

Gout Drugs



Deposition of urate microcrystals in:

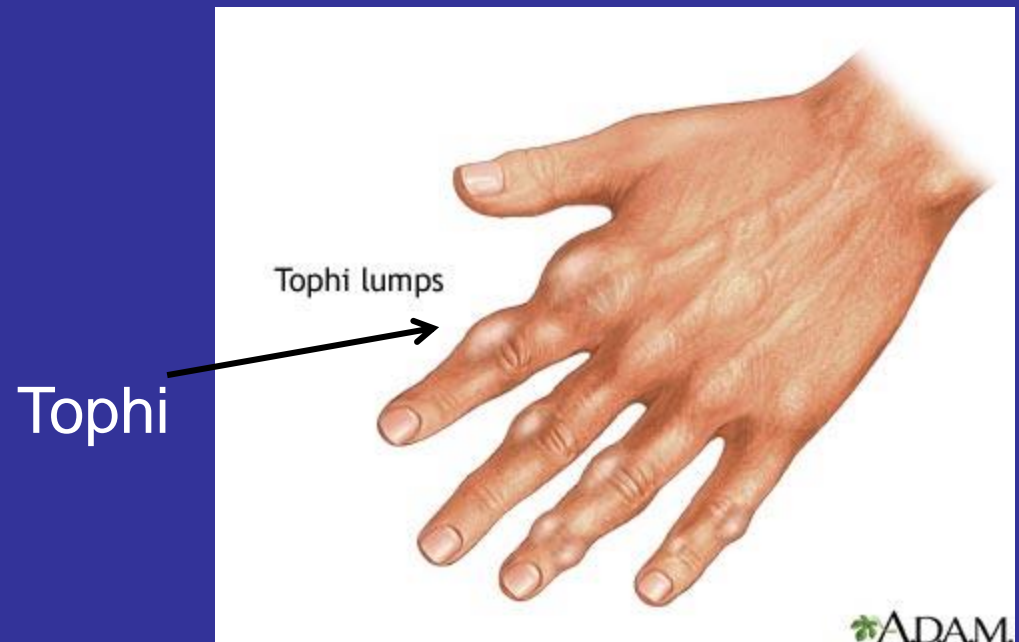
Joints

Extra-articular Tissues

Renal tubules

Subcutaneous tissue

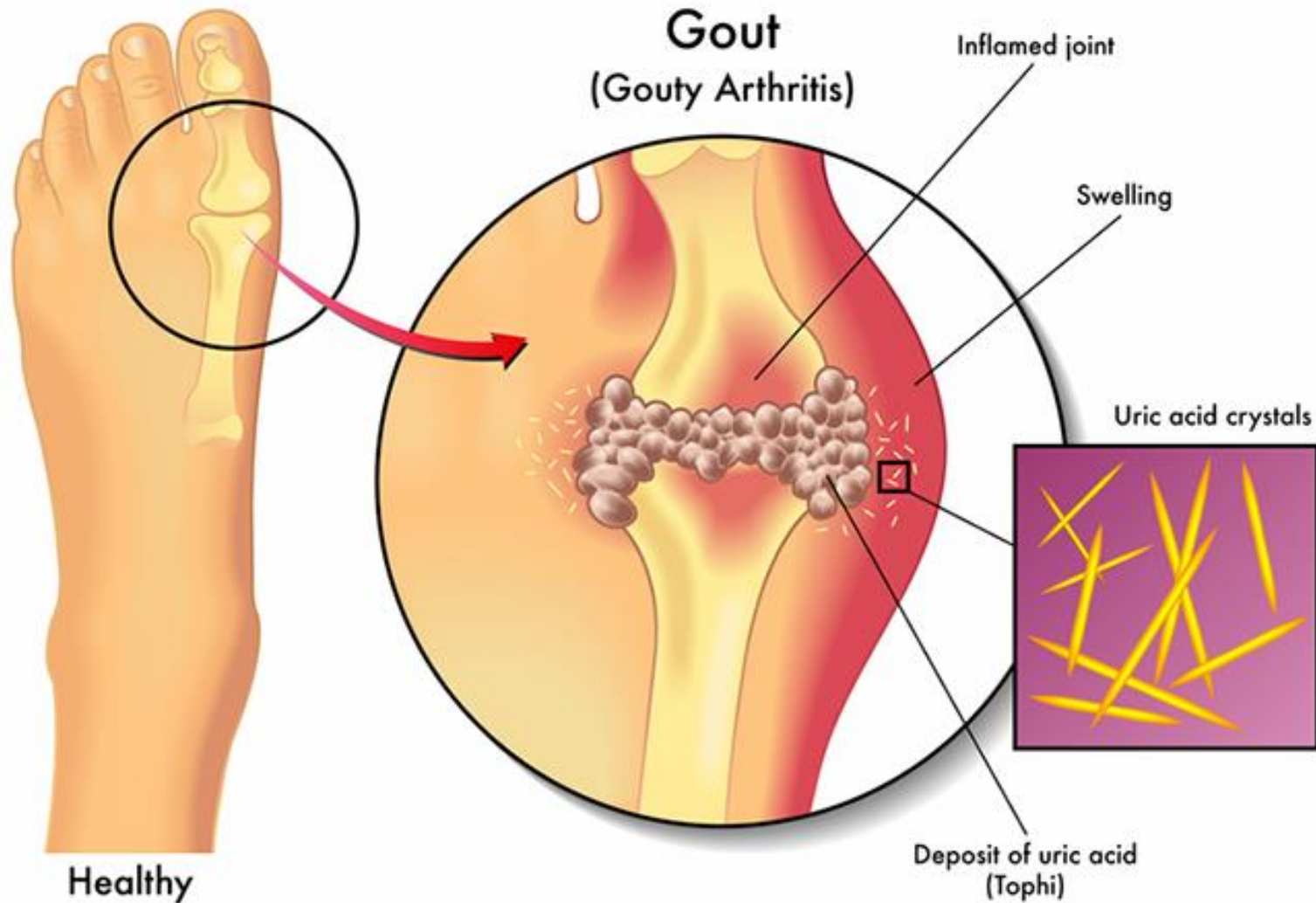
Gout arthritis



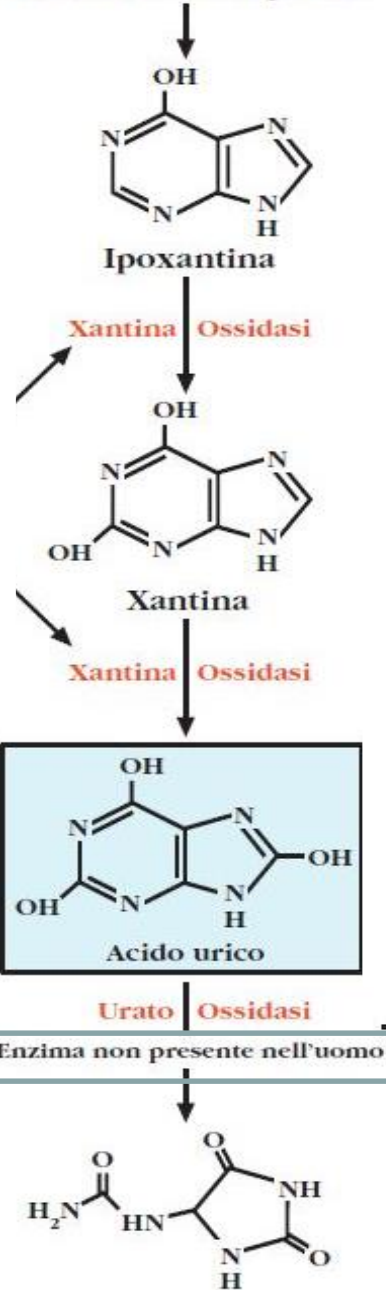
Risk factors associated with increased urate:

- Age
- Gender
- Meat, seafood, beer, liqueurs (foods with high purine content)
- Diabetes, hyperlipidemia, hypertension, obesity

Inflammation in Gout



Catabolismo delle purine



Biosynthesis and
biotransformation
processes
of uric acid

Mechanisms for decreasing Uric Acid (UA)

- **Interference with synthesis of UA**
- **Inhibition of leukocyte entry in the joint**
- **UA excretion increase**
- **Decreased re-absorption of UA**

Drugs used in gout



- To treat an acute attack:
 - non-steroidal anti-inflammatory drugs have anti-inflammatory action and reduce pain
 - **colchicine** reduces leucocyte migration into joints.
- For prophylaxis:
 - **allopurinol** inhibits uric acid synthesis
 - probenecid increases uric acid excretion.
- Drugs used for prophylaxis must not be started until the acute attack has resolved.

