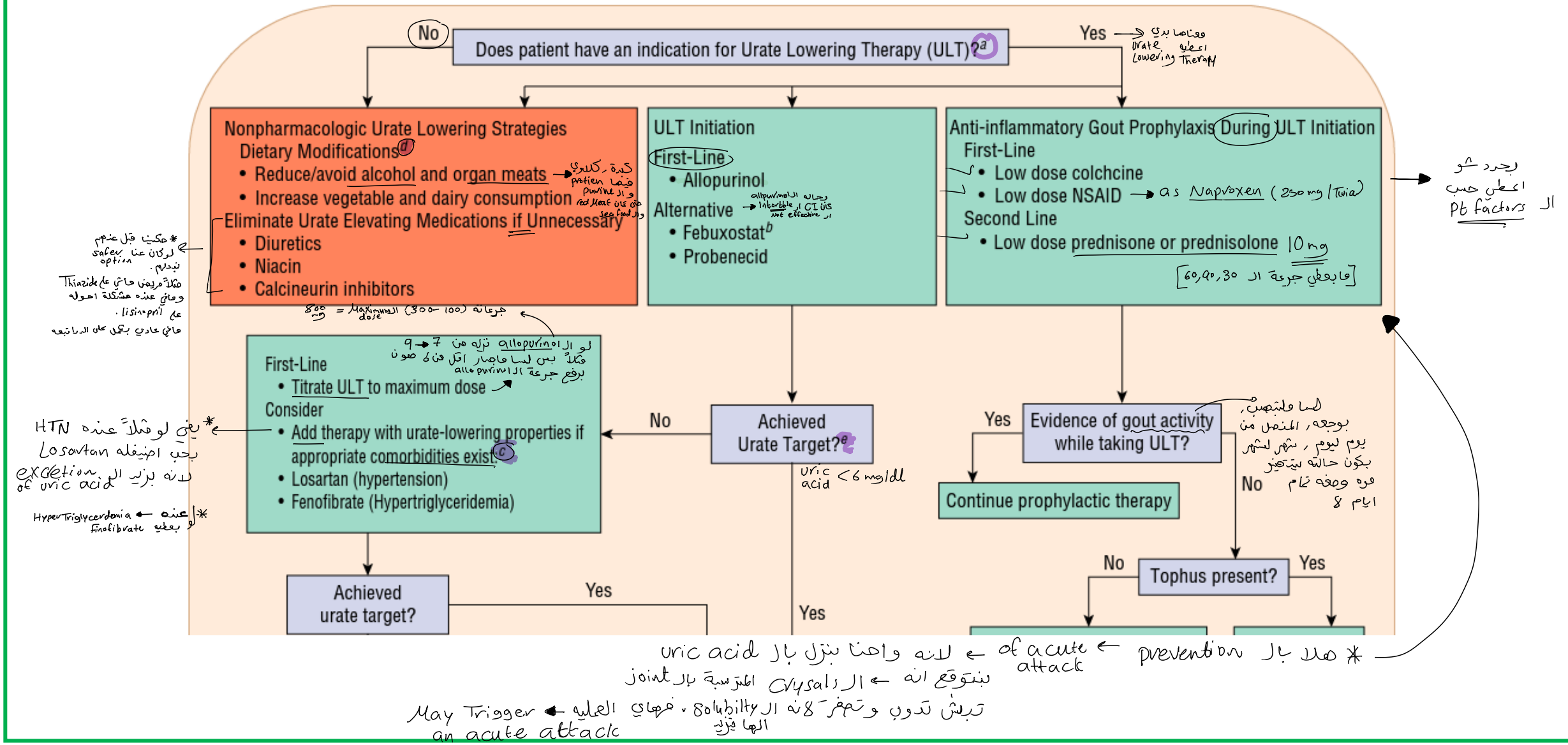
- ✓ The use of PEG-uricase has been associated with severe infusion reactions in a small minority of patients; this and its high cost are likely to limit its use.

X Not for Long - Term

- ✓ Immunogenicity issues associated with pegloticase therapy may limit the duration with which pegloticase therapy may be used effectively (pegloticase antibodies resulted in a loss of efficacy by month 4).

* بصير immune response من الجسم تجاه
هاد الدوا وبصير في Anti bodies بتقلل فعاليته
* هو مين قديه ممكن نفضي عليه قبل ما تقل فعاليته بس غالباً الموضوع من Pt لـ Pt بختلف

Algorithm for management of hyperuricemia in gout. (Algorithm derived from 2017 ACP, 2016 EULAR and 2012 ACR gout guidelines.)



* نزول ال uric acid بختلف من مريض لمريض

* كأن ال indication شوابي بجد

Tophus present?

