Gout—is adequate attention devoted to preventing haemorrhagic risk when benzbromarone is administered with warfarin?

Benzbromarone, although unapproved by Medsafe, has been reimbursed by New Zealand’s Pharmaceutical Management Agency (PHARMAC) for gout patients in New Zealand from 1 July 2013.

Centre for Adverse Reactions Monitoring (CARM) has already received at least one report of increased bleeding in a gout patient co-prescribed benzbromarone and warfarin.² Winnard et al report in this Journal that around 23% of New Zealand patients with gout also have cardiovascular disease (CVD).²

We know that S-warfarin is metabolised by CYP2C9 and that R-warfarin is metabolised by CYP1A2.³ It is also known that benzbromarone is metabolised by both CYP2C9 and CYP1A2.⁴ The enhanced anticoagulation effects of benzbromarone with warfarin have been reported as far back 1996, where the authors (Shimodaira et al) concluded:⁵

> These results verified that the anticoagulant action of warfarin is enhanced by concurrent administration of benzbromarone. Accordingly, adequate consideration must be devoted to the prevention of grave hemorrhagic tendencies when these two drugs are administered concurrently.

It is therefore recommended that patients are not co-prescribed benzbromarone and warfarin because of the increased risk of bleeding and that if co-prescription is necessary there is closer monitoring of INR levels.

Current BPAC guidelines acknowledge that the monthly LFT monitoring necessary with benzbromarone may be difficult due to adherence in these patients. These low adherence problems simply serve to frustrate the necessary closer INR monitoring and thereby increase the risks of bleeds.⁶ However, since benzbromarone is not approved by Medsafe in New Zealand there is no Datasheet available to carry such a warning. Neither do the current Special Authority criteria for benzbromarone carry a warning regarding co-prescription with warfarin.

If benzbromarone is to remain an unapproved yet funded medicine then it is paramount that its prescribing is limited to specialists and that the Special Authority criteria carry a recommendation not to co-prescribe with warfarin. The high level of warfarin co-prescription in gout patients poses a high likelihood of potentially life-threatening bleeds with benzbromarone.

From a medicolegal perspective there is an added onus on the prescriber to alert the patient to such risks when seeking informed consent. Urgent action is needed to better manage the risks associated with benzbromarone (both bleeds with warfarin and intrinsic hepatotoxicity).

In contrast, febuxostat has been shown to minimally inhibit the activity of any CYP and does not affect the plasma binding of warfarin.⁷
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**Competing interests:** Shareholder of the company supplying febuxostat in New Zealand.

**References:**

1. Personal communication CARM, 23 August 2013.