Sulfinpyrazone blocks AU reabsorption in the renal tubule
Benzbromarone increases AU excretion

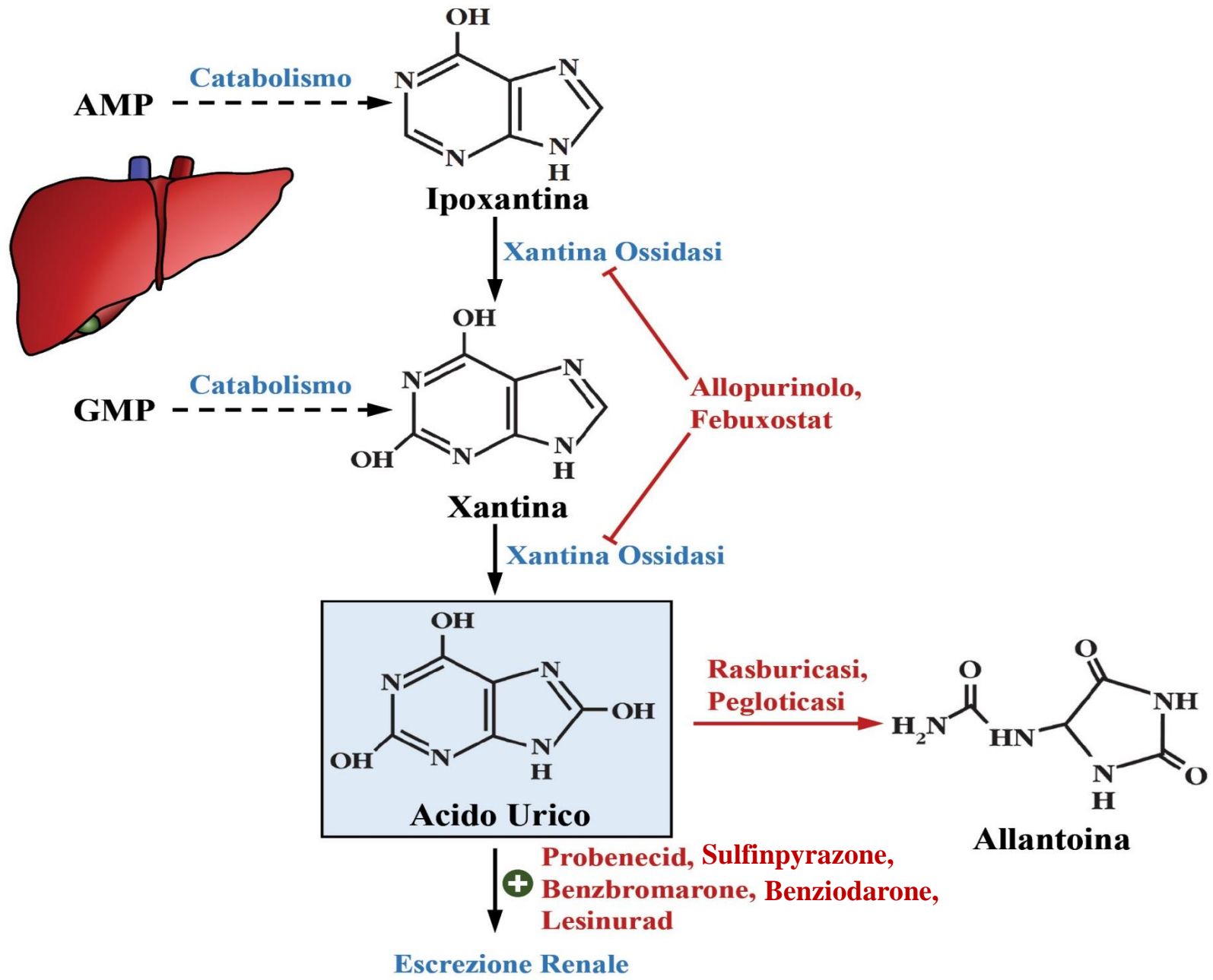