- Yes → Discontinue prophylactic therapy after six months following achievement of urate target
- No → Discontinue prophylactic therapy after the greater of: 1) Six months OR 2) Three months following achievement of urate target

Achieved urate target?

- Yes → Continue all measures needed to maintain serum urate <6 mg/dL (<357 µmol/L) indefintely[e]
- No → If using maximized xanthine oxidase inhibitor, consider add-on therapy:
  - Lesinurad
  - Probenecid

Achieved urate target?

- Yes → Continue all measures needed to maintain serum urate <6 mg/dL (<357 µmol/L) indefintely[e]
- No → Switch to pegloticase

Yes (presence of Tophi) → Continue all measures needed to maintain serum urate <6 mg/dL (<357 µmol/L) indefintely[e]

a) Indications for urate-lowering therapy include: 1) presence of tophus 2) ≥ 2 gout attacks per year 3) kidney disease 4) past urolithiasis. EULAR, but not ACR or ACP Guidelines, also recognize the following indications for ULT: 1) first diagnosis of gout at age < 40 years 2) uric acid > 8.0 mg/dL 3) high-risk comorbidities (hypertension, ischemic heart disease, hear failure)

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ممكن يكون precense of Tophi ← وال Tophi عشان تذوب بدها عدة اشهر معناها حتى لو نزل ال uric acid بس ال Tophi لسا موجوده ما دايت بدي اكملها لتروح تماما بدها ٦ اشهر ممكن او اكثر

dual Therapy ← يكون هوه فاني ع ال allopurinol الي بشتغل ع ال over production ما لما اجي بدي اعطيه add on بده يكون الدوا التاني different MOA

من ال uricase – uric agents

(Febuxostat) b) لما انشروا ال guidlines من ال 2012 طلعت دراسات انه بزيد ال CU complications عشان هيك ال algorithm حطوه ال 1st line مو alternative

* هوه في ال guidline الجديدة مو First-line

يعني لو ال Pt ال uric acid = 8 وخلال شهرين صار 5.5 معناها يا اما بكمل لتكمل ٣ اشهر بصير فاني ع الدوا تبعه 5 اشهر او بكمل لـ 6 اشهر (الفترة الاطول هيه الي بختارها) بصادف المثال اني هوه ال 6 اشهر

بعد ما نزل ال level ل 6 >

ازاي Tophi بتوقف ال drug بعد 6 اشهر من لما تصير ال uric acid عنه (< 6 mg/dl)

الي طلعوا من ال acute attack

* المرضى بختلفو

في Pt عنه Low disease activity

وفي ناس عندهم High disease activity

وهوه مو بعد acute attack ما خلص ال affected joint بس ال 6 لسا في شي مو normal.

اذا ال indication ← نفس فكرة ال losartan

حاجة مكانها فوق بس بلا تغير

inconclusive → انو ال data الي جمعوها وعملوها ما قدرتهم بالاخير ال Conclusion ما استنتجوا شي معين. (هاد الحكي بس من ال 2017 institution)

يعني ال diatry intervention effect

بيهاي ال guidlins تاعت ال 2017 اعتبرت انه ال uric acid تحت ال 6 ← Inconclusive ما كان في evidance كافي بالنسبة الهم الدراسة الموجودة عشان احكي انه بدي اخلي ال uric acid < 6

* بس تاعت 2020 الي اعتقدوها هيه < 6

[guidline 2020]

Table 1. Indications for pharmacologic urate-lowering therapy (ULT)*

Recommendation	PICO question	Certainty of evidence
For patients with 1 or more subcutaneous tophi, we strongly recommend initiating ULT over no ULT.	1	High
For patients with radiographic damage (any modality) attributable to gout, we strongly recommend initiating ULT over no ULT.	2	Moderate
For patients with frequent gout flares (≥2/year), we strongly recommend initiating ULT over no ULT.	3	High
For patients who have previously experienced >1 flare but have infrequent flares (<2/year), we conditionally recommend initiating ULT over no ULT.	4	Moderate
For patients experiencing their first flare, we conditionally recommend *against* initiating ULT over no ULT, with the following exceptions.	5	Moderate
For patients experiencing their first flare and CKD stage ≥3, SU >9 mg/dl, or urolithiasis, we conditionally recommend initiating ULT.	5	Very low
For patients with asymptomatic hyperuricemia (SU >6.8 mg/dl with no prior gout flares or subcutaneous tophi), we conditionally recommend *against* initiating any pharmacologic ULT (allopurinol, febuxostat, probenecid) over initiation of pharmacologic ULT.	57	Hight

Strongly recommend | Conditionally recommend | Strongly recommend against | Conditionally recommend against

