Allopurinol: MOA, Indication, Dose, Interaction and Side effects

Allopurinol is a purine analog and a xanthine oxidase inhibitor primarily used in the long-term management of **chronic gout** and in the **prevention of hyperuricemia** associated with **tumor lysis syndrome** in patients undergoing chemotherapy for hematologic malignancies.

By inhibiting xanthine oxidase, the enzyme responsible for converting hypoxanthine to xanthine and then to uric acid, allopurinol effectively reduces serum and urinary uric acid levels.

Mechanism of Action

Allopurinol acts as a **uricostatic agent** by competitively inhibiting **xanthine oxidase** , decreasing the production of uric acid. It is converted in vivo to its active metabolite **oxypurinol (alloxanthine)** , which continues to inhibit xanthine oxidase.

- **Reduces total uric acid burden**
- Prevents urate crystal formation and deposition
- Promotes the gradual mobilization and resolution of tophi
- Inhibits de novo purine synthesis (secondary mechanism)

Allopurinol is **not a uricosuric agent** .

Clinical Indications

FDA-Approved Uses

- Chronic tophaceous gout (urate-lowering therapy)
- Prevention of uric acid nephropathy during cancer chemotherapy
- Recurrent uric acid nephrolithiasis
- Hyperuricemia in malignancies
- Recurrent calcium oxalate stones (with hyperuricosuria)

Off-Label/Orphan Uses

- **Chagas disease** , **cutaneous and visceral leishmaniasis**
- Amelioration of **fluorouracil-induced granulocytopenia**
- Mouthwash for **stomatitis prevention** in chemotherapy

Pharmacokinetics

Property	Details
Absorption	~80% oral bioavailability
Onset (oral)	Delayed; peak action in days to weeks
Metabolism	Hepatic to alloxanthine

Property	Details
Half-life	Allopurinol: 1–2 h; Oxypurinol: 18–30 h
Protein Binding	<1%
Excretion	Renal
Dialyzable	Yes (hemodialysis, peritoneal)

Encourage **2.5–3 L/day fluid intake** to minimize risk of nephrolithiasis. Take with food to reduce GI side effects.

Dosing Guidelines

Adults

- **Initial dose:** 100 mg/day PO
- **Maintenance:** Titrate weekly by 100 mg until serum uric acid <6 mg/dL (target <0.42 mmol/L)
- **Typical dose:** 200–300 mg/day (up to 800 mg/day based on severity)
- **Tumor lysis syndrome prevention:** 600–800 mg/day PO for 2–3 days prior to chemotherapy
- **Recurrent calcium oxalate stones:** 200–300 mg/day PO (adjust based on 24-hour urinary urate)

Pediatric

- <6 years: 150 mg/day PO
- 6–10 years: 300 mg/day PO
- **Parenteral:** 200 mg/m²/day IV in divided doses

Geriatrics/Renal Impairment

Creatinine Clearance (mL/min)	Recommended Dose
10–20	200 mg/day
<10	100 mg/day
<3	Adjust interval based on uric acid levels

Special Considerations

- Initiate only **after resolution** of an acute gout attack.
- Colchicine or NSAIDs are co-administered during early therapy to **prevent gout flare-ups** .
- Long-term therapy is required, often **lifelong** .
- Do **not mix** with other IV drugs—many **incompatibilities** exist.
- Pregnancy Category: **C**
- Safety in **children and pregnancy** not well established

Adverse Effects

Common

- Rash, pruritus
- GI upset (nausea, vomiting)
- Acute gout flare (early in treatment)

Serious

- **Stevens-Johnson Syndrome/TEN**
- **Hepatotoxicity**
- **Bone marrow suppression**
- **Hypersensitivity syndrome (AHS)** – can be fatal

Contraindications and Cautions

- Hypersensitivity to allopurinol
- Use caution in:
    - Hepatic or renal impairment
    - Pregnancy or lactation
    - Blood dyscrasias
- Avoid alcohol (may worsen hyperuricemia)

Patient Counseling Points

- Take medication after meals
- Ensure adequate hydration
- Do not discontinue abruptly
- Alert clinician if rash, fever, or flu-like symptoms appear
- Compliance is essential for chronic management