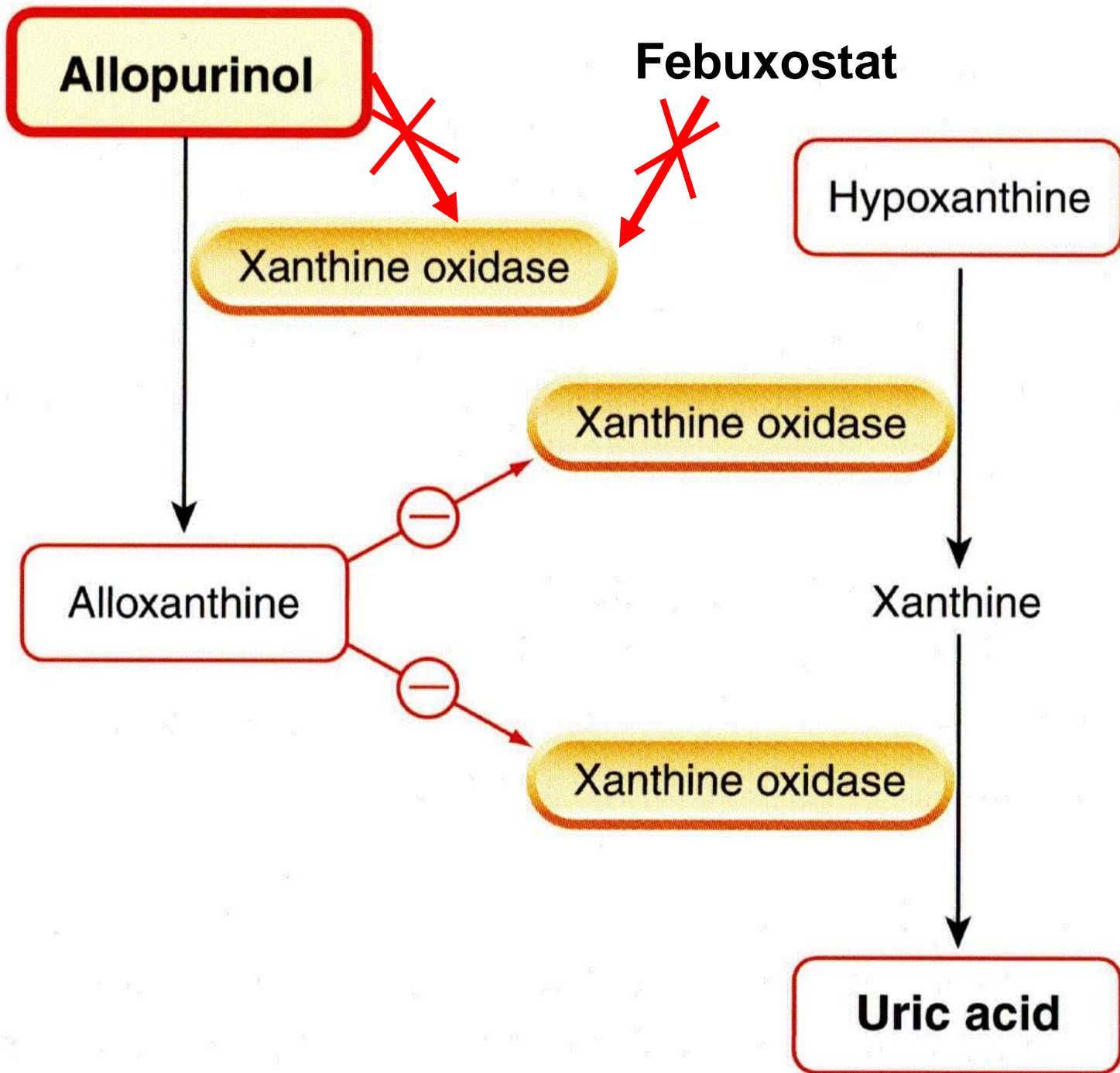
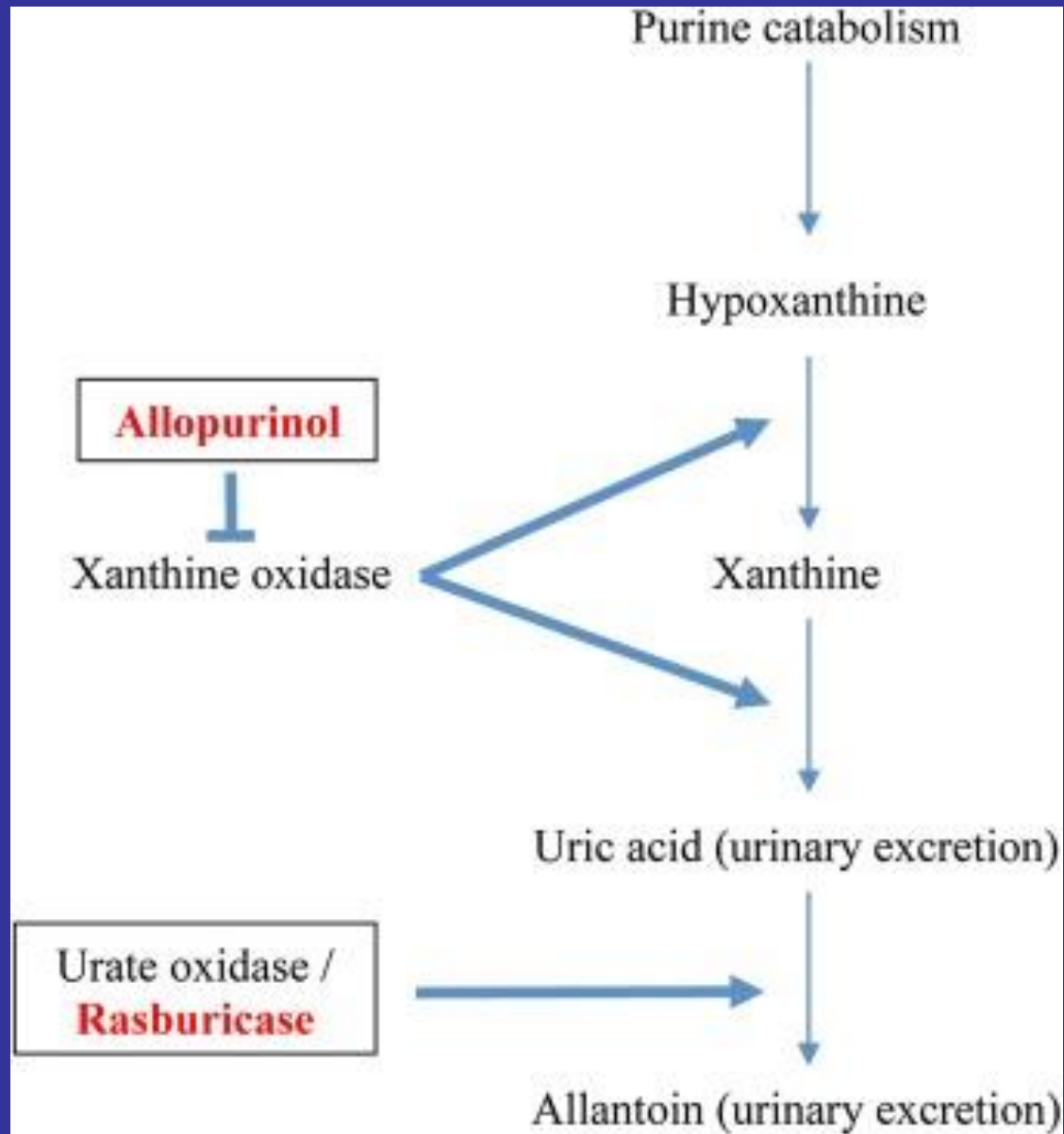


