**BENZBROMARONE PRESCRIBER INFORMATION**

**What is benzbromarone and what is it used for?**

- Benzbromarone is a uricosuric agent that increases the excretion of uric acid through the kidneys.
- In New Zealand benzbromarone is available for gout prophylaxis for patients with hyperuricaemia who have failed to achieve the target serum urate (<0.36mmol/l) with allopurinol and probenecid.
- PHARMAC Special Authority is required.

**What must you consider before prescribing benzbromarone?**

- Benzbromarone is a Section 29 drug that is not registered in NZ, although it is funded.
- You are required to inform the patient that their medicine is not licensed, the basis for its use, and any potential risks.
- Patient consent for its use must be documented and you must advise the patient that the information about supply of the medicine will be forwarded to Medsafe and recorded on a database as a requirement of the Medicines Act.

**Contraindications and precautions:**

- Urate lowering can be associated with gout flares, particularly in the first 3-6 months, and consideration should be given to prophylaxis with low dose colchicine, NSAIDs or steroids.
- Benzbromarone has been associated with severe hepatotoxicity and the risk is increased in patients with existing liver disease or previous episodes of hepatotoxicity. Benzbromarone should not be used in patients with known liver disease. It should be used with caution in patients with a history of hepatic impairment or patients who are also taking other medicines which may be potentially hepatotoxic. Patients who have an excess intake of alcohol are also likely to be more at risk of liver toxicity.
- Porphyria – in vitro studies suggest benzbromarone is porphyrinogenic, do not use.

**Dose and administration**

- The usual dose of benzbromarone is 100 mg orally once daily.
- Doses of 50 – 200 mg per day may be used.

**Potential Adverse effects**

**Hepatotoxicity**

- Benzbromarone has been associated with severe hepatotoxicity, including fatalities.
- Most cases of hepatotoxicity have been with doses greater than 100mg/daily.
- Liver function tests should be monitored regularly – monthly for the first 6 months then three monthly.
- Patients should be advised to stop benzbromarone and seek urgent medical attention if they develop nausea, vomiting, abdominal pain or jaundice.

**Renal Stones**

- Benzbromarone increases renal urate excretion, which can cause uric acid kidney stones. Patients should be warned of this. Alkalinisation of the urine with Ural® sachets can reduce the risk.
Gout flares

Other possible adverse-effects:
- Occasionally: gastrointestinal symptoms such as nausea, vomiting, bloating and diarrhoea.
- Seldom: hives
- Very seldom: eosinophilic pneumonitis, headache, conjunctivitis, allergic skin rash, urate calculus, gout, increased urge to urinate.

Drug Interactions

Likely clinically significant:
- Benz bromarone inhibits the metabolism of:
  - Warfarin: Bleeding risk is increased. Consider reducing warfarin dose by 30% when initiating benz bromarone. INR should be closely monitored for two weeks after benz bromarone is started, stopped or the dose is changed.
  - Sulphonylureas: check capillary blood gluoses for one week after benz bromarone is started, stopped or the dose is changed.
  - Phenytoin: check phenytoin concentrations before starting or stopping benz bromarone and repeat 3 and 7 days after starting or stopping benz bromarone.

Benz bromarone metabolism is affected by:
- Fluconazole: inhibits benz bromarone metabolism - the combination should be avoided.
- Rifampicin: induces benz bromarone metabolism, such that it is likely to be ineffective.

Possibly clinically significant:
- Other CYP2C9 substrates (e.g. most NSAIDs, losartan). Benz bromarone is a moderate inhibitor of CYP2C9 and may increase concentrations of drugs (substrates) primarily metabolised by this enzyme. Monitor for an increase in effect.
- Other hepatotoxic drugs - benz bromarone may cause hepatotoxicity which could theoretically be additive with other hepatotoxic drugs.
- Other inhibitors or inducers of CYP2C9 (e.g. amiodarone or carbamazepine): may affect benz bromarone clearance but are unlikely to be clinically important in most cases.

Overdose
- There is limited experience of benz bromarone overdose and there is no specific antidote.
- If overdose occurs gastric decontamination should be considered (e.g. activated charcoal) and supportive care provided.
- The half-life of benz bromarone is prolonged in overdose due to saturation of metabolism.

Pregnancy and lactation

Benz bromarone should not be used in pregnancy or lactation. There are no reports of benz bromarone use in pregnant humans, and animal experiments have shown evidence of foetal malformation.

Prescribing Points
- Benz bromarone is effective in chronic kidney disease for patients with eGFR down to 30ml/min.

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