Te Awakairangi Health NETWORK

Medicines Update **September 2013**

Benzbromarone (Benzbromaron®)

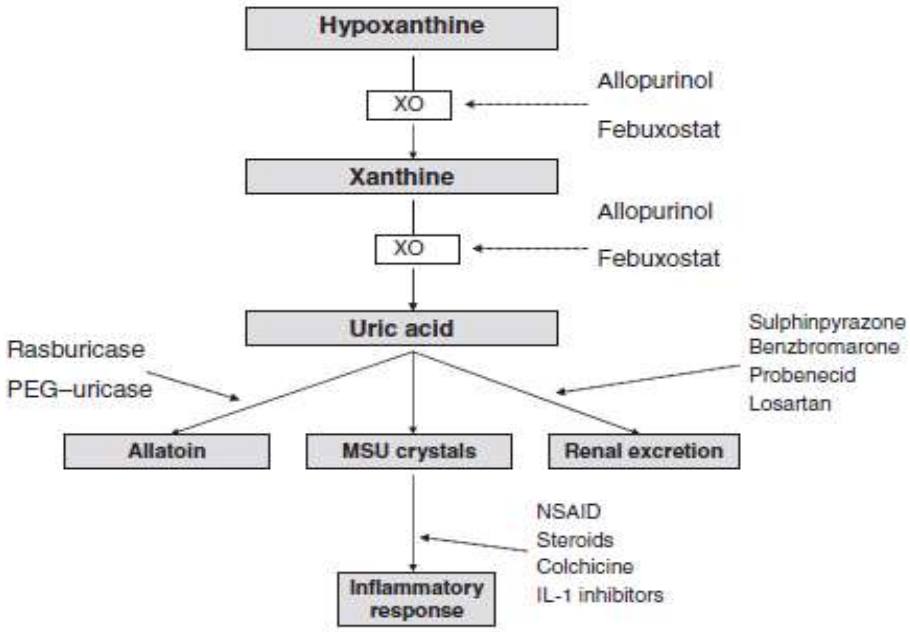
Benzbromarone has been recently funded under Special Authority criteria for the chronic treatment of gout when allopurinol and/probenecid is not tolerated, contraindicated or ineffective despite optimal treatment doses.[1,2]

Key Messages:

- 100mg tablets are fully subsidised under Special Authority since 1 April 2013.
- Unapproved medicine supplied under section 29, not a new medicine.
- Discuss suitable patients with rheumatologist prior to initiation.
- Effective in moderate renal impairment (avoid use if CrCl < 20ml/min).[1,2]
- Effective at lowering uric acid, reducing the number of acute attacks and size reduction, and resolution of tophi.[1]
- Should not be used in patients with known hepatic disease, hepatic impairment or at risk of hepatotoxicity and in patients with a past history of kidney stones.[4]
- Generally well tolerated; 3-4% of patients discontinued because of diarrhoea, estimated risk of hepatotoxicity reported as 1 in 17000, elevated liver enzymes seen in over 0.1% of patients in clinical trials (no cases of jaundice reported).[2]
- Requires baseline LFT and monthly LFTs – stop treatment if significant elevation in transaminases occurs (i.e. ALT and AST >2.5 to 3x the ULN). Hepatic injury arises after 1 to 6 months of therapy presenting with jaundice, fatigue and transaminase elevations.[4,6]
- Start low and go slow, use target serum Uric Acid (sUA) level of <0.36mmol/L to guide dose increases over the first 6 months however most patients achieve target sUA levels with a dose of 100mg once daily.[4](refer to www.nzformulary.org.nz)
- When initiating benzbromarone concomitant low dose NSAID or colchicine should be prescribed to prevent early gout flares.
- Patients tolerating optimal doses of allopurinol can continue to take it in combination with benzbromarone.[2]
- Patients should be advised to maintain a high fluid intake, report any signs of jaundice and fatigue and other adverse effects immediately.
- Benzbromarone inhibits CYP2C9 and is known to increase the effect of warfarin - monitor INR and adjust dose of warfarin.

Mechanism of Action of Medicines Used in Acute and Chronic Treatment of Gout[3]

FIG. 3 Summary of the final part of purine metabolism and site of drug action (XO = xanthine oxidase).



Genetics of Gout

- Benzbromarone inhibits the action of urate transporters SLC2A9, URAT1 and ABCG2 in the renal tubules.
- SLC2A9 is a key regulator for urate homeostasis.[3]
- Research indicates that inheriting one variant of SLC2A9 can increase the risk of developing gout by 30-70%. [3]
- On going research shows that people of Maori and Pacific ancestry have inherited a specific SLC2A9 variant that increases their risk of developing gout by five times.[5]

References

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3. Rider, TG and Jordan, KM. The modern management of gout. *Rheumatology* 2010;49:5-14
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