Figura 41.1. Processi di biosintesi dell'acido urico. In blu sono indicati i processi e gli enzimi coinvolti, in rosso sono indicati i farmaci.

Allopurinol, Febuxostat



Rasburicase



Comparison of cost for rasburicase and allopurinol/sodium bicarbonate

Drug	Average dose per day	Maximum duration	Cost per day*	Cost of 5 days of therapy
Allopurinol sodium (intravenous)	300 mg	NA	\$473.89	\$2369.45
Oral allopurinol	600 mg	NA	\$0.28	\$1.40
Sodium bicarbonate intravenous (90 mEq)‡	4000 ml (rate, 150–200 mL/h)	NA	\$0.74	\$29.60
Rasburicase	13.5 mg‡ (based on 0.2 mg/kg for 70-kg patient)	5 days	\$2724.84	\$13, 624.20

Probenecid, Sulfinpirazone,
Benziodarone, Benzbromarone

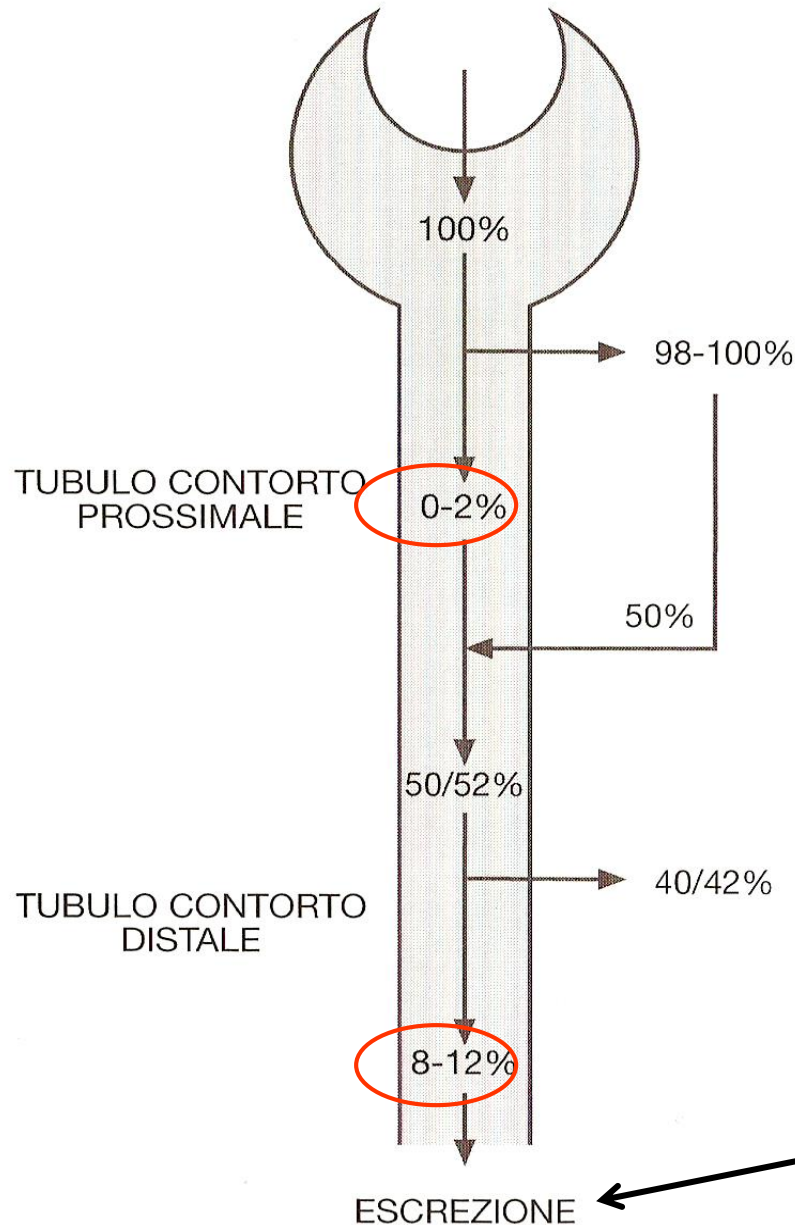
Uricosuric drugs

1 filtration

Probenecid (an organic acid), binds preferentially to OAT instead of uric acid, preventing its reabsorption and increasing excretion

Lesinurad (urate transporter inhibitor)