* PICO = population, intervention, comparator, outcomes; CKD = chronic kidney disease; SU = serum urate.
† There is randomized clinical trial data to support the benefit that ULT lowers the proportion of patients who develop incident gout. However, based on the attributable risk, 24 patients would need to be treated for 3 years to prevent a single (incident) gout flare leading to the recommendation against initiating ULT in this patient group.

advanced CKD → dosage adjusment

Table 2. Recommendations for choice of initial urate-lowering therapy (ULT) in patients with gout*

Recommendation	PICO question	Certainty of evidence
For patients starting any ULT, we strongly recommend allopurinol over all other ULT as the preferred first-line agent for all patients, including in those with CKD stage ≥3.	10	Moderate
We strongly recommend a xanthine oxidase inhibitor over probenecid for those with CKD stage ≥3.		
For allopurinol and febuxostat, we strongly recommend starting at a low dose with subsequent dose titration to target over starting at a higher dose (e.g., ≤100 mg/day [and lower in patients with CKD] for allopurinol or ≤40 mg/day for febuxostat).	7	Moderate
For probenecid, we conditionally recommend starting at a low dose (500 mg once or twice daily) with dose titration over starting at a higher dose.		
We strongly recommend initiating concomitant antiinflammatory prophylaxis therapy (e.g., colchicine, NSAIDs, prednisone/prednisolone) over no antiinflammatory prophylaxis. The choice of specific antiinflammatory prophylaxis should be based upon patient factors.	9	Moderate
We strongly recommend continuing prophylaxis for 3–6 months rather than <3 months, with ongoing evaluation and continued prophylaxis as needed if the patient continues to experience flares.	9	Moderate
When the decision is made that ULT is indicated while the patient is experiencing a gout flare, we conditionally recommend starting ULT during the gout flare over starting ULT after the gout flare has resolved.	6	Moderate
We strongly recommend *against* pegloticase as first-line therapy.	10	Moderate†

Strongly recommend | Conditionally recommend | Strongly recommend against | Conditionally recommend against

[safety cause]

* PICO = population, intervention, comparator, outcomes; CKD = chronic kidney disease; NSAIDs = nonsteroidal antiinflammatory drugs.

† Moderate evidence is in support of the efficacy of pegloticase, but due to cost, safety concerns, and favorable benefit-to-harm ratios of other untried treatment options, the recommendation is *against* using pegloticase as first-line agent.

[X pelgoticase → X 1st line]

indication for urate lowering Therapy

* مريض اول مره يدخل بـ gout attack فبدي اعالج هاي الـ attack , رح يبين معي بس يدخل لو عنده مثلاً ال serum uric acid >9 مع انها الـ Tophi عنده , first attack

When the decision is made that ULT is indicated while the patient is experiencing a gout flare, we conditionally recommend starting ULT during the gout flare over starting ULT after the gout flare has resolved.	6	Moderate

عشان انا لزا بدي احكيله يرجع بعد ما الـ attack تخلص بخاف يروح وما يرجع. صار pain free حسى انه هو بخير.

Starting ULT during a flare has conceptual benefits, including the time efficiency offered by initiating therapy during the concurrent flare visit rather than risking the patient not returning for ULT initiation. Furthermore, input from the **Patient Panel** emphasized that patients are likely to be highly motivated to take ULT due to the symptoms related to the current flare. However, concerns about starting ULT during a flare include potential *extension or worsening of a flare*, as well as the possibility of *information overload* for patients, which may lead to conflating flare management and long-term ULT. Two small RCTs and an observational study support the hypothesis that starting ULT during a flare does not significantly extend flare duration or severity. Input from the **Patient Panel**, citing their own ability to simultaneously process information related to flare treatment and ULT initiation together, along with their preference to start on a treatment path sooner to prevent future flares, **influenced the final recommendation**. As with all conditional recommendations, there may be patient factors or preferences that would **reasonably support the alternative** of delaying ULT initiation until the flare has resolved.

* اذا قبل هيك انه بنعطي الـ ULT بعد ما تخلص الـ attack بس هاي النقطة بتحكي العكس

لـ الي هوه انه بعد ما تخلص الـ attack نبلش بالـ ULT

* معناها الجهتين مريح حسب الـ Pt factor

انه لو استخدمنا الـ ULT خلال الـ attack يصير worsening وتزيد مدة الـ attack او مثلاً بدل ما تكون صارت بـ one joints تصير بـ 2joints , يزيد الـ inflamm الـ crystal بلش تتوب من الـ ULT

Table 3. Recommendations for all patients taking urate-lowering therapy (ULT)*

Recommendation	PICO question	Certainty of evidence
For all patients taking ULT, we strongly recommend a treat-to-target strategy of ULT dose management that includes dose titration and subsequent dosing guided by serial SU values to achieve an SU target over a fixed, standard-dose ULT strategy.	13	Moderate
For all patients taking ULT, we strongly recommend continuing ULT to achieve and maintain an SU target of <6 mg/dl over no target.	14	High
For all patients taking ULT, we conditionally recommend delivery of an augmented protocol of ULT dose management by nonphysician providers to optimize the treat-to-target strategy that includes patient education, shared decision-making, and treat-to-target protocol.	8	Moderate
We conditionally recommend continuing ULT indefinitely over stopping ULT.	19	Very low

Strongly recommend | Conditionally recommend | Strongly recommend against | Conditionally recommend against

* PICO = population, intervention, comparator, outcomes; SU = serum urate.

