JPP Feb 2022: Allopurinol

Day 1: 1950s cancer drug investigations led to the discovery of 6-mercaptopurine; the kinetics revealed the breakdown role of xanthine oxidase (XO). Further tests showed that an analogue to naturally occurring hypoxanthine, [#allopurinol](https://twitter.com/search?q=%23allopurinol), could block XO & treat gout. Approved in USA 1966

Day 2: [#allopurinol](https://twitter.com/search?q=%23allopurinol) tablet used for prevention of gout/kidney stones in adults. Also for the prevention of hyperuricaemia from cytotoxic drugs re increased cell turnover (>1 month old). 100-300mg once/day titrated using serum urate response; use divided doses > 300mg/day. Max dose 900mg/day if safe renal function

Day 2 (cont) [#allopurinol](https://twitter.com/search?q=%23allopurinol) is NOT used for acute gout; initial decline of serum urate levels causes urate crystals to shed from cartilage into the joint space. Start after acute attack settled if indicated. If already on when attack happens, can continue allopurinol, with attack managed separately

Day 3: [#allopurinol](https://twitter.com/search?q=%23allopurinol) kinetics; good oral absorption & moderate volume of distribution, as concentrated in gut & liver. Liver breakdown releases active metabolite 'oxypurinol', also a xanthine oxidase inhibitor. Mainly renal elimination of metabolites; ~20% in faeces. T½ 1-2 hours

Day 4: [#allopurinol](https://twitter.com/search?q=%23allopurinol) & active metabolite are xanthine oxidase inhibitors, which block the breakdown pathway of hypoxanthine>xanthine>uric acid. The reduced production of uric acid leads to lower serum levels; can take a few months to lower uric acid levels as effective for prevention. Historical concerns re the accumulation of xanthine were not realised; the increased recycling for purine synthesis via HGPRTase led to negative feedback & less purine synthesis, aiding reduced uric acid levels

Day 5: Common adverse drug effects; skin reactions, rash & increased TSH. Serious/rare; blood disorders, hepatitis, paralysis (NOT exhaustive). Allergic reactions e.g anaphylaxis, DRESS, SJS are rare, but increased genetic risk for Han Chinese,Thai & Korean; HLA screen & use alternative if positive where possible. Rarely [#allopurinol](https://twitter.com/search?q=%23allopurinol) can cause skin hyperpigmentation, alopecia & hair colour change (poorly understood)

Day 6: DDIs [#allopurinol](https://twitter.com/search?q=%23allopurinol): a small number, but most are ‘severe’. Diuretics (oppose uric acid excretion), ACEi (increase risk hypersensitivity/haematological reactions); could reduce effect capecitabine & icrease risk toxicity with azathioprine, as breakdown pathway needs xanthine oxidase (NOT exhaustive)

Day 7 [#allopurinol](https://twitter.com/search?q=%23allopurinol): Monitor liver function in early stages of therapy & reduce dose if impairment. Reduce dose to below 100mg/day if renal impairment, or increase dosing intervals

**CPD-** in addition to the tweets, read the BNF section treatment summary on gout, as well as the monograph on allopurinol

[**https://bnf.nice.org.uk/treatment-summary/gout.html**](https://bnf.nice.org.uk/treatment-summary/gout.html)

[**https://bnf.nice.org.uk/drug/allopurinol.html**](https://bnf.nice.org.uk/drug/allopurinol.html)

**The SPC for allopurinol also contains some useful information**

[**https://www.medicines.org.uk/emc/product/6007/smpc**](https://www.medicines.org.uk/emc/product/6007/smpc)

1. Allopurinol is the first -line treatment for prevention of gout in the UK

TRUE or FALSE

1. There are multiple formulations of allopurinol available for adults

TRUE or FALSE

1. Which of the following is TRUE?
2. Allopurinol is just used for gout
3. Allopurinol is not used in the management of an acute attack
4. Allopurinol is only ever used in adults
5. The maximum dose is 300mg/day
6. Which of the below best describes the mechanism of action for allopurinol
7. It reduces inflammatory pathways inside the joint
8. It inhibits cell division and suppresses bone marrow functions
9. It moderates prostaglandin production
10. It inhibits xanthine oxidase, the enzyme needed for the final stages of uric acid production
11. Which of the following is a common adverse drug effect?
12. Increase in thyroid stimulating hormone (TSH)
13. Angioedema
14. Visual impairment
15. Alopecia
16. Allopurinol is not used for acute gout because it takes too long to work

TRUE or FALSE

1. It is safe to take aspirin at all doses together with allopurinol

TRUE or FALSE

1. People from East/South-East Asia may be more prone to hypersensitivity reactions

TRUE or FALSE

1. Dose reduction in liver and renal impairment is important

TRUE or FALSE

1. A rare side-effect of allopurinol is a change in hair colour

TRUE or FALSE