ASA competes with UA
reduces effect of probenecid



Sulfinpirazone

2

~~Riassorbimento~~

3

secretion + distal

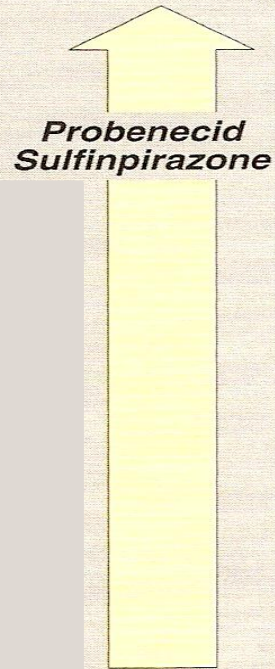
4

~~Riassorbimento~~

Benziodarone

Fig. 7.7. Escrezione renale dell'acido urico nell'uomo.

Diminuzione della escrezione di urato
(controindicata nei pazienti con gotta)



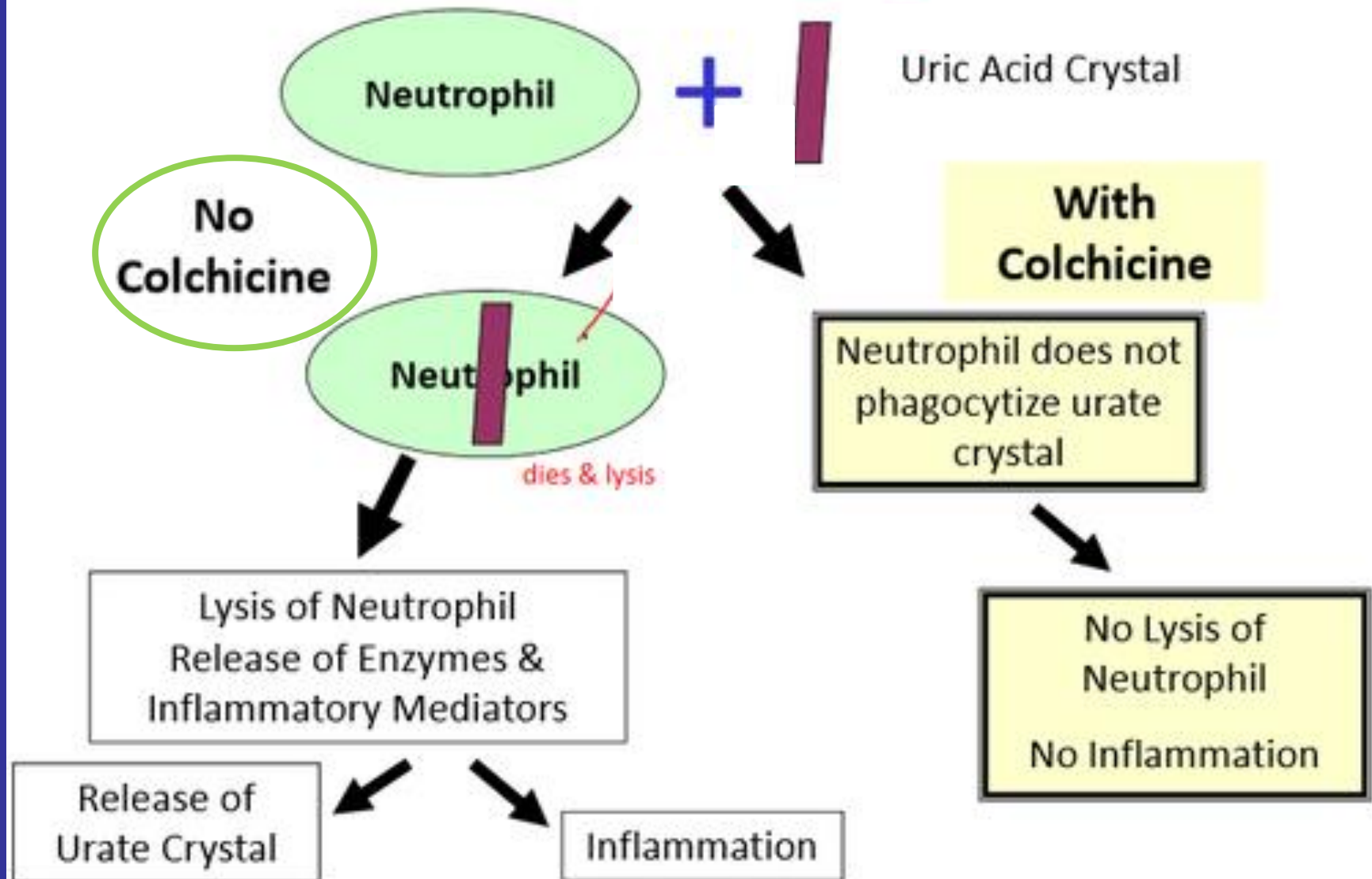
Salicilati

INTERACTION WITH OTHER DRUGS

Low/medium doses (1-2 g)

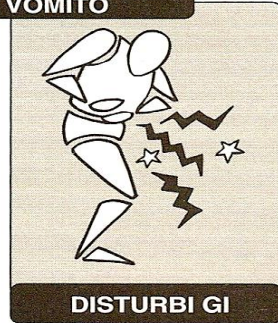
Colchicine

Colchicine: Mechanism of Action

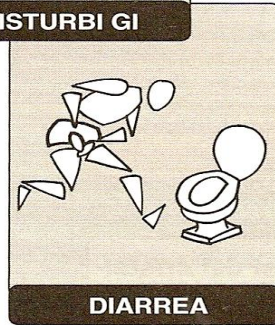




**NAUSEA E
VOMITO**



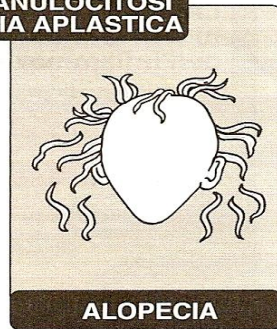
DISTURBI GI



DIARREA



**AGRANULOCITOSI
ANEMIA APLASTICA**



ALOPECIA

Side effects of colchicine

Tabella 41.1. Principali proprietà farmacocinetiche, indicazioni terapeutiche e tossicità dei farmaci antigottosi.

FARMACO	POSOLOGIA (mg/die)	EMIVITA (ORE)	LEGAME PROTEINE (%)	ESCREZIONE	INDICAZIONI	Tossicità ²
Allopurinolo	100-900 ¹ Orale	1-2 (Ossipurinolo 13-30)	Nulla	Renale	Iperuricemia non controllata con la dieta; nefropatia uratica; dissoluzione di calcoli di acido urico; prevenzione della formazione di calcoli di ossalato; in chemioterapia per il trattamento di nefropatia da acido urico (bambini); disturbi ereditari associati a deficit enzimatici (bambini)	Reazioni cutanee