هاد geno Type معين موجود ب certin races زي مثلاً chinese, korea people
ازا هاي geno Type موجودة بيتزيد ال senstivity لل allopurinol واي ممكن تكون Sirouse

Table 4. Recommendations for patients taking specific urate-lowering therapy (ULT) medications*

Recommendation	PICO question	Certainty of evidence
Allopurinol		
We conditionally recommend testing HLA–B*5801 prior to starting allopurinol for patients of Southeast Asian descent (e.g., Han Chinese, Korean, Thai) and African American patients, who have a higher prevalence of HLA–B*5801.	12	Very low
We conditionally recommend *against* HLA–B*5801 testing in all others.		
For patients with a prior allergic response to allopurinol who cannot be treated with other oral ULT, we conditionally recommend using allopurinol desensitization.	23	Very low
Febuxostat		
For patients with gout taking febuxostat with a history of CVD or a new CV event, we conditionally recommend switching to an alternative ULT agent if available and consistent with other recommendations in this guideline.	22	Moderate
Uricosurics		
For patients considered for, or taking uricosuric treatment, prior to starting any uricosuric treatment, we conditionally recommend *against* checking urinary uric acid over checking urinary uric acid.	28	Very low
For patients taking uricosuric treatment, we conditionally recommend *against* alkalinizing urine.	29	Very low

Strongly recommend | Conditionally recommend | Strongly recommend against | Conditionally recommend against

* PICO = population, intervention, comparator, outcomes; CVD = cardiovascular disease.

→ انه بنحاول نعوده وحده ما يطلع يصيرله sensitization منه

بنعطي جرعة صغيرة بالمايكرو جرام وبنصير نرفع شوي شوي

اول. بعد ال Diet بتجمع ال urine لمدة 24hr وبتشوف كم ال uric acid
over producer ← يعتبر = > 600 mg
under excreter يعتبر = < 600mg

* هيه Clinicaly فاعملوا هيك انه ما بروحوا بيشوفوا كم في uric acid بال urine. بس كيف بعملوها يحسبوا uric acid لمدة 24hr بدنا نجمع ال urine لـ 24 ونشوف. بخلو ال Pt عـ purine free diet من يومين لثلاث قبل الفحص (هاد الشي كتير صعب انه تخلي pt لاكثر من يوم عـ purine free diet ممكن ليوم بس هوه بدك تمشي عليه (3-4) ايام والي صعب لانه اغلب الاكل في purine

احنا ما بتنصحهم يروحوا يشيكوا كم ال uric acid بال urine

* يعني مع اي وصلت لل Maximum dose من allpurinol
(2≤ in one year) freq attack ولما عنده ≤ 6 < uric acid
او عنده Tophi ولسا موجودة حاديت .
معناها انه ال Therapy تبع الكريمن مو كافيه
بهاي الحالة بنفضل نبدل الدوا لـ XOI تاني
احسن منه نضيف on add Therapy

Table 5. When to consider switching to a new urate-lowering therapy (ULT) strategy*

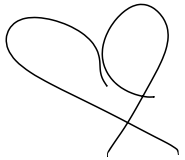
first-line allopuri

Recommendation	PICO question	Certainty of evidence
For patients with gout taking their first XOI monotherapy at maximum-tolerated or FDA-indicated dose who are not at SU target and/or have continued frequent gout flares or nonresolving subcutaneous tophi, we conditionally recommend switching the first XOI to an alternate XOI agent over adding a uricosuric agent.	24	Very low
For patients with gout where XOI, uricosurics, and other interventions have failed to achieve SU target and who have frequent gout flares or nonresolving subcutaneous tophi, we strongly recommend switching to pegloticase over continuing current ULT.†	27	Moderate
For patients with gout for whom XOI, uricosurics, and other interventions have failed to achieve serum urate target and who have infrequent gout flares (<2 flares/year) and no tophi, we strongly recommend *against* switching to pegloticase over continuing current ULT.‡	~~27~~ ما بنعملها	Moderate

