

International Evidence-Based Clinical Guidelines for Refractory Gout

(For healthcare professionals or those with a medical background only)

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Introduction

A 53-year-old male patient expressed frustration: "...Could we schedule a call to discuss my gout? I've been using both Western and Chinese medicine with little effect." "During flare-ups, I take colchicine, and when not in pain, I take febuxostat, along with Chinese herbal medicine prescribed in Shenzhen for four weeks without noticeable improvement." "It seems that just managing uric acid levels doesn't get to the root cause." "Various hospitals have prescribed febuxostat solely to control uric acid, but the pain recurs sporadically."

(Attached: Blood uric acid test results)

For the treatment of refractory gout, a combination therapy with multiple urate-lowering drugs is often considered to enhance efficacy and speed up uric acid metabolism. According to several evidence-based guidelines (NICE, 2023 Egyptian Consensus), combination therapy is a recommended approach when monotherapy fails to reduce uric acid effectively or if the patient has frequent flare-ups. Below are combination therapy approaches and strategies:

1. Indications for Combination Therapy

- **Monotherapy Ineffectiveness:** When a single xanthine oxidase inhibitor (such as allopurinol or febuxostat) does not reduce serum uric acid to below 6 mg/dL.
- **Frequent Gout Flare-ups or Persistent Tophi:** Combination therapy may help stabilize uric acid levels and reduce tophi formation.

2. Recommended Drug Combinations

- **Xanthine Oxidase Inhibitors (XOIs) + Uricosuric Agents (e.g., Probenecid):** A common combination involving allopurinol or febuxostat with probenecid. XOIs reduce uric acid production, while probenecid enhances uric acid excretion, increasing total uric acid clearance.
- **XOIs + Pegloticase:** For chronic, refractory gout or patients intolerant to other medications, pegloticase, a uricase enzyme, accelerates uric acid breakdown. This combination is suitable for severe cases and should be administered under specialist supervision.

3. Monitoring and Dose Adjustment in Combination Therapy

- Gradual Dose Increase: Start at a low dose and adjust gradually, observing side effects and uric acid levels.
- Regular Monitoring: Liver and kidney function should be monitored during combination therapy to avoid cumulative side effects. Uric acid levels should be reassessed every three months to adjust dosage as needed.

4. Anti-Inflammatory Adjuncts

Combination therapy, especially during initial phases, may provoke gout attacks. Low-dose colchicine, NSAIDs, or corticosteroids can be used to prevent flare-ups.

Summary

For refractory gout patients, combination therapy offers enhanced uric acid control. However, it should be managed under professional guidance to ensure safety and efficacy.

References:

1. National Institute for Health and Care Excellence (NICE). (2022). Gout: Diagnosis and management (NICE guideline NG219).
2. El Miedany, Y., Gadallah, N. A., Mansour, M., El Gaafary, M., Mortada, M., Eissa, M., ... & Galal, S. (2022). Egyptian consensus on treat-to-target approach of gout: Evidence-based clinical practice guidelines for the management of gout. *Egyptian Rheumatology and Rehabilitation*, 49(1), 28. <https://doi.org/10.1186/s43166-022-00123-3>

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检测指标	结果	参考值
尿素	5.90 (mmol/L)	(3.10-8.00)
肌酐	109 (umol/L) ↑	(57-97)
肾小球滤过率	67 (ml/min/1.73 m ²)	
尿酸	640 (umol/L) ↑	(90-420)