Colchicina	3 ¹ Orale	31	39	Prevalentemente biliare, renale	Attacco acuto di artrite gottosa; trattamento profilattico dell'artrite gottosa ricorrente	Nausea; vomito; diarrea; dolori addominali; Se usata cronicamente: agranulocitosi, trombocitopenia, miopatia prossimale
Febuxostat	80-120 Orale	5-8	99.2	Epatica, renale	Trattamento dell'iperuricemia cronica con deposito di urato	Attacchi acuti di gotta; alterazioni della funzionalità epatica; diarrea; nausea; cefalea; eruzioni cutanee ed edema
Lesinurad	200 Orale	5	98	Epatica, renale	Iperuricemia gottosa severa non adeguatamente trattabile con un inibitore della xantina ossidasi in monoterapia	Insufficienza renale; sindrome simil-influenzale; reflusso gastroesofageo
Probenecid	250-2000 ¹ Orale	5-8	85-95	Prevalentemente urinaria	Iperuricemia non controllata con la dieta.	Reazioni a carico del sistema gastrointestinale, il sovradosaggio può causare convulsioni e depressione respiratoria
Rasburicasi	0.2 mg/kg Infusione e.v.	15.7-22.5	—	—	Trattamento e profilassi dell'iperuricemia acuta	Febbre

¹ La posologia varia a seconda dell'indicazione terapeutica, per ulteriori dettagli vedi il testo.