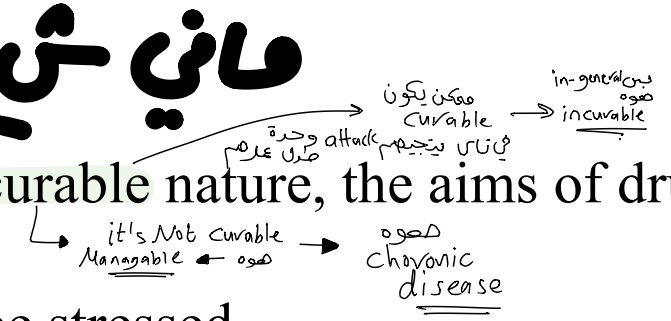
3rd line agent

Strongly recommend | Conditionally recommend | Strongly recommend against | Conditionally recommend against

* PICO = population, intervention, comparator, outcomes; XOI = xanthine oxidase inhibitor; FDA = Food and Drug Administration.
† There is moderate certainty of evidence about the efficacy of the benefits, harms, and high certainty about the costs of pegloticase. For patients with high disease activity, the magnitude of potential benefits outweighs the harms and costs of the drug.
‡ For patients with minimal disease activity, the smaller potential benefits do not outweigh the harms and costs of the drug.



✓ Preventing gout flare:



- It is important to inform patients about the disease, its curable nature, the aims of drug therapy and how to prevent and handle flares.
- The need for dietary and lifestyle changes should also be stressed.
- In over-weight patients, gradual weight loss should be encouraged.
- Low purine diets are difficult to adhere to.
- The importance of avoiding or reducing alcohol consumption should also be emphasised.
- The patient should be clear on what dose to take, when to initiate therapy, how long to take the medication for and any possible side effects to look out for.
- The patient should also be advised to avoid certain OTC medicines which may exacerbate an attack as the use of aspirin as an analgesic.
- Those taking long-term prophylactic therapy need to understand the importance of continuing therapy despite being asymptomatic.
- They should avoid running out of medication, as a short gap in therapy may precipitate an attack.
- Patients receiving uricosuric agents should be advised to maintain a fluid intake of at least 2 L/day to reduce the risk of uric acid stone formation in the kidneys.

Table 7. Management of lifestyle factors*

Recommendation	PICO question	Certainty of evidence
For patients with gout, regardless of disease activity, we conditionally recommend limiting alcohol intake.	41	Low
For patients with gout, regardless of disease activity, we conditionally recommend limiting purine intake.	42	Low
For patients with gout, regardless of disease activity, we conditionally recommend limiting high-fructose corn syrup.	43	Very low
For overweight/obese patients with gout, regardless of disease activity, we conditionally recommend weight loss.	46	Very low
For patients with gout, regardless of disease activity, we conditionally recommend *against* adding vitamin C supplementation.	48	Low

Strongly recommend | Conditionally recommend | Strongly recommend against | Conditionally recommend against

* PICO = population, intervention, comparator, outcomes.

* في Data بتحكي انه الـ Vit C بجرعات كبيرة زي 1500 mg بزيد الـ excretion للـ uric acid في ناس مثلاً بيشرب عصير برتقال . واني الـ pt recommend This

* بس حكينا قبل شوي انه كمان [High-fructose] بده يكون Moderate (انه قديه بيشرب)

* هو احد الحلويات : Corn-syrup (cheap alternative) الصناعية بكون High-fructose الـ Fructose بدخل لـ liver وبدخل الـ Glycolysis لإنتاج الطاقة وبطلع منه intermediate الي الجسم بالاخير بتحولهما لـ uric acid

* هو بس الـ Corn Syrup كمان العصائر و الصومات الجاهزه صدول High fructose

Table 8. Management of concurrent medications*

Recommendation	PICO question	Certainty of evidence
For patients with gout, regardless of disease activity, we conditionally recommend switching hydrochlorothiazide to an alternate antihypertensive when feasible.	47	Very low
We conditionally recommend choosing losartan preferentially as an antihypertensive when feasible.	47	Very low
We conditionally recommend *against* stopping low-dose aspirin (in those who are taking this medication for appropriate indications).	47	Very low
We conditionally recommend *against* adding or switching to fenofibrate.	47	Very low

Strongly recommend | Conditionally recommend | Strongly recommend against | Conditionally recommend against

* PICO = population, intervention, comparator, outcomes.

✓ Evaluation of Therapeutic Outcomes:

- Baseline blood work for patients receiving hypouricemic medications chronically should include kidney function, liver enzymes, CBC, and electrolytes.

- During titration of ULT, uric acid should be monitored every 2 to 5 weeks; once the urate target is achieved, uric acid should be monitored every 6 months.

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- Because of the high rates of comorbidities associated with gout, including DM, CKD, HTN, obesity, MI, HF, and stroke, elevated uric acid concentrations or gout should prompt evaluations for signs of CV disease and the need for appropriate risk reduction measures.

