

Dear Dave

Dave and other members of the bpac^{nz} team answer your clinical questions

If you have a clinical question email it to
dave@bpac.org.nz

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My drug interaction programme warns of a potentially serious drug interaction between ACE inhibitors and allopurinol. What is the significance of this warning and is it safe to use these drugs together?

The warning about concurrent use of ACE inhibitors and allopurinol originates from several reports of hypersensitivity syndromes when allopurinol has been prescribed for patients already taking captopril, especially in people with pre-existing renal impairment. In three of the reported cases, Stevens-Johnson syndrome developed (one fatal) three to five weeks after starting the allopurinol.¹ Milder cases of hypersensitivity (arthralgia, myalgia, fever) and exfoliative facial dermatitis have also been reported with concurrent use of captopril and allopurinol but there appear to be few similar reports with the other ACE inhibitors.² A case of anaphylaxis and myocardial infarction was reported in a man taking enalapril who was given allopurinol.³

As a separate issue the manufacturers of most ACE inhibitors warn of a possible increased risk of leucopenia when they are given with allopurinol especially in people with renal impairment.

It is not known if these reactions are due to an effect of the drug combination or caused by allopurinol itself, as this drug alone can cause severe hypersensitivity reactions and leucopenia. Whatever the cause, such events appear to be very rare and unpredictable and concurrent use is not contraindicated. However, patients should be advised to report possible signs of hypersensitivity (skin rash, arthralgia) or signs of low white cell count (infection, sore throat fever), especially in the first few weeks of concurrent treatment if they have a degree of renal impairment. This advice would also apply to patients taking allopurinol alone.

To put this interaction in to perspective we analysed Pharmhouse data for the last three months of 2006 and found that over 25, 000 patients had received both an ACE inhibitor and allopurinol during that time. We can't determine if use was always concurrent but we expect this to be the case in most patients.

Bottom Line

If this is an interaction it appears to be very rare and it is possible that the reported cases were actually due to allopurinol hypersensitivity. Concurrent use is widespread. Monitor all patients starting on allopurinol (as described above) irrespective of whether they are already taking an ACE inhibitor.

Note: In an up coming issue of best practice journal we will be covering the common clinically significant drug interactions relevant to General Practice.

References

1. Pennell DJ, Nunan TO, O'Doherty MJ, Croft DN. Fatal Stevens-Johnson syndrome in a patient on captopril and allopurinol. *Lancet* 1984;1(8374): 463.
2. Stockley's Drug Interactions: 2007. Pharmaceutical Press.
3. Ahmad S. Allopurinol and enalapril. Drug induced anaphylactic coronary spasm and acute myocardial infarction. *Chest* 1995; 108: 586.

Who is Dave?

Pharmaceutical Programme Manager Dave Woods is a graduate of Manchester University (BSc. [Hons]) and the University of Otago (MPharm). Dave has extensive experience in hospital pharmacy, drug information, rational use of drugs and quality assurance. He has published on a range of subjects and holds editorial positions for several international journals.

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