TABLE 109-7 Drug Monitoring

Drug	Adverse Drug Reaction	Monitoring Parameter	Comments
NSAIDs	Impaired kidney function (acute and chronic [Chapter 61], gastritis (worse with concurrent aspirin), fluid retention, blood pressure elevation	Therapeutic (efficacy) Resolution of pain Avoidance of gout attacks when used for prophylaxis Toxic Blood pressure Kidney function Edema Dark stools	Avoid for patients with peptic ulcer disease, active bleeding (Melena) Use caution in congestive heart failure, dehydration, impaired kidney function Consider coadministration with a proton-pump inhibitor when used long term for patients at risk for GI bleeding
Systemic corticosteroids	GI upset, increased appetite, nervousness/restlessness, transient glucose intolerance, fluid retention, blood pressure elevation	Therapeutic Resolution of pain Avoidance of gout attacks when used for prophylaxis Toxic Glucose levels in patients with diabetes	Limit duration of therapy in patients with diabetes
Intra-articular corticosteroids	Injection pain, rebound arthritis	Therapeutic Resolution of pain Toxic Signs of rebound arthritis (pain relief followed by reemergence of pain)	Avoid if joint sepsis cannot be ruled out
Corticotropin	Increased appetite, nervousness/restlessness, transient glucose intolerance, fluid retention, blood pressure elevation	Therapeutic Resolution of pain	Requires intact pituitary–adrenal axis Less effective for patients receiving long-term oral corticosteroid therapy

Colchicine	Dose-dependent GI adverse effects (diarrhea, nausea, vomiting), rare myelosuppression, and reversible neuromyopathy	Therapeutic Resolution of pain Avoidance of gout attacks when used for prophylaxis Toxic GI symptoms Complete blood count	
Interleukin-1 inhibitors	Injection site reaction, neutropenia, immune hypersensitivity reaction, infectious disease, malignancy	Therapeutic Resolution of pain Avoidance of gout attacks when used for prophylaxis Toxic Neutrophil count (prior to initiation, monthly for the first 3 months of therapy then after 6, 9, and 12 months of therapy) Temperature (periodically to detect infection)	Safety for use in acute gout and gout prophylaxis during initiation of urate-lowering therapy has not yet been established; not FDA approved for use in gout
Allopurinol	Rash, potential for fatal hypersensitivity syndrome	Therapeutic Serum urate level Reduced frequency of gout attacks Toxic Rash Kidney function	Can be used in both urate overproduction and urate underexcretion
Febuxostat	Liver enzyme elevation, nausea, arthralgias, rash, cardiovascular risk	Therapeutic Serum urate level Reduced frequency of gout attacks Toxic Liver function tests Kidney function	Can be used in both urate overproduction and urate underexcretion

Probenecid	Urolithiasis	Therapeutic Serum urate level Reduced frequency of gout attacks Toxic Kidney function	Useful in urate underexcretion Avoid for patients with history of urolithiasis
Pegloticase	Acute gout attack during treatment initiation, anaphylaxis, GI symptoms (constipation, nausea, vomiting), chest pain, nasopharyngitis	Therapeutic Serum urate levels Reduced frequency of gout attacks Toxic Signs/symptoms of anaphylaxis following infusion	Reserved for patients with gout refractory to conventional therapies Can be used in both urate overproduction and urate underexcretion
Lesinurad	Acute gout attack during treatment initiation, headache, GERD, acute kidney injury, major adverse cardiovascular events have been observed, although a causal relationship has not been established	Therapeutic Serum urate levels Reduced frequency of gout attacks Toxic Kidney function	Reserved for patients with hyperuricemia associated with gout who do not achieve target serum uric acid levels with conventional therapies Can be used in both urate overproduction and urate underexcretion Must be used in combination with a xanthine oxidase inhibitor due to increased risk of acute kidney injury with monotherapy

FDA, Food and Drug Administration; GERD, gastroesophageal reflux disease; GI, gastrointestinal; NSAID, nonsteroidal anti-inflammatory drug.

TABLE 109-9 Pharmacotherapy Considerations in Gout

Conditions and Situations	Limitations to Pharmacotherapy	Alternative Therapies
Impaired Kidney Function	NSAIDs may lead to exacerbation of kidney impairment	Consider reduced-dose colchicine or corticosteroids for short-term treatment of acute gout Consider reduced-dose colchicine for prophylaxis during initiation of urate-lowering therapy
	Uricosuric therapy is ineffective in patients with impaired kidney function	Consider allopurinol or febuxostat
	Lesiurad is not indicated in patients with impaired kidney function	Consider allopurinol or febuxostat for first-line urate lowering therapy; consider pegloticase for refractory cases
GI disease	Colchicine may cause GI upset and diarrhea	Consider corticosteroids for treatment of acute gout If monoarticular, consider joint injection
	NSAIDs may cause GI bleeding or ulceration	Consider gastroprotection with coadministration of proton-pump inhibitor when NSAID therapy is used Consider colchicine or corticosteroids for treatment of acute gout Consider low-dose colchicine for prophylaxis during initiation of urate-lowering therapy
Congestive heart failure	NSAIDs may cause a congestive heart failure exacerbation	Consider colchicine for treatment of acute gout Consider colchicine for prophylaxis during initiation of urate-lowering therapy
	Concurrent use of diuretic may increase serum urate	If diuretic remains necessary, consider initiating urate-lowering therapy Consider losartan as a therapy for congestive heart failure given its uricosuric properties

Hypertension	Diuretics may increase uric acid	Consider losartan as alternative or additional antihypertensive therapy given its uricosuric properties Consider addition of urate-lowering therapy if diuretic remains necessary
	NSAIDs may worsen blood pressure control	Consider colchicine or corticosteroids for treatment of acute gout Consider colchicine for prophylaxis during initiation of urate-lowering therapy
Polypharmacy	CYP3A4 inhibitors and P-glycoprotein inhibitors interact with colchicine leading to elevated colchicine levels	Reduce the dose of colchicine used for the treatment and prophylaxis of acute gout Consider NSAIDs or corticosteroids for treatment of acute gout Consider NSAIDs for prophylaxis during initiation of urate-lowering therapy
	Added pharmacotherapy may be undesirable in a patient with a large medication burden	Consider losartan as urate-lowering therapy in patients with comorbid hypertension Consider fenofibrate as urate-lowering therapy in patients with hypertriglyceridemia
Financial limitations	Febuxostat and colchicine are considerably more costly compared with other gout treatments	Consider allopurinol as urate-lowering therapy Consider NSAIDs or corticosteroids for treatment of acute gout Consider NSAIDs for prophylaxis of gout during initiation of urate-lowering therapy

CYP, cytochrome P450; GI, gastrointestinal; NSAID, nonsteroidal anti-inflammatory drug.

Starting from this slide, material is just for your own knowledge.

TABLE 109-6 Pharmacotherapy of Acute Gout, Anti-Inflammatory Prophylaxis during Initiation of Urate-Lowering Therapy and Hyperuricemia in Gout[a]

Drug	Brand Name	Initial Dose	Usual Range	Special Population Dose	Other
Acute Gout					
NSAIDs					In general, not recommended in patients with advanced kidney disease as NSAID use may decrease kidney function; use with caution in patients with mild-to-moderate kidney impairment
Etodolac	Lodine, various	300 mg twice daily	300-500 mg twice daily		
Fenoprofen	Nalfon, various	400 mg three times daily	400-600 mg three to four times daily		
Ibuprofen	Advil, various	400 mg three times daily	400-800 mg three to four times daily		
Indomethacin	Indocin	50 mg three times daily	50 mg three times daily initially until pain is tolerable then rapidly reduce to complete cessation		
Ketoprofen	Orudis, various	75 mg three times daily or 50 mg four times daily	50-75 mg three to four times daily	Severe kidney impairment (GFR <25 mL/min [0.42 mL/s]): 100 mg maximum daily dose Mildly impaired kidney function: 150 mg maximum daily dose Impaired liver function with serum albumin <3.5 g/dL (<35 g/L): 100 mg maximum daily dose	

Naproxen	Naprosyn, various	750 mg followed by 250 mg every 8 hours until the attack has subsided		Not recommended in severe kidney impairment (creatinine clearance <30 mL/min [<0.5 mL/s])	
Piroxicam	Feldene	20 mg once daily or divided twice daily			
Sulindac	Clinoril	200 mg twice a day	150-200 mg twice daily for 7-10 days		
Meloxicam	Mobic	5 mg daily	7.5-15 mg daily	Not recommended if creatinine clearance <15 mL/min	
Celecoxib	Celebrex	800 mg followed by 400 mg on day one then 400 mg twice daily for 1 week			Option for patients with GI contraindications to nonselective NSAIDs; unclear risk-to-benefit ratio at this time due to cardiovascular concerns
Oral colchicine	Colcrys	1.2 mg initially, followed by 0.6 mg 1 hour later		See Table 109-8	Dose adjustment recommended when used with selected CYP3A4 and P-glycoprotein inhibitors
Corticosteroids					
Oral		0.5 mg/kg prednisone equivalent daily for 5-10 days followed by discontinuation or 0.5 mg/kg daily for 2-5 days followed by tapering for 7-10	30-60 mg prednisone equivalent once daily for 3-5 days, then taper in 5-mg decrements spread over 10-14 days until discontinuation		The use of an oral methylprednisolone dose pack may be considered

		days		
Intramuscular		Triamcinolone acetonide 60 mg IM once; methylprednisolone 100 mg IM once	Triamcinolone acetonide 60 mg IM once; methylprednisolone 100-150 mg IM daily for 1-2 days	Administration of intramuscular triamcinolone is to be followed by oral prednisone or prednisolone
Intra-articular	Kenalog	Triamcinolone acetonide 10 mg (large joints), 5 mg (small joints)	Triamcinolone acetonide 10-40 mg (large joints), 5-20 mg (small joints)	Intra-articular administration is acceptable when only one to two joints involved and should be used in combination with NSAIDs, colchicine, or oral corticosteroids

(*Continued*)

TABLE 109-6 Pharmacotherapy of Acute Gout, Anti-Inflammatory Prophylaxis during Initiation of Urate-Lowering Therapy and Hyperuricemia in Gout[a] (*Continued*)

Drug	Brand Name	Initial Dose	Usual Range	Special Population Dose	Other
Corticotropin	H.P. Acthar Gel	40 units IM or SC every 72 hours	40-80 units IM or SC every 24-72 hours		Contraindicated for IV administration
Interleukin-1 inhibitors					Reserve use for refractory cases; use for gout is an off-label indication
Anakinra	Kineret	100-mg SC daily for 3 days			
Canakinumab	Ilaris	Single dose 150-mg SC			
Anti-Inflammatory Prophylaxis During Initiation of Urate-Lowering Therapy					
NSAIDs			Lowest effective dosage		
Oral colchicine	Colcrys	0.6 mg daily	0.6 mg once or twice daily	See Table 109-8	
Prednisone or prednisolone		≤10 mg daily			Second-line therapy; recommended only if colchicine and NSAIDs are both contraindicated, ineffective, or not tolerated

Interleukin-1 inhibitors					Reserve use for refractory cases Studied for 16-week duration
Rilonacept	Arcalyst	320-mg loading dose followed by 160 mg weekly (SC)			
Canakinumab	Ilaris	Single SC dose (50-300 mg) or four times weekly SC dosing (50 mg—50 mg—25 mg—25 mg)			
Hyperuricemia in Gout					
Xanthine oxidase inhibitors					
Allopurinol	Lopurin, Zyloprim	100 mg daily	100-800 mg daily to achieve serum urate concentration <6 mg/dL (<357 μmol/L)	Start at dose of 50 mg daily for patients with a glomerular filtration rate <30 mL/min/1.73 m^2 (<0.29 mL/s/m^2)	

Febuxostat	Uloric	40 mg daily	40-80 mg/daily	No dosage adjustment necessary for patients with mild-to-moderate kidney impairment (creatinine clearance 30-89 mL/min [0.5-1.49 mL/s]) Insufficient data in patients with creatinine clearance <30 mL/min (<0.5 mL/s)	
Uricosurics					
Probenecid	Probalan	250 mg twice daily for 1 week	500-2,000 mg/day (target serum urate concentration <6 mg/dL [<357 mol/L])	Not recommended if creatinine clearance <50 mL/min (<0.83 mL/s)	
Lesinurad	Zurampic	200 mg once daily in combination with a xanthine oxidase inhibitor		Not recommended if creatinine clearance <45 mL/min (<0.75 mL/s) Not studied in patients with severe hepatic disease Contraindicated in tumor lysis syndrome and Lesch-Nyhan syndrome	Should be used in combination with a xanthine oxidase inhibitor due to increased risk of acute kidney injury with lesinurad monotherapy Use is not recommended in patients taking allopurinol doses <300 mg daily (normal kidney function) or <200 mg daily (creatinine clearance <60 mL/min)

TABLE 109-6 Pharmacotherapy of Acute Gout, Anti-Inflammatory Prophylaxis during Initiation of Urate-Lowering Therapy and Hyperuricemia in Gout[a] (*Continued*)

Drug	Brand Name	Initial Dose	Usual Range	Special Population Dose	Other
Combination Therapy					
Lesinurad/ Allopurinol	Duzallo	Lesinurad 200 mg/ allopurinol 300 mg: one tablet daily		Lesinurad 200 mg/ allopurinol 200 mg: one tablet daily recommended if creatinine clearance is 45-60 mL/min Not recommended if creatinine clearance <45 mL/min (<0.75 mL/s)	See above for lesinurad and allopurinol comments
Other					
Pegloticase	Krystexxa	8 mg IV every 2 weeks			Optimal treatment duration has not been established

[a]Agents available in the United States.

CYP, cytochrome P; GFR, glomerular filtration rate; IM, intramuscular; IV, intravenous; NSAID, nonsteroidal anti-inflammatory drug; SC, subcutaneous.

[What Happens During a Gout Attack | WebMD – YouTube]
1:33

[Gout – YouTube